IFFS SARS-COV-2 LITERATURE MONITORING REPORT

August 2021 Update

An IFFS-Merck Collaboration
## Contents

### Section

**Report Objectives**

### Literature monitoring

- Effects of SARS-COV-2 infection on pregnancy outcomes
- Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death
- Effects of SARS-COV-2 vaccination on pregnancy
- Effects of SARS-COV-2 infection on Male fertility
- Effects of SARS-COV-2 infection on Female fertility
- Effect of SARS-COV-2 infection on assisted reproductive technique (ART)
- Effects of COVID-19 vaccination on ART
Report Objective

This literature monitoring report has been developed as a scientific collaboration between Merck and IFFS, to provide an overview of the emerging situation around COVID-19 and Reproductive Health-related topics.

It highlights the publications and/or discussions regarding the global SARS-CoV-2 pandemic, vaccination and fertility/conception/pregnancy to help colleagues keep abreast of developments in the literature

• It highlights the publications concerning the impact of the global SARS-CoV-2 pandemic on fertility, conception, pregnancy and lactation, to help colleagues keep updated in developments in the literature from November 1st, 2020 to August 12th, 2021.

• As from our previous report, a new section has been introduced to track the reports on COVID-19 vaccination and pregnancy on Reproductive Health issues
SARS-CoV-2 taskforce – literature monitoring

Date of Search: 01 November 2020 – 12 Aug 2021

- The following slides highlight the publications and/or discussion regarding the global SARS-CoV-2 pandemic and fertility/conception/pregnancy to help Merck colleagues keep abreast of developments in the literature. Selection was focused on meta-analyses, systematic reviews or good quality review articles.

- This report will focus on:
  - The link between placental infection with SARS-CoV-2 and miscarriage, stillbirth, preterm delivery and perinatal death.
  - Monitoring any effects of COVID-19 vaccination on pregnancy, fertility and ART

- The following key search terms were used:


Last updated
12/08/2021
SARS-CoV-2 taskforce – literature monitoring

Date of Search: 01 November 2020 – 12 Aug 2021

3. Effects of COVID-19 vaccination on pregnancy - ('vaccine' OR 'vaccination' OR 'Pfizer' OR 'AstraZeneca' OR 'coronavirus vaccine' OR 'COVID-19 vaccine' OR 'inoculation' OR 'immunization' OR 'immunization' OR 'immunized' OR 'immunized' OR 'antibodies' OR 'COV' OR 'covid 19' OR 'covid 19' OR 'coronavirus' OR 'cov-19' OR 'sar-cov-2' OR 'sar-cov 2' OR 'corona virus' OR 'covid-19 vaccin*' OR 'sars-cov-2 vaccine' OR 'chadox1-s' OR 'pfizer-biontech covid-19 vaccine' OR 'bnt162b2' OR 'comirnaty' OR 'mmn-a-1273' OR 'mmn-a vaccine' OR 'ad26.cov2.s vaccine' OR 'nvx-cov2373 vaccine' OR 'sputnik-v' OR 'gam-covid-vac' OR 'janssen' OR 'jansen' OR 'J&J' And 'Pregnant' OR 'pregnancy' OR 'neonate' OR 'child' OR 'conceive' OR 'gravid' OR 'parturient' OR 'expectant' OR 'maternal' OR 'fetal' OR 'miscarriage' OR 'abortion' OR 'termination' OR 'placental infection' OR 'premature delivery' OR 'pregnancy loss' OR 'stillbirth' OR 'preterm delivery' OR 'perinatal death' OR 'fetal death' OR 'fetal demise' OR 'neonatal death' OR 'neonatal death' OR 'pregnant' OR 'pregnancy' OR 'newborn' OR 'prenatal death' OR 'neonate' OR 'neonatal' OR 'vertical transmission')

4. For Effects of COVID-19 vaccination on fertility - ('vaccine' OR 'vaccination' OR 'Pfizer' OR 'AstraZeneca' OR 'coronavirus vaccine' OR 'COVID-19 vaccine' OR 'inoculation' OR 'immunization' OR 'immunization' OR 'immunized' OR 'immunized' OR 'antibodies' OR 'COV' OR 'covid 19' OR 'covid 19' OR 'coronavirus' OR 'cov-19' OR 'sar-cov-2' OR 'sar-cov 2' OR 'corona virus' OR 'covid-19 vaccin*' OR 'sars-cov-2 vaccine' OR 'chadox1-s' OR 'pfizer-biontech covid-19 vaccine' OR 'bnt162b2' OR 'comirnaty' OR 'mmn-a-1273' OR 'mmn-a vaccine' OR 'ad26.cov2.s vaccine' OR 'nvx-cov2373 vaccine' OR 'sputnik-v' OR 'gam-covid-vac' OR 'janssen' OR 'jansen' OR 'J&J' And 'fertility' OR 'conception' OR 'reproductive system' OR 'gamete' OR 'orchitis' OR 'sperm' OR 'ovary' OR 'ovaries' OR 'gametogenesis')

5. Effects of COVID-19 vaccination on ART – ('vaccine' OR 'vaccination' OR 'Pfizer' OR 'AstraZeneca' OR 'coronavirus vaccine' OR 'COVID-19 vaccine' OR 'inoculation' OR 'immunization' OR 'immunization' OR 'immunized' OR 'immunized' OR 'antibodies' OR 'COV' OR 'covid 19' OR 'covid 19' OR 'coronavirus' OR 'cov-19' OR 'sar-cov-2' OR 'sar-cov 2' OR 'corona virus' OR 'covid-19 vaccin*' OR 'sars-cov-2 vaccine' OR 'chadox1-s' OR 'pfizer-biontech covid-19 vaccine' OR 'bnt162b2' OR 'comirnaty' OR 'mmn-a-1273' OR 'mmn-a vaccine' OR 'ad26.cov2.s vaccine' OR 'nvx-cov2373 vaccine' OR 'sputnik-v' OR 'gam-covid-vac' OR 'janssen' OR 'jansen' OR 'J&J' And 'assisted reproductive technology':ab,ti,tn OR 'in vitro fertilization':ab,ti,tn OR 'ovulation trigger':ab,ti,tn OR 'ovulation induction':ab,ti,tn OR 'ovarian stimulation':ab,ti,tn OR 'controlled ovarian stimulation':ab,ti,tn OR 'embryo transfer':ab,ti,tn OR 'intrauterine insemination':ab,ti,tn OR 'intrauterine insemination syndrome':ab,ti,tn OR 'ovarian hyperstimulation syndrome':ab,ti,tn OR 'ovary hyperstimulation':ab,ti,tn OR 'ohss':ab,ti,tn OR 'hypogonadotropic hypogonadism':ab,ti,tn OR 'spermatogenesis':ab,ti,tn OR 'vitrification':ab,ti,tn OR 'cryopreservation':ab,ti,tn OR 'cryopreservation':ab,ti,tn OR 'preimplantation genetic':ab,ti,tn OR 'pgd':ab,ti,tn OR 'pgd':ab,ti,tn OR 'gavi':ab,ti,tn OR 'geri':ab,ti,tn OR 'cryopreservation':ab,ti,tn OR 'preimplantation genetic':ab,ti,tn OR 'embryoscope':ab,ti,tn OR 'embryoscope':ab,ti,tn OR 'embryoscope':ab,ti,tn OR 'primo vision':ab,ti,tn OR 'miri':ab,ti,tn OR 'ccm ivf':ab,ti,tn OR 'cryopreservation':ab,ti,tn OR 'rapid':ab,ti,tn OR 'rapid':ab,ti,tn OR 'ccm-iBIS':ab,ti,tn)

SARS-CoV-2 taskforce – literature monitoring

Date of Search: 01 November 2020 – 12 Aug 2021
SARS-CoV-2 taskforce – literature monitoring

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7. **Effect of covid-19 on ART** – ('assisted reproductive technology':ab,ti,tn OR 'assisted reproductive technologies':ab,ti,tn OR 'in vitro fertilization':ab,ti,tn OR 'ovulation trigger':ab,ti,tn OR 'ovulation induction':ab,ti,tn OR 'ovarian stimulation':ab,ti,tn OR 'controlled ovarian stimulation':ab,ti,tn OR 'assisted reproduction':ab,ti,tn OR 'medical assisted reproduction':ab,ti,tn OR 'intracytoplasmic sperm injection':ab,ti,tn OR 'embryo transfer':ab,ti,tn OR 'mild stimulation':ab,ti,tn OR 'infertility therapy':ab,ti,tn OR 'reproductive technologies':ab,ti,tn OR 'ivf':ab,ti,tn OR 'oi':ab,ti,tn OR 'icsi':ab,ti,tn OR 'iui':ab,ti,tn OR 'intrauterine insemination':ab,ti,tn OR 'ovarian hyperstimulation syndrome':ab,ti,tn OR 'ovary hyperstimulation':ab,ti,tn OR 'ohss':ab,ti,tn OR 'hypogonadotrophic hypogonadism':ab,ti,tn OR 'spermatogenesis':ab,ti,tn OR 'time lapse':ab,ti,tn OR 'cryopreservation':ab,ti,tn OR 'preimplantation genetic':ab,ti,tn OR 'pgd':ab,ti,tn OR 'pgt':ab,ti,tn OR 'gavi':ab,ti,tn OR 'geri':ab,ti,tn OR 'eeva':ab,ti,tn OR 'gidget':ab,ti,tn OR 'gems':ab,ti,tn OR 'vitrolife':ab,ti,tn OR 'origio':ab,ti,tn OR 'irvine scientific':ab,ti,tn OR 'lifeglobal':ab,ti,tn OR 'kitazato':ab,ti,tn OR 'embryoscope':ab,ti,tn OR 'embryoscope+':ab,ti,tn OR 'primo vision':ab,ti,tn OR 'ccm ivf':ab,ti,tn OR 'cryotop':ab,ti,tn OR 'rapid i':ab,ti,tn OR 'rapid vit':ab,ti,tn OR 'cm-bis':ab,ti,tn AND ('coronavirus disease 2019' OR '2019 novel coronavirus disease' OR '2019 novel coronavirus infection' OR '2019-ncov disease' OR '2019-ncov infection' OR 'sars coronavirus 2 infection' OR 'sars-cov-2 disease' OR 'sars-cov-2 infection' OR 'sars-cov2 disease' OR 'sars-cov2 infection' OR 'wuhan coronavirus disease' OR 'wuhan coronavirus infection' OR 'severe acute respiratory syndrome coronavirus 2' OR '2019 new coronavirus' OR '2019 novel coronavirus' OR '2019-ncov' OR 'hcov-19' OR 'human coronavirus 2019' OR 'ncov-2019' OR 'novel 2019 coronavirus' OR 'novel coronavirus 2019' OR 'novel coronavirus-19' OR 'sars coronavirus 2' OR 'sars-cov-2' OR 'sars2' OR 'wuhan coronavirus' OR 'wuhan seafood market pneumonia virus')

- Each publication title is hyperlinked to the abstract (if available) on PubMed/relevant data source for further reference
- Publications may be eligible for inclusion in multiple sections and are usually included once in their most relevant section. However, some articles may be deemed significantly relevant across multiple topics. In these instances, publications may be duplicated in order to avoid these articles being overlooked by those focusing in only one area. Because of the rapidly evolving events surrounding the COVID-19, the presented information may have changed since the date of search mentioned in this document.
Literature Monitoring

Topic Covered

Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

Duration:

1\textsuperscript{st} Nov 2020 to 12\textsuperscript{th} Aug 2021
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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</table>
| 1   | Management of maternal COVID-19: considerations for anesthesiologists | Author: Bernstein K, Landau R  
Study Citation: Curr Opin Anaesthesiol. 2021 Jun 1;34(3):246-253.  
Study Type: Review  
Patients No.: NA | Study describe the pragmatic approach for COVID-19 and evaluate pregnancy impact on severity of COVID-19.  
• Pregnancy puts women at higher risk of severe COVID-19 and adverse birth outcomes.  
• Pregnant women are more likely to be admitted to ICU and receive mechanical ventilation than non-pregnant COVID-19 patients  
• Early neuraxial labor analgesia with a indwelling epidural catheter may reduce need for general anesthesia for cesarean delivery |
| 2   | A snapshot of the prevalence of endocrine disorders in pregnancies complicated by coronavirus disease 2019: A narrative review with meta-analysis | Author: Angela J et al  
Study Citation: Int J Gynaecol Obstet. 2021 Aug;154(2):204-211  
Study Type: Review  
Patients No.: NA | This review study evaluated the prevalence of endocrine disorders in pregnancies involving COVID-19, and its impact on maternal outcomes.  
• Prevalence of obesity ranged from 16% - 46% and hyperglycemia in pregnancy (HIP) ranged from 8% - 12%. HIP and obesity were risk factors for severe disease.  
• Mortality risk was higher in women with diabetes and obesity. |

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Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 3   | A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: Clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity | Author: Lassi ZS et al Study Citation: J Glob Health. 2021 Jun 30;11:05018. Study Type :Meta-analysis Patients No. :31 016 | This meta-analysis studied the clinical presentation, risk factors, and pregnancy and perinatal outcomes in pregnant women with confirmed COVID-19.  
  • 16.4% developed severe COVID-19.  
  • 7% were admitted to the ICU, 8% required mechanical ventilation, and 2% of the women died.  
  • 80% of women delivered; 48.4% had cesarean births.  
  • Among newborns, 23.4% were preterm (<37 weeks), 16.6% were low birth weight, and 23.7% were admitted to neonatal ICU.  
  • 1.6% were stillbirths; 1.6% neonatal deaths were recorded, while 3.5% babies were COVID-19 positive.  
  • The risk of severe COVID-19 was significantly higher among women who were obese, had smoked, diabetic, and had pre-eclampsia.  
  • The risk of preterm birth was almost 2.4 folds among women with severe COVID-19. |
| 4   | Convalescent Plasma for Pregnant Women with COVID-19: A Systematic Literature Review | Author: Franchini M et al Study Citation: Viruses. 2021 Jun 22;13(7):1194 Study Type : Case report Patients No. :12 | Findings from the case report study suggests that convalescent plasma administered to pregnant women with severe COVID-19 provides benefits for both the mother and the fetus. |

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# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 5   | Immunological and physiopathological approach of COVID-19 in pregnancy | Author: Ferrer-Oliveras R et al  
Study Citation: Arch Gynecol Obstet. 2021;304(1):39-57.  
Study Type: Review  
Patients No.: NA | This review study emphasizes that a severe COVID-19 form is mainly a hyperinflammatory, immune-mediated disorder, triggered by a viral infection.  
Due to their particular immunological features, pregnant women may be susceptible to complication by intracellular infections as well as immunological disturbances. |
| 6   | A systematic review of pregnant women with COVID-19 and their neonates | Author: Mirbeyk M et al  
Study Citation: Arch Gynecol Obstet. 2021 Jul;304(1):5-38.  
Study Type: Systematic review  
Patients No.: 364 | This systematic review considered the impact of COVID-19 on pregnancy and neonatal outcome.  
- majority of pregnant patients were in their third trimester and 12.4% in first or second trimester.  
- The most common symptoms were fever (62.4%) and cough (45.3%).  
- 6.0% pregnant patients developed severe pneumonia.  
- 23.6% were preterm neonates. Neonatal COVID-19 positivity rate was 5%  
- One baby was born dead from a mother who also died from COVID-19. Of the babies born alive from mothers with COVID-19, 5 newborns faced critical conditions, and 2 later died. |

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| 7   | Maternal and perinatal outcomes related to COVID-19 and pregnancy: An overview of systematic reviews | Author: Vergara-Merino L et al Study Citation: Acta Obstet Gynecol Scand. 2021 Jul;100(7):1200-1218 Study Type: Review Patients No.: NA | This systematic review analyzed the current evidence on prognosis of COVID-19 in pregnant women.  
- The rates of maternal death varied from 0% to 11.1%, admission to intensive care from 2.1% to 28.5%, preterm deliveries before 37 weeks from 14.3% to 61.2%, and cesarean delivery from 48.3% to 100%.  
- Regarding neonatal outcomes, neonatal death varied from 0% to 11.7% and the estimated infection status of the newborn varied between 0% and 11.5%. |
| 8   | Depression and anxiety in pregnancy during COVID-19: A rapid review and meta-analysis | Author: Tomfohr-Madsen LM et al Study Citation: Psychiatry Res. 2021 Jun;300:113912 Study Type: Meta-analysis Patients No.: 47677 | This study reviewed the prevalence of depression and anxiety among pregnant women during the COVID-19 pandemic. Findings suggests that prevalence of depression was 25.6% & anxiety was 30.5%. |
| 9   | Effects of the COVID-19 pandemic on pregnancy outcomes            | Author: Elsaddig M et al Study Citation: Best Pract Res Clin Obstet Gynaecol. 2021 Jun;73:125-136. Study Type: Review Patients No.: NA | This review study explored the effect of COVID-19 on pregnant women and their babies. Findings from the study suggests that  
- pregnant women with COVID-19 may be more likely to require ICU admission in the third trimester.  
- caesarean section rates among pregnant women with COVID-19  
- there is higher frequency of preterm births among women with COVID-19 |

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| 10  | A systematic review involving 11,187 participants evaluating the impact of COVID-19 on anxiety and depression in pregnant women | Author: Sun F et al Study Citation: J Psychosom Obstet Gynaecol. 2021 Jun;42(2):91-99. Study Type: Meta-analysis Patients No.: 11187 | This meta-analysis was conducted to analyze mental health in pregnant and delivery women. The prevalence of  
- depression was 30%  
- anxiety was 34% and  
- both anxiety and depression was 18%  

| 11  | Pregnant women with COVID-19: the placental involvement and consequences | Author: Aghaamoo S et al Study Citation: J Mol Histol. 2021 Jun;52(3):427-435. Study Type: Review Patients No.: NA | This review investigated the features of COVID-19 in pregnant women and its feto-neonatal consequences.  
- The higher risk of abruption, preterm labor, maternal death, stillbirth, IUGR, and newborns with fetal distress were adverse pregnancy and perinatal outcomes of COVID-19.  
- There was no agreement on the mother-child vertical transmission.  
- Feto-neonatal consequences might be associated with placental abnormalities like feto-maternal vascular malperfusion. |
Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<td>12</td>
<td>Editorial: Maternal SARS-CoV-2 Infection and Pregnancy Outcomes from Current Global Study Data</td>
<td>Author: Parums DV et al. Study Citation: Med Sci Monit. 2021 Jul 5;27:e933831. Study Type: Review Patients No.: NA</td>
<td>This review article summarizes current understanding about maternal SARS-CoV-2 infection and pregnancy outcomes from multinational studies. Findings from study suggests that • most maternal infections with SARS-CoV-2 occur during the third trimester and result in a small increase in hospital admission, admission to the ICU, mechanical ventilation, preterm birth, and increased cesarean sections in mothers infected with SARS-CoV-2. • transplacental transmission of SARS-CoV-2 to the fetus may occur</td>
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<tr>
<td>13</td>
<td>Supporting parents as essential care partners in neonatal units during the SARS-CoV-2 pandemic</td>
<td>Author: van Veenendaal NR et al. Study Citation: Acta Paediatr. 2021 Jul;110(7):2008-2022. Study Type: Review Patients No.: 442</td>
<td>This review highlights that SARS-CoV-2 pandemic-related hospital restrictions had adverse effects on care delivery and outcomes for neonates, families and staff. restricting parents' access and participation in neonatal care had negative impact on breastfeeding, parental bonding, participation in caregiving and parental mental health.</td>
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<td>14</td>
<td>Breast Milk and COVID-19: From Conventional Data to &quot;Omics&quot; Technologies to Investigate Changes Occurring in SARS-CoV-2 Positive Mothers</td>
<td>Author: Bardanzellu F et al. Study Citation: Int J Environ Res Public Health. 2021;18(11):5668 Study Type: Review Patients No.: NA</td>
<td>Findings from this review suggests that there is a sustained beneficial effects of breast milk in the case of mothers affected by SARS-COV-2, hence should continue to breastfeed. There is a possible protective effect of breast milk against COVID-19 also for the transfer of antibodies that can exert an antiviral action protecting respiratory and gastrointestinal systems.</td>
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### Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 15  | SARS-CoV-2 infection during pregnancy and pregnancy-related conditions: Concerns, challenges, management and mitigation strategies-a narrative review | Author: Kumar R et al Study Citation: J Infect Public Health. 2021 Jul;14(7):863-875. Study Type : Review Patients No. : NA | This review analyzed the potency of the high risk of infection, morbidity and mortality of COVID-19 in pregnant women. It evaluated the chances vertical transmission of SARS-CoV-2 during pregnancy and breastfeeding. Findings suggests that  
• pregnant women are considered to be a vulnerable group during the ongoing COVID-19 pandemic.  
• the possibility of vertical transmission is unclear |
| 16  | SARS-CoV-2 Infection in Pregnant Women: Neuroimmune-Endocrine Changes at the Maternal-Fetal Interface | Author: Granja MG et al Study Citation: Neuroimmunomodulation. 2021;28(1):1-21. Study Type : Review Patients No. : NA | This review studied the possible harmful outcomes to the offspring brains of mothers infected by SARS-CoV-2.  
• Evidence indicating vertical transmission of SARS-CoV-2 are not stronger; however, the exacerbated inflammatory response observed in the disease may influence the neurodevelopment of the fetus. |
| 17  | The Psychological Impact of COVID-19 Pandemic on Women’s Mental Health during Pregnancy: A Rapid Evidence Review | Author: Ahmad M et al Study Citation: Int J Environ Res Public Health. 2021 Jul 2;18(13):7112. Study Type :Review Patients No. :NA | This review studied the psychological impact of the COVID-19 pandemic on women during pregnancy and the first year postpartum. Findings suggests that COVID-19 pandemic can have a significant impact on maternal mental health in the form of anxiety and depressive symptoms.  
Psychological support should be provided to pregnant women with COVID-19 to protect their mental health and minimize the risks of long-term effects on child development. |

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# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<td>18</td>
<td>Effects of Covid-19 on pregnancy: An overview</td>
<td>Author: Siddiqui S et al. Study Citation: Saudi Med J. 2021 Jul;42(7):798-800</td>
<td>This review study stated that there is a considerable effect on the coagulation, respiratory, immune, and cardiovascular functions in pregnant women due to physiological variations and this may highly affect the COVID-19 progression in them positively or negatively.</td>
</tr>
</tbody>
</table>
| 19  | Maternal death related to COVID-19: A systematic review and meta-analysis focused on maternal comorbidities and clinical characteristics | Author: La Verde M et al. Study Citation: Int J Gynaecol Obstet. 2021 Aug;154(2):212-219. | This review study evaluated the characteristics of pregnant women who died due to COVID-19. Findings suggest that  
  • obesity doubled the risk of death  
  • at least one severe co-morbidity showed a twofold increased risk of death  
  • admission to intensive care was related to a fivefold increased risk of death |
| 20  | Clinical Features and Maternal-fetal Results of Pregnant Women in COVID-19 Times | Author: Godoi APN et al. Study Citation: Rev Bras Ginecol Obstet. 2021 May;43(5):384-394. | Findings from this review suggests that  
  • Clinical manifestations in pregnant women are similar to those of non-pregnant patients.  
  • no significant scientific evidence of vertical transmission of SARS-CoV-2.  
  • SARS-CoV-2 infection in pregnant women may cause fetal distress, breathing difficulties and premature birth. |

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| 21  | Maternal nutrients and effects of gestational COVID-19 infection on fetal brain development | Author: Hoffman MC et al  
Study Citation: Clin Nutr ESPEN. 2021 Jun;43:1-8.  
Study Type: Review  
Patients No.: NA | This review aimed to evaluate the impact of maternal nutrients status during gestational infection on fetal brain development.  
• Higher maternal choline levels have positive effects on the infant brain development of mothers who experienced viral infections in early pregnancy.  
• Choline supplements could be helpful for women planning or already pregnant who are exposed or infected with SARS-CoV-2. |
| 22  | Maternal medicine in the COVID era                                   | Author: Relph S et al  
Study Type: Review  
Patients No.: NA | This review summarizes the current evidence on COVID-19's impact on high-risk pregnant women and their babies.  
• Pregnant women with medical co-morbidities or complications are at higher risk of COVID-19 including ICU admissions, need for invasive ventilation and death.  
• Both COVID-19 and reduced mobility may increase the risk of thromboembolic complications.  
• Pregnant women have an increased risk to develop symptoms of anxiety or depression. |

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| 23  | The Differences in Clinical Presentation, Management, and Prognosis of Laboratory-Confirmed COVID-19 between Pregnant and Non-Pregnant Women: A Systematic Review and Meta-Analysis | Author: Khan DSA et al Study Citation: Int J Environ Res Public Health. 2021 May 24;18(11):5613. Study Type: Meta-analysis Patients No.: 591,058 | This review investigated the differences in clinical presentation, management, and prognosis of COVID-19 infection in pregnant and non-pregnant women.  
• The risk of experiencing fever (26%), headache (33%), myalgia (8%), diarrhea (60%), chest tightness (14%), and expectoration (55%) were greater amongst non-pregnant COVID-19-infected women.  
• Non-pregnant women had a higher frequency of chronic cardiac disease (42%), renal disease (55%), and malignancy (18%) vs COVID-19-infected pregnant women.  
• The risk of ICU admission and requirement of invasive mechanical ventilation were 2 times higher amongst pregnant women. |
| 24  | The severity of COVID-19 among pregnant women and the risk of adverse maternal outcomes | Author: Samadi P e al Study Citation: Int J Gynaecol Obstet. 2021 Jul;154(1):92-99. Study Type: cross-sectional Patients No.: 258 | This study evaluated the relationship between the severity of COVID-19 during pregnancy and the risk of adverse maternal outcomes.  
• 79.8% pregnant women had mild to moderate disease,  
• 16.7% had severe disease, and  
• 3.5% were in the critical stage  
• 3.1% died and 12.8% required ICU admission  
• Pregnant women with severe and critical disease had a high rate of cesarean delivery and ICU admission. |

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| 25  | Health-related quality of life and quality of care in pregnant and postnatal women during the coronavirus disease 2019 pandemic: A cohort study | Author: Alaya F et al Study Citation: Int J Gynaecol Obstet. 2021 Jul;154(1):100-105. Study Type: cohort Patients No. :38 | This cohort study compared self-reported health-related quality of life (HRQoL) and hospital quality of care among perinatal women with and without COVID-19.  
  • There was a significantly greater burden on physical health among pregnant women with COVID-19.  
  • There was no difference in mental health and well-being between cohorts. |
| 26  | COVID-19 pandemic and population-level pregnancy and neonatal outcomes: a living systematic review and meta-analysis | Author: Yang J et al Study Citation: Acta Obstet Gynecol Scand. 2021 Jun 6:10.1111/aogs.14206. Study Type: Living Systematic review Patients No. :21 028 650 | This living systematic review studies reporting pregnancy and neonatal outcomes by comparing the pandemic and pre-pandemic periods. Findings suggests that  
  • The COVID-19 pandemic period may be associated with a reduction in preterm birth.  
  • There was no difference in stillbirth between the pandemic and pre-pandemic period. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 27  | Diabetes Management Delivery and Pregnancy Outcomes in Women with Gestational Diabetes Mellitus during the First Wave of the 2020 COVID-19 Pandemic: A Single-Reference Center Report | Author : Wilk M et al Study Citation: J Diabetes Res. 2021 Jul 3;2021:5515902. Study Type : Cohort Patients No. : 155 | This single center cohort study evaluated the impacts of the first COVID-19 wave on GDM treatment, glycemic control, and pregnancy outcomes.  
- almost 50% GDM women used telemedicine.  
- incidence of prolonged labor and preeclampsia were different in COVID-19 period vs non-COVID-19 period, (16.4% vs 3.7%; p ≤ 0.01) & (0 vs 8.5%; p = 0.01), respectively.  
- first wave of the COVID-19 pandemic had no negative impact on pregnancy outcomes in GDM women. |
| 28  | COVID-19 positivity associated with traumatic stress response to childbirth and no visitors and infant separation in the hospital | Author : Mayopoulos GA et al. Study Citation: Sci Rep 11, 13535 (2021) Study Type : Cohort Patients No. : 2344 | This matched-control survey-based studied women confirmed/ suspected COVID-19 matched with COVID-19 negative recruited during the first wave of the pandemic in the US.  
- 50% of COVID positive women had acute traumatic stress symptoms  
- COVID positive group reported higher levels of pain in delivery, lower newborn weights, and more infant NICU admissions.  
- COVID-19 positive pregnant women are at increased risk for traumatic childbirth and psychiatric morbidity risk |

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# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 29  | The Psychological Impact of the Coronavirus Disease 2019 Pandemic on Pregnant Women in China | Author: Zheng Z et al.  
Study Citation: Front Psychiatry. 2021 Jul 2;12:628835.  
Study Type: cross-sectional  
Patients No.: 2,798 | This study investigated the psychological impact in pregnant women during this COVID-19 pandemic.  
- Significantly higher rates of depression and insomnia among pregnant women were found during the COVID-19 pandemic.  
- Over one third reported mild depression  
- Around 20% experienced mild generalized anxiety  
- About one third reported sleep issues  
- >15% felt mild psychological stress  
- Depression issue was more in 1st trimester  
- Insomnia and psychological stress reported more in 3rd trimester |
| 30  | Fetal and perinatal outcome following first and second trimester covid-19 infection: Evidence from a prospective cohort study | Author: Rosen H et al.  
Study Citation: J Clin Med. 2021 May 16;10(10):2152.  
Study Type: cohort  
Patients No.: 55 | This cohort study investigated the effect of first and second trimester maternal COVID-19 disease on fetal and perinatal outcomes.  
- SARS-CoV-2 infection at early gestation showed no association of vertical transmission and resulted in favorable obstetric and neonatal outcomes.  
- Pregnancies resulted in perinatal survival of 100%  
- Preterm birth rate was 3.4% |

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## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 31  | Study of pregnancy with COVID-19 and its clinical outcomes in a tertiary care teaching hospital in Western India | Author: Kapadia SN et al  
Study Citation: J South Asian Feder Obst Gynae 2021;13(2):125–130.  
Study Type: Cohort  
Patients No.: 50 | This cohort study investigated the cases of pregnancy with COVID-19 and its clinical outcome.  
- The main complaint was fever (44%), followed by dry cough (18%), sore throat (8%), headache (4%), malaise (14%), and diarrhea in (4%) of patients.  
- elevated C-reactive protein level – 44%  
- Lymphopenia – 34%  
- elevation of the D-dimer level – 38%  
- increased interleukin 6 levels – 16%  
- 52% patients underwent C-section, and 46% delivered vaginally  
- there was no evidence of poor fetal outcome, intrauterine fetal deaths, or premature deliveries.  
- no evidence of the virus in the vaginal fluid, cord blood, or breast milk supporting vertical transmission of COVID-19 in the third trimester of pregnancy. |
| 32  | Consequences of SARS-CoV-2 disease on maternal, perinatal and neonatal outcomes: A retrospective observational cohort study | Author: Sahar H et al  
Study Citation: Clinical and Experimental Obstetrics & Gynecology, 2021, 48(2): 353-358.  
Study Type: Cohort  
Patients No.: 62 | The cohort study aimed to describe maternal and fetal outcomes among mothers with confirmed maternal SARS-CoV-2 infection.  
- 22.5% presented with obvious typical symptoms of COVID-19  
- Length of hospital stay was more in positive cases |

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# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 33  | Clinical relevance of SARS-CoV-2 infection in late pregnancy | Author: Ruggiero M et al. Study Citation: BMC Pregnancy Childbirth. 2021 Jul 12;21(1):505. Study Type: Cohort Patients No.: 315 | This cohort aimed to understand the impact of SARS-CoV-2 infection in late pregnancy.  
- Overall, 8.9% women had a diagnosis of SARS-CoV-2 infection in pregnancy.  
- Symptoms significantly associated with Covid-19 in pregnancy included fever, cough, dyspnea and anosmia.  
- Pregnancy outcome in women with and without SARS-CoV-2 infection did not differ much. |
| 34  | Maternal and fetal effects of COVID-19 virus on a complicated triplet pregnancy: a case report | Author: Rabiei, M et al. Study Citation: J Med Case Reports 15, 87 (2021). Study Type: Case report Patients No.: 1 | This was a case report of a woman with a triplet pregnancy and a history of primary infertility, as well as hypothyroidism and GDM.  
- after maternal infection with COVID-19 (mild symptoms), exacerbated placental insufficiency occurred in two of the fetuses, and the 3rd fetus had a positive COVID-19 test after birth.  
- Two babies died 3 and 13 days after birth, respectively, due to collapsed white lung and sepsis. |

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## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 35  | Maternal and perinatal outcomes of pregnant women with SARS-CoV-2    | Author: Gurol-Urganci I et al  
Study Citation: Am J Obstet Gynecol. 2021 May 20:S0002-9378(21)00565-2.  
Study Type: Cohort  
Patients No.: 342,080 | This cohort study aimed to determine the association between SARS-CoV-2 infection at the time of birth and maternal and perinatal outcomes.  
• Risk of fetal death and preterm birth was twice more common in women with SARS-CoV-2 infection than those without.  
• The risk of preeclampsia or eclampsia, birth by emergency cesarean delivery, and prolonged admission after birth were significantly higher by 55%, 63% and 57% for women with SARS-CoV-2 infection, respectively.  
• The risk of neonatal adverse outcome, need for specialist neonatal care, and prolonged neonatal admission after birth were all significantly higher by 45%, 24% and 61% for infants with positive mothers, respectively. |
| 36  | Maternal and perinatal outcomes of pandemic Covid-19 in pregnancy in Basrah | Author: Sharief M et al  
Study Citation: European Journal of Molecular & Clinical Medicine, 2021; 8(3): 517-529.  
Study Type: Cohort  
Patients No.: 135 | This cohort study aimed to evaluate the maternal, fetal and neonatal complications in pregnant women with Covid-19 infection.  
• 41.48% patient experienced mild disease & 17.77% were having severe conditions.  
• The maternal risk factors that may worse the prognosis were maternal hypertension (5.1%) and diabetes (2.9%).  
• Vaginal delivery (4.4%), abdominally delivery (6.6%).  
• 17.03% neonates admitted to ICU  
• 3.7% perinatal deaths were observed |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 37  | Impact of Covid-19 on attendances for a 1st episode of reduced fetal movements: A retrospective observational study | Author: Marques-Fernandez L et al Study Citation: PLoS One. 2021 Jun 25;16(6):e0253796. Study Type: Cohort Patients No.: 810 | • This cohort study showed that there was a significant decrease in 1st attendances for reduced fetal movements (RFM) during COVID-19 pandemic.  
• Primiparous women were 1.4 times more likely to attend with RFM. |
| 38  | Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study | Author: José Villar et al Study Citation: JAMA Pediatr. 2021;175(8):817-826 Study Type: Cohort Patients No.: 706 | • In this multinational cohort study, COVID-19 in pregnancy was associated with consistent and substantial increases in severe maternal morbidity and mortality and neonatal complications when pregnant women with and without COVID-19 diagnosis were compared.  
• The findings should alert pregnant individuals and clinicians to implement strictly all the recommended COVID-19 preventive measures. |
| 39  | Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study | Author: Aris T Papageorghiou et al Study Citation: Am J Obstet Gynecol. 2021 Jun 26;S0002-9378(21)00561-5 Study Type: observational Patients No.: 2184 | • COVID-19 during pregnancy is strongly associated with preeclampsia, especially among nulliparous women.  
• Women with preeclampsia should be considered a particularly vulnerable group with regard to the risks posed by COVID-19. |

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# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 40  | Coronavirus Disease 2019 in Pregnancy and Outcomes Among Pregnant Women and Neonates: A Literature Review | Author: Mark EG et al. Study Citation: Pediatr Infect Dis J. 2021 May 1;40(5):473-478. Study Type: Review Patients No.: NA | This review included the studies published February 1, 2020, through August 15, 2020.  
- Among pregnant women with COVID-19, 11% required ICU admission and 8% required mechanical ventilation.  
- Among women who delivered, 28% had a preterm birth, and 57% had a Caesarean section. 4% neonates with reported testing had at least 1 positive severe acute respiratory syndrome coronavirus 2 polymerase chain reaction test.  
- The most common symptom among neonates was respiratory distress (21%).  
- There were 14 neonatal deaths |
| 41  | Relationship of COVID-19 with pregnancy | Author: Umme Salma Study Citation: Taiwan J Obstet Gynecol. 2021 May; 60(3): 405–411. Study Type: Review Patients No.: 149 | This review included the most recent data on 149 pregnant women and 96 newborns.  
- 4 infants had shown COVID-19 positive, while 91 were COVID-19 negative.  
- 1 had died due to DIC and multiple organ failure.  
- Total 6 neonate has complication after delivery, 3 had fever, cough, 1 had fatigue, 1 had GI and respiratory symptoms and 1 had slightly decreased responsiveness and muscle tone respectively.  
- Last updated 12/08/2021 |
# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 42  | Coronavirus infection in neonates: a systematic review                 | Author: Trevisanuto D et al. Study Citation: Arch Dis Child Fetal Neonatal Ed. 2021 May;106(3):330-335. Study Type: Systematic Review Patients No.: 44 | This systematic review evaluated 26 observational studies (18 case reports and 8 case series) and identified 44 newborns with confirmed SARS-CoV-2 infection.  
• Half of neonates had a documented contact with the infected mother.  
• Most neonates were asymptomatic or presented mild symptoms.                                                                                     |
| 43  | Perinatal SARS-CoV-2 Infection and Neonatal COVID-19: A 2021 Update   | Author: Sankaran D et al. Study Citation: Neoreviews. 2021 May;22(5):e284-e295. Study Type: Review Patients No.: NA | This review summarizes the impact of SARS-CoV-2 infection on pregnancy and childbirth and examined care and possible outcomes for neonates with Covid-19-positive mothers.  
• Neonatal infection was reported in 1% to 3% of births.  
• Preterm birth were reported 12.9%  
• Low birthweight, cesarean section, and NICU admissions were frequently observed among COVID-19 deliveries.                                                                                           |
| 44  | Vertical transmission of Severe Acute Respiratory Syndrome Coronavirus 2: A scoping review | Author: Tolu LB et al. Study Citation: PLoS One. 2021 Apr 22;16(4):e0250196. Study Type: Meta-analysis Patients No.: 336 | This meta-analysis evaluated 51 studies (30 case series, 20 case reports, 1 case-control study) reporting 336 newborns screened for COVID-19.  
• 4.4% were positive and 95.6% were negative for RT-PCR.  
• 11.9% births were preterm (<37 weeks) and all were live births except for one stillbirth at 20 weeks.  
• 6.25% were low birth weight (<2500g).  
• 8.3% required admission to the NICU.                                                                                                                  |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<td>45</td>
<td>The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis</td>
<td>Author: Wei SQ et al. Study Citation: CMAJ. 2021 Apr 19;193(16):E540-E548. Study Type: Meta-analysis. Patients No.: 438,548</td>
<td>This meta-analysis included 42 studies involving 438,548 pregnant women. COVID-19 during pregnancy was associated with increased risk of preeclampsia, preterm birth and stillbirth. Severe COVID-19 was strongly associated with preeclampsia, preterm birth, gestational diabetes and low birth weight.</td>
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| 46  | Adverse Pregnancy Outcomes Among Individuals With and Without Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): A Systematic Review and Meta-analysis | Author: Huntley BJF et al. Study Citation: Obstet Gynecol. 2021 Apr 1;137(4):585-596. Study Type: Meta-analysis. Patients No.: 4,473 | This meta-analysis included 6 studies with 4,473 pregnant individuals.  
  - 16.0% individuals had laboratory-confirmed SARS-CoV-2 infection.  
  - The incidences of intrauterine fetal death and neonatal death were similar among individuals who tested positive compared with negative for SARS-CoV-2 when admitted to labor and delivery. |
| 47  | The effects of COVID-19 on pregnancy and implications for reproductive medicine | Author: Joseph NT et al. Study Citation: Fertil Steril. 2021 Apr;115(4):824-830. Study Type: Review. Patients No.: NA | This review summarizes that pregnancies complicated by SARS-CoV-2 infection are associated with increased likelihood of cesarean delivery and preterm birth with rare possibility of intrauterine transmission. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 48  | Inositol and vitamin D may naturally protect human reproduction and women undergoing assisted reproduction from Covid-19 risk | Author : Bezerra Espinola MS et al  
Study Citation : J Reprod Immunol. 2021 Apr;144:103271.  
Study Type : Review  
Patients No. : NA | This review summarizes the COVID-19 and pregnant women association and role of Vitamin D and Myo-inositol as preventive treatment for pregnant women or women undergoing assisted reproductive technologies (ART). |
# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 49  | Mindfulness Effects in Obstetric and Gynecology Patients During the Coronavirus Disease 2019 (COVID-19) Pandemic: A Randomized Controlled Trial | **Author:** Smith RB et al.  
**Study Citation:** Obstet Gynecol. 2021 Jun 1;137(6):1032-1040.  
**Study Type:** RCT  
**Patients No.:** 101 | This study showed that outpatient obstetric and gynecology patients who used the prescribed consumer-based mobile meditation app during the COVID-19 pandemic had significant reductions in perceived stress, depression, anxiety, and sleep disturbance compared with standard care. |
| 50  | Immunological and physiopathological approach of COVID-19 in pregnancy | **Author:** Ferrer-Oliveras R et al.  
**Study Citation:** Arch Gynecol Obstet. 2021 Jul;304(1):39-57.  
**Study Type:** Review  
**Patients No.:** NA | This review discusses that immune-thrombosis has been identified as a common immune-mediated and pathogenic phenomenon both in COVID-19, in obstetric diseases and in COVID-19 pregnant women. |
| 51  | Vertical transmission and COVID-19: a scoping review                 | **Author:** Oliveira KF et al.  
**Study Citation:** Rev Bras Enferm. 2021 May 21;74(suppl 1):e20200849.  
**Study Type:** Review  
**Patients No.:** NA | In this review a small percentage of neonates tested positive for COVID-19, but these cases were not attributed to vertical transmission. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 52  | A literature review of 2019 novel coronavirus (SARS-CoV2) infection in neonates and children | **Author:** Di Nardo M et al.  
**Study Citation:** Pediatr Res. 2021 Apr;89(5):1101-1108.  
**Study Type:** Review  
**Patients No.:** NA | This review highlights the impact of COVID-19 in children which is usually a mild form of disease, rarely requiring high-intensity medical treatment in pediatric ICU. Vertical transmission is unlikely, but not completely excluded. |
| 53  | European consensus recommendations for neonatal and paediatric retrievals of positive or suspected COVID-19 patients | **Author:** Terheggen U et al.  
**Study Citation:** Pediatr Res. 2021 Apr;89(5):1094-1100.  
**Study Type:** Review  
**Patients No.:** NA | This consensus recommendations aim to define current best-practice and aim help guide transport teams dealing with infants and children with COVID-19 to work safely and effectively. |
| 54  | Breast Milk and COVID-19: From Conventional Data to "Omics" Technologies to Investigate Changes Occurring in SARS-CoV-2 Positive Mothers | **Author:** Bardanzellu F et al.  
**Study Citation:** Int J Environ Res Public Health. 2021 May 25;18(11):5668.  
**Study Type:** Review  
**Patients No.:** NA | This review study summarizes the current knowledge on SARS-CoV-2 effects on breast milk, resuming both "conventional data" (antibodies) and "omics technologies" (metabolomics and microbiomics). |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 55  | A systematic review of pregnant women with COVID-19 and their neonates | **Author**: Mirbeyk M. et al.  
**Study Citation**: Arch Gynecol Obstet. 2021 Jul;304(1):5-38.  
**Study Type**: Review  
**Patients No.**: 364 | A systematic review confirm that the course of COVID-19 in pregnant women resembles that of other populations. However, there is not sufficient evidence to establish an idea that COVID-19 would not complicate pregnancy. |
| 56  | A systematic review involving 11,187 participants evaluating the impact of COVID-19 on anxiety and depression in pregnant women | **Author**: Sun F et al.  
**Study Citation**: J Psychosom Obstet Gynaecol. 2021 Jun;42(2):91-99.  
**Study Type**: Systematic review  
**Patients No.**: 11187 | This meta-analysis was conducted about mental health in pregnant and delivery women. The results showed that the prevalence of depression was 30%, anxiety was 34% and prevalence of both anxiety and depression was 18%. |
| 57  | Pregnant women with COVID-19: the placental involvement and consequences | **Author**: Aghaamoo S et al.  
**Study Citation**: J Mol Histol. 2021 Jun;52(3):427-435.  
**Study Type**: Review  
**Patients No.**: NA | In this study, the potential undesirable maternal and feto-neonatal consequences of COVID-19, and the related pathophysiological alterations in mother, neonate, and especially in the placenta as a vital organ, were investigated.  
The higher risk of abruption, preterm labor, maternal death, stillbirth, intrauterine growth restriction, and newborns with fetal distress were adverse pregnancy and perinatal outcomes of COVID-19. |

Last updated 12/08/2021
### Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 58  | Diffuse trophoblast damage is the hallmark of SARS-CoV-2-associated fetal demise | **Author:** Garrido-Pontnou M et al.  
**Study Citation:** Mod Pathol. 2021 May 18;1-6.  
**Study Type:** Cohort  
**Patients No.:** 198 | This study report findings of vertical transmission associated with placental SARS-CoV-2 infection that may result in fetal loss depending on the extent of the lesion. Although placental infection occurs at a low rate, it can cause diffuse trophoblastic damage which can result in fetal death. |
| 59  | Investigating the risk of maternal-fetal transmission of SARS-CoV-2 in early pregnancy | **Author:** Halici-Ozturk F et al.  
**Study Citation:** Placenta. 2021 Mar;106:25-29.  
**Study Type:** Cohort  
**Patients No.:** 210 | This cohort study evaluated the possibility of intrauterine vertical transmission of SARS-CoV-2 in early pregnancy (before 24 weeks of gestation).  
- 24 (11.4%) pregnant women had positive rt-PCR results.  
- However, placenta and curettage material samples of these patients (21 samples) were negative for SARS CoV-2 RNA.  
- No evidence of vertical transmission of SARS-CoV-2 in early pregnancy. |
| 60  | Severe SARS-CoV-2 placenta infection can impact neonatal outcome in the absence of vertical transmission | **Author:** Cribiù F.M, et al.  
**Study Citation:** J Clin Invest. 2021 Mar 15;131(6):e145427  
**Study Type:** Cohort  
**Patients No.:** 37 | This cohort study showed that SARS-CoV-2 RNA could be detected in the placenta in 47% of SARS-CoV-2–positive women by PCR.  
- Presence of the virus was not associated with any maternal or neonatal features  
- Placental damage induced by the virus may be detrimental for the neonate independently of vertical transmission. |
# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 61  | SARS-CoV-2 Infection in Pregnant Women: Neuroimmune-Endocrine Changes at the Maternal-Fetal Interface | **Author:** Granja M.G et al.  
**Study Citation:** Neuroimmunomodulation. 2021;28(1):1-21.  
**Study Type:** Review  
**Patients No.:** NA | • This review suggests that although evidence of vertical transmission are rare, infection by SARS-CoV-2 disturbs the maternal-fetal interface, changing immune cells signaling present there.  
• This in turn leads to an increase in inflammatory cytokines that cross the placenta and can influence the neurodevelopment of the fetus. |
| 62  | Association of Maternal SARS-CoV-2 Infection in Pregnancy with Neonatal Outcomes | **Author:** Norman M et al.  
**Study Citation:** JAMA. 2021 May 25;325(20):2076-2086.  
**Study Type:** Cohort  
**Patients No.:** 88 159 | In this cohort study maternal SARS-CoV-2 infection in pregnancy was significantly associated with small increase in some neonatal morbidities.  
Risk of admission for neonatal care was 47% high, mortality risk and respiratory distress syndrome was 2 times high among infants of SARS-CoV-2-positive mothers versus comparator infants of SARS-CoV-2-negative mothers. |
| 63  | Fetal inflammatory response syndrome associated with maternal SARS-CoV-2 infection | **Author:** McCarty K.L et al.  
**Study Citation:** Pediatrics. 2020 Oct 29;e2020010132.  
**Study Type:** Case report  
**Patients No.:** 1 | This case report describe an infant of a SARS-CoV-2-positive mother born prematurely with signs of a systemic inflammatory response. The neonate was tested negative for SARS-CoV-2.  
It should be considered that virus may act as a nidus for a fetal inflammatory response syndrome even if infant test negative for SARS-CoV-2. |
Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 64  | Pregnancy and neonatal outcomes in COVID-19: Study protocol for a global registry of women with suspected or confirmed SARS-CoV-2 infection in pregnancy and their neonates, understanding natural history to guide treatment and prevention | **Author:** Banerjee J. et al.  
**Study Citation:** BMJ Open. 2021 Jan 29;11(1):e041247.  
**Study Type:** Cohort  
**Patients No.:** NA | The pregnancy and neonatal outcomes in COVID-19 (PAN-COVID) registry are an observational study collecting focused data on outcomes of pregnant mothers who have had suspected COVID-19 in pregnancy or confirmed SARS-CoV-2 infection and their neonates via a web-portal.  
The latest information till 12 April 2021 showed results as  
- Pre-term birth – 8.2%  
- Miscarriage – 1%  
- Intrauterine death /stillbirth – 0.4%  
- Fetal growth restriction – 4.3% |
| 65  | Consequences of SARS-CoV-2 disease on maternal, perinatal and neonatal outcomes: A retrospective observational cohort study | **Author:** Abdulghani S.H et al.  
**Study Citation:** Clinical and Experimental Obstetrics and Gynecology (2021) 48:2 (353-358)  
**Study Type:** Cohort  
**Patients No.:** 62 | This observational study showed that the median length of stay was higher in symptomatic cases vs asymptomatic cases (6 vs 4 days).  
Absence of perinatal morbidities or mortalities among symptomatic and asymptomatic mothers. |
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Study Citation: JAMA Pediatr. 2021 Apr 22;e211050.  
Study Type: Cohort  
Patients No.: 2130 | This cohort study compared the maternal and neonatal outcomes in infected and not-infected pregnant individuals.  
• Women with COVID-19 diagnosis were at 76% higher risk for preeclampsia/eclampsia.  
• More than 3 times higher risk of severe infection and 5 times higher risk of ICU admission & 22 times higher risk of mortality.  
• 59% increase risk of preterm birth  
• Cesarean delivery was associated with 2X risk of neonatal test positivity. |
| 67  | Obstetrical and Newborn Outcomes Among Patients With SARS-CoV-2 During Pregnancy | Author: Trahan M.-J et al.  
Study Citation: J Obstet Gynaecol Can.2021 Mar 27;S1701-2163(21)00298-X  
Study Type: Cohort  
Patients No.: 270 | Outcomes of 45 patients with SARS-CoV-2 during pregnancy were compared with those of 225 patients without infection.  
• 16% of patients with SARS-CoV-2 delivered preterm, compared with 9% of patients without.  
• The rate of cesarean delivery was 29% for patients with SARS-CoV-2. |
| 68  | Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study | Author: Gurol-Urganci I et al.  
Study Citation: Am J Obstet Gynecol.2021 May 20;S0002-9378(21)00565-2.  
Study Type: Cohort  
Patients No.: 342080 | This cohort analysis included 342,080 women, of whom 3,527 had laboratory-confirmed SARS-CoV-2 infection.  
Preterm birth & fetal death occurred 2 times more in women with infection than those without. Risk of preeclampsia/eclampsia, birth by Cesarean delivery and prolonged admission following birth were significantly higher for women with infection by 55%, 63% and 57%, respectively. Risk of neonatal adverse outcome, need for specialist neonatal care and prolonged neonatal admission following birth were all significantly higher for infants with positive mothers. |
### Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 69  | Maternal nutrients and effects of gestational COVID-19 infection on fetal brain development | **Author**: Hoffman M.C et al.  
**Study Citation**: Clin Nutr ESPEN  
**Study Type**: Review  
**Patients No.**: NA | This review has highlighted that SARS-CoV-2 produces maternal inflammatory responses during pregnancy similar to previously studied common respiratory viruses. This study encourages choline supplementation which can have positive effects on the development of brain function for infants of mothers who experienced viral infections in early pregnancy. |
| 70  | The association between SARS-CoV-2 infection and preterm delivery: a prospective study with a multivariable analysis | **Author**: Martinez-Perez O et al.  
**Study Citation**: BMC Pregnancy Childbirth  
2021 Apr 1;21(1):273  
**Study Type**: Cohort  
**Patients No.**: 1009 | Among 1009 screened pregnancies, 246 were SARS-CoV-2 positive.  
• Compared to negative mothers, SARS-CoV-2 infection increased the odds of preterm birth by 2 times.  
• Risk of premature rupture of membranes at term increased by 70% and neonatal ICU admissions was 4 times more common in positive mothers. |
| 71  | Should COVID-19 Mother Breastfeed her Newborn Child? A Literature Review on the Safety of Breastfeeding for Pregnant Women with COVID-19 | **Author**: Bhatt H  
**Study Citation**: Curr Nutr Rep  
2021 Mar;10(1):71-75  
**Study Type**: Review  
**Patients No.**: NA | This review study evaluated the possibility of vertical transmission through breastmilk. Although rare data suggests that virus can be detected in breastmilk and the infants were diagnosed with COVID-19, the disease was transmitted through breastmilk or direct contact or through delivery remain unclear. As breastmilk of COVID-19 positive mothers can give immunity to the child, direct breastfeeding or extracted breastmilk should be encouraged. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 72  | Retrospective Analysis of Clinical Characteristics and Neonatal Outcomes of Pregnant Women with SARS-COV-2 Infection | Author: Chen Y et al.  
Study Citation: Curr Med Sci  
2021 Apr;41(2):306-311  
Study Type: Cohort  
Patients No.: 8 | This cohort study investigated the neonatal outcomes of pregnant women with SARS-COV-2. Finding from the study suggested the possibility of vertical transmission of SARS-CoV-2. |
| 73  | Pregnancy outcome, antibodies and placental pathology in sars-cov-2 infection during early pregnancy | Author: Jang W.-K., et al.  
Study Citation: Int J Environ Res Public Health  
2021 May 26;18(11):5709  
Study Type: Cohort  
Patients No.: 7 | This cohort study considered 7 pregnant women diagnosed with SARS-CoV-2 infection during pregnancy at a mean gestational age of 14.5 weeks.  
The rt-PCR results for maternal plasma, cord blood, placenta, and amniotic fluid were negative and IgG antibodies were detected in maternal plasma and cord blood.  
Findings suggest that maternal antibodies are passed to the fetus, which results in a period of immunity. |
| 74  | Effect of SARS-CoV-2 infection during the second half of pregnancy on fetal growth and hemodynamics: A prospective study | Author: Rizzo G et al.  
Study Citation: Acta Obstet Gynecol Scand  
2021 Jun;100(6):1034-1039  
Study Type: Case-control  
Patients No.: 147 | Findings from this study suggests that pregnancies complicated by SARS-CoV-2 infection are not at higher risk of developing fetal growth restriction through impaired placental function. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 75  | Adverse pregnancy outcomes, maternal complications, and severe illness among U.S. delivery hospitalizations with and without a COVID-19 diagnosis | Author: Ko J.Y, et al.  
Study Citation: Clin Infect Dis. 2021 May 12;ciab344  
Study Type: Cohort  
Patients No.: 489,471 | The incidence of COVID-19 positive case was 1.3% in this delivery hospitalized patients.  
• COVID-19 was associated with increased risk for ARDS, sepsis, mechanical ventilation, shock ICU admission, acute renal failure, thromboembolic disease and preterm delivery.  
• Risk for any maternal complications or for any severe illness did not significantly differ by race/ethnicity. |
| 76  | Villitis of unknown etiology in the placenta of a pregnancy complicated by COVID-19 | Author: Ozer E et al.  
Study Citation: Turk Patoloji Derg. 2021;37(2):167-171.  
Study Type: Case-report  
Patients No.: 1 | Findings from this case-report hypothesize that Villitis of unknown etiology (VUE) may represent a maternal anti-viral immune response in SARS-CoV-2 positive mother and may result in fetal growth restriction and stillbirth. |
| 77  | The severity of COVID-19 among pregnant women and the risk of adverse maternal outcomes | Author: Samadi P et al.  
Study Citation: Int J Gynaecol Obstet. 2021 Apr 9.  
Study Type: Cohort  
Patients No.: 258 | Findings from this cross-sectional study suggest that pregnant women with severe and critical disease had a high rate of cesarean delivery and admission to the ICU (12.8%). Mortality rate was more than 3%. |
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| 78  | Fetal and perinatal outcome following first and second trimester covid-19 infection: Evidence from a prospective cohort study | **Author:** Rosen H et al.  
**Study Citation:** J Clin Med. 2021 May 16;10(10):2152.  
**Study Type:** Cohort  
**Patients No.:** 55 | This was a prospective cohort study considered pregnant women with SARS-COV-2 infection contracted prior to 26 weeks. Study concluded that SARS-CoV-2 infection at early gestation was not associated with vertical transmission and resulted in favorable obstetric and neonatal outcomes. |
| 79  | Influence of socioeconomic status on sars-cov-2 infection in spanish pregnant women. The moacc-19 cohort | **Author:** Llorca J et al.  
**Study Citation:** Int J Environ Res Public Health. 2021 May 12;18(10):5133  
**Study Type:** Cohort  
**Patients No.:** 988 | This study analyzed the relationship between educational, occupational, and housing variables with SARS-CoV-2 infection in a cohort of 988 pregnant women. Housing characteristics, but not occupational or educational variables, were associated with SARS-CoV-2 infection. |
| 80  | SARS-COV-2 infection in pregnant women and newborns in a Spanish cohort (GESNEO-COVID) during the first wave | **Author:** Carrasco I et al.  
**Study Citation:** BMC Pregnancy Childbirth. 2021 Apr 26;21(1):326.  
**Study Type:** Cohort  
**Patients No.:** 105 | The possibility of vertical transmission has not been reported in this cohort. The prognosis of newborns could be worsened by SARS-CoV-2 infection during pregnancy as COVID-19 pneumonia increased the risk of caesarean section deliveries and preterm births. |
Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 81  | Third trimester stillbirth during the first wave of the SARS-CoV-2 pandemic: Similar rates with increase in placental vasculopathic pathology | Author: Bunnell M.E et al.  
Study Citation: Placenta. 2021 Apr 19;109:72-74  
Study Type: Cohort  
Patients No.: 18000 | This study compared third trimester stillbirth rates (28 weeks or greater) during the first wave of the COVID-19 pandemic to those in equivalent time periods in 2019 and 2018.  
The study demonstrated no change in the rates of third trimester stillbirth during the first five months of the COVID-19 pandemic. |
| 82  | The differences in clinical presentation, management, and prognosis of laboratory-confirmed covid-19 between pregnant and non-pregnant women: A systematic review and meta-analysis | Author: Khan D.S.A et al  
Study Type: Review  
Patients No.: 591,058 | This review investigated the differences in clinical presentation, management, and prognosis of COVID-19 infection in pregnant and non-pregnant women.  
COVID-19-infected pregnant women had a higher requirement of ICU admission and invasive mechanical ventilation compared to non-pregnant COVID-19-infected women. |
Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 83  | Characteristics, clinical and laboratory data and outcomes of pregnant women with confirmed SARS-CoV-2 infection admitted to Al-Zahra tertiary referral maternity center in Iran: a case series of 24 patients | **Author**: Vaezi M et al.  
**Study Citation**: BMC Pregnancy Childbirth. 2021 May 17;21(1):378  
**Study Type**: case-series  
**Patients No.**: 24 | This study evaluated clinical and laboratory characteristics and outcomes of COVID-19 pregnant patients and their newborns. Findings suggest that clinical symptoms in pregnancy were similar to non-pregnant women, no rise in risk of premature labor or abortion was seen, and vertical transmission was not observed in any of cases. |
| 84  | A rare but devastating cause of twin loss in a near-term pregnancy highlighting the features of severe SARS-CoV-2 placentitis | **Author**: Libbrecht S et al.  
**Study Citation**: Histopathology. 2021 May 13.  
**Study Type**: Case-report  
**Patients No.**: 2 | This study reports 2 cases of severe SARS-CoV-2 placentitis, which is rare, but can have an impact on pregnancy outcome.  
- The main histopathological features of SARS-CoV-2 placentitis were syncytiotrophoblast necrosis, histiocytic intervillositis and strong positive immunohistochemistry for SARS-CoV2 nucleocapsid protein.  
- Deposition of C4d was an additional hallmark. |
| 85  | Pregnancy outcomes of women positive for SARS-CoV-2 compared to women tested negative | **Author**: Mattern J et al.  
**Study Citation**: Topics in Antiviral Medicine. (2021) 29:1 (222-223)  
**Study Type**: Cohort  
**Patients No.**: 123 | In a symptomatic pregnant population tested positive for SARS-CoV-2 compared to negative patients with same characteristics, COVID-19 infection seemed to increase medically indicated preterm births. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 86  | Clinical features and outcomes of neonatal COVID-19: A systematic review | **Author:** Lim K.H et al.  
**Study Citation:** J Clin Virol. 2021 Jun;139:104819.  
**Study Type:** Systematic review  
**Patients No.:** 99 | This study aimed to determine the clinical manifestations of neonatal COVID-19 and outcomes based on severity groups. Of 99 neonates diagnosed with COVID-19 infection, 27.3% were asymptomatic. 30.3% had severe-critical illness. Amongst symptomatic neonates, respiratory symptoms were common — dyspnoea (36.1%), nasal symptoms (19.4%), cough (18.1%); 55.6% had fever. More neonates in the severe group were symptomatic, admitted to the ICU, had dyspnoea and abnormal chest radiographic findings. Mild-moderately ill neonates had increased incidence of fever and gastrointestinal symptoms. |
| 87  | Maternal death related to COVID-19: A systematic review and meta-analysis focused on maternal comorbidities and clinical characteristics | **Author:** La Verde M et al.  
**Study Citation:** Int J Gynaecol Obstet. 2021 Apr 30.  
**Study Type:** Review  
**Patients No.:** 154 | The aim of this review was to evaluate the characteristics of pregnant women who died due to COVID-19. Obesity doubled the risk of death. Admission to ICU was related to a fivefold increased risk of death |
| 88  | Comparison of Laboratory and Radiological Findings of Pregnant and Non-Pregnant Women with Covid-19 | **Author:** Ozer K.B et al.  
**Study Citation:** Rev Bras Ginecol Obstet. 2021 Mar;43(3):200-206.  
**Study Type:** Cohort  
**Patients No.:** 34 | The aim of this article was to determine whether the laboratory results and radiological findings were different in non-pregnant women (NPWs) of reproductive age and pregnant women (PWs) diagnosed with the Covid-19 infection. The laboratory findings and imaging studies may differ between pregnant and non-pregnant populations. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 89  | The impact of the COVID-19 pandemic on maternal mortality in Brazil: 523 maternal deaths by acute respiratory distress syndrome potentially associated with SARS-CoV-2 | **Author**: Nakamura-Pereira M. et al.  
**Study Citation**: Int J Gynaecol Obstet. 2021 May;153(2):360-362  
**Study Type**:  
**Patients No.**: | Abstract NA                                                                                                                                                                                                |
| 90  | Prevalence, clinical features, and outcomes of SARS-CoV-2 infection in pregnant women with or without mild/moderate symptoms: Results from universal screening in a tertiary care center in Mexico City, Mexico | **Author**: Cardona-Pérez J.A et al.  
**Study Citation**: PLoS One. 2021 Apr 22;16(4):e0249584.  
**Study Type**: Case-control  
**Patients No.**: 240 | In this cohort study prevalence of COVID-19 was 29%; 86% of the patients were asymptomatic.  
The proportion of preeclampsia was higher in positive women than negative women.  
No differences were found for other perinatal outcomes. |
| 91  | Impact of the COVID-19 pandemic on preterm birth and stillbirth: a nationwide, population-based retrospective cohort study | **Author**: Simon E et al.  
**Study Citation**: Am J Obstet Gynecol. 2021 May 19;S0002-9378(21)00563-9  
**Study Type**: Cohort  
**Patients No.**: 518,798 | This study showed that lockdown may be associated with beneficial effects on perinatal morbidity.  
Also there was no increase in the rate of stillbirth since the beginning of the pandemic. |
# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 92  | The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: A national cohort study using the UK Obstetric Surveillance System (UKOSS) | **Author:** Vousden N et al.  
**Study Citation:** PLoS One. 2021 May 5;16(5):e0251123.  
**Study Type:** Cohort  
**Patients No.:** NA | This cohort study aimed to describe the outcomes of symptomatic & asymptomatic hospitalized pregnant women with SARS-CoV-2.  
Hospitalized symptomatic patients were more likely to be admitted to ICU.  
Cesarean births and neonatal unit admission were increased regardless of symptom status.  
The risks of stillbirth or neonatal death were not significantly increased, regardless of symptom status. |
| 93  | Were pregnant women more affected by COVID-19 in the second wave of the pandemic? | **Author:** Kadiwar S et al.  
**Study Citation:** Lancet. 2021 Apr 24;397(10284):1539-1540  
**Study Type:** Review  
**Patients No.:** NA | This review summarises, that pregnant and peripartum women experienced more severe illness in the second wave of the COVID-19 pandemic than was observed in the first wave. However, the true cause of this change was not clear. |
| 94  | Placenta histopathology in SARS-CoV-2 infection: analysis of a consecutive series and comparison with control cohorts | **Author:** Bertero L et al.  
**Study Citation:** Virchows Arch. 2021 May 1;1-14.  
**Study Type:** Cohort  
**Patients No.:** 11 | This study showed that compared to control cohort, chronic villitis/VUE, chronic deciduitis, microvascular thrombosis, presence of infarction areas and of accelerated villous maturation showed higher frequencies in placentas delivered by women with COVID-19. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 95  | Coronavirus disease 2019 in pregnant and non-pregnant women: a retrospective study | Author : Zha Y et al.  
Study Citation : Chin Med J (Engl)  
Study Type : Cohort  
Patients No. : 285 | This cohort study showed that pregnant and non-pregnant women with COVID-19 infection had similar epidemiological characteristics, but pregnant patients presented relatively mild clinical manifestations, shorter symptom-to-discharge duration, and pregnancy-related specific laboratory examination characteristics. |
Study Citation : Am J Obstet Gynecol MFM  
. 2021 Feb 20;3(4):100329  
Study Type : Cohort  
Patients No. : 887 | This study aimed to evaluate maternal and perinatal outcomes in high- and low-risk pregnancies complicated by SARS-CoV-2.  
Findings suggest that high-risk pregnancies with SARS-CoV-2 were at higher risk of adverse maternal outcomes. |
| 97  | Potential SARS-CoV-2 interactions with proteins involved in trophoblast functions – An in-silico study | Author : Seethy A.A et al.  
Study Citation : Placenta  
. 2021 Jan 1;103:141-151.  
Study Type : Cohort  
Patients No. : NA | This study showed that SARS-CoV-2 can potentially interact with proteins having crucial roles in the placental function. |
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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| 98  | Impact of SARS-Cov-2 on ectopic pregnancies management in the United Kingdom: a multicentre observational study | **Author**: Platts S et al.  
**Study Citation**: BJOG 2021 May 16. doi: 10.1111/1471-0528.16756  
**Study Type**: Cohort  
**Patients No.**: 341 | - In this cohort study, consecutive patients diagnosed clinically and/or radiologically with ectopic pregnancy were entered into the Covid-ectopic pregnancy registry (CEPR) and results were compared to the non-Covid ectopic pregnancy registry (NCEPR) cohort.  
- A significantly lower percentage of women underwent surgical management vs non-surgical management in the CEPR vs NCEPR  
- In medically managed patients, the CEPR had a significantly lower median number of hospital visits vs NCEPR.  
- There was no observed difference in complication rates between cohorts. |
# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<tr>
<td>99</td>
<td>Impact of COVID-19 on maternal and neonatal outcomes: a systematic</td>
<td>Author: Di Toro F et al Study Citation: Clin Microbiol Infect. 2021 Jan;27(1):36-46.</td>
<td>This systematic review and meta-analysis stated that in most cases the disease does not threaten the mother, and vertical transmission has not been clearly demonstrated. Therefore, COVID-19 should not be considered as an indication for elective caesarean section.</td>
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<tr>
<td></td>
<td>review and meta-analysis</td>
<td>Study Type: Meta-analysis Patients No.: 1100</td>
<td></td>
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<tr>
<td>100</td>
<td>Maternal and perinatal outcomes in pregnant women infected by SARS-CoV-2: A meta-analysis</td>
<td>Author: Bellos I et al Study Citation: Eur J Obstet Gynecol Reprod Biol. 2021 Jan;256:194-204. Study Type: Meta-analysis Patients No.: NA</td>
<td>This meta-analysis showed that the maternal and neonatal clinical course the infection is typically mild, presenting low mortality rates. The risk of vertical transmission is suggested to be low and may not be affected by the severity of maternal disease.</td>
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## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<tr>
<td>101</td>
<td>Maternal Coronavirus Infections and Neonates Born to Mothers with SARS-CoV-2: A Systematic Review</td>
<td>Author: Amaral WND et al Study Citation: Healthcare (Basel). 2020 Nov 24;8(4):511 Study Type: Review Patients No.: 1457</td>
<td>This review showed that COVID-19 during pregnancy can result in maternal, fetal, and neonatal complications. Moreover, SARS-CoV-2 viral exposure of neonates during pregnancy and delivery cannot be ruled out. Further, long-term follow-up studies are required to establish the full implications of SARS-CoV-2 infection in these children.</td>
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<tr>
<td>102</td>
<td>Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review</td>
<td>Author: Centeno-Tablante E et al Study Citation: Ann N Y Acad Sci. 2021 Jan;1484(1):32-54. Study Type: Systematic review Patients No.: 77</td>
<td>This systematic review analyzed breast milk samples, and reported that 9 of the 68 analyzed breast milk samples from mothers with COVID-19 were positive for SARS-CoV-2 RNA, and out of exposed infants 4 were positive and two were negative for COVID-19. More number of studies are needed to confirm the viral presence in breast milk.</td>
</tr>
<tr>
<td>103</td>
<td>Clinical Presentation and Outcomes of Pregnant Women With Coronavirus Disease 2019: A Systematic Review and Meta-analysis</td>
<td>Author: Matar R et al Study Citation: Clin Infect Dis. 2021 Feb 1;72(3):521-533. Study Type: Systematic review Patients No.: 136</td>
<td>This systematic review and meta-analysis reported preterm birth rate as 37.7% and cesarean delivery rate as 76%. There was 1 maternal death. There were 2 fetal COVID-19 cases. Overall findings suggested that clinical picture in pregnant women with COVID-19 did not differ from the nonpregnant population; however, the rate of preterm birth and cesarean delivery are considerably higher than international averages.</td>
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# Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<td>104</td>
<td>Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review</td>
<td>Author: Novoa RH et al.  Study Citation: Travel Med Infect Dis. 2021 Jan-Feb;39:101919. Study Type: Systematic review. Patients No.: 322</td>
<td>This systematic review stated that fever and cough were the main clinical characteristics among pregnant women with COVID-19, and it was less frequent than non-pregnant women with COVID-19. Iatrogenic preterm birth is the main adverse obstetric outcome. Moreover, findings of this study did not support vertical transmission in third trimester.</td>
</tr>
<tr>
<td>105</td>
<td>Clinical characteristics and outcomes of pregnant women with COVID-19 and the risk of vertical transmission: a systematic review</td>
<td>Author: Chi J et al.  Study Citation: Arch Gynecol Obstet. 2021 Feb;303(2):337-345. Study Type: Systematic review. Patients No.: 230</td>
<td>This systematic review showed that cesarean section was more common than vaginal delivery for pregnant women with COVID-19. Premature delivery was the main adverse event for newborns. The vertical transmission rate calculated by SARS-CoV-2 nucleic acid tests was 3.91%.</td>
</tr>
<tr>
<td>106</td>
<td>Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews</td>
<td>Author: Papapanou M et al.  Study Citation: Int J Environ Res Public Health. 2021 Jan 12;18(2):596. Study Type: Systematic review. Patients No.: NA</td>
<td>This systematic review demonstrated maternal mortality rate as &lt;2%, while stillbirth, neonatal ICU admission and mortality rates were &lt;2.5%, 3.1-76.9% and &lt;3%, respectively. Cesarean delivery and preterm births were higher in COVID-19 infected pregnant women. Also, the probability of vertical transmission cannot be excluded in this study. Thus, more studies are required to be evaluated in women of all trimesters.</td>
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Last updated 12/08/2021
## Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<td>107</td>
<td>Clinical manifestation, outcomes in pregnant women with COVID-19 and the possibility of vertical transmission: a systematic review of the current data</td>
<td>Author: Han Y et al Study Citation: J Perinat Med. 2020 Nov 26;48(9):912-924 Study Type: Systematic review Patients No.: NA</td>
<td>This systematic review showed that premature delivery risk was higher, leading to greater risk of NICU admission and low neonatal birthweight. Vertical transmission of SARS-CoV-2 from mother to child was found to be unlikely.</td>
</tr>
<tr>
<td>108</td>
<td>Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its effect on gametogenesis and early pregnancy</td>
<td>Author: Singh B et al Study Citation: Am J Reprod Immunol. 2020 Nov;84(5):e13351. Study Type: Meta-analysis Patients No.: NA</td>
<td>This meta-analysis states that early reports from SARS-CoV, MERS-CoV, and other respiratory infections suggest that there may be a lesser severe impact with SARS-CoV-2 on early pregnancy physiology, as suggested by a lesser comparative miscarriage rate.</td>
</tr>
<tr>
<td>109</td>
<td>Clinical Characteristics and Neonatal Outcomes of Pregnant Patients With COVID-19: A Systematic Review</td>
<td>Author: Islam MM et al Study Citation: Front Med (Lausanne). 2020 Dec 3;7:573468. Study Type: Systematic review Patients No.: 235</td>
<td>This systematic review shows that the clinical, laboratory and radiological characteristics of pregnant women with COVID-19 were similar to those of the general populations.</td>
</tr>
<tr>
<td>110</td>
<td>A multicenter study on epidemiological and clinical characteristics of 125 newborns born to women infected with COVID-19 by Turkish Neonatal Society</td>
<td>Author: Oncel MY et al Study Citation: Eur J Pediatr. 2021 Mar;180(3):733-742. Study Type: Cohort Patients No.: 125</td>
<td>This multicenter cohort study showed that COVID-19 in pregnant women has important impacts on perinatal and neonatal outcomes. Maternal mortality, higher rates of preterm birth and cesarean section, suspected risk of vertical transmission, and low rate of breastfeeding show that family support should be a part of the care in the NICU.</td>
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### Effects of COVID-19 on pregnancy outcomes: miscarriage, stillbirth, preterm delivery and perinatal death

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<tr>
<td>111</td>
<td>Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: A systematic review and meta-analysis</td>
<td>Author: Jafari M et al Study Citation: Rev Med Virol. 2021 Jan 2:e2208. Study Type: Review Patients No.: 138176</td>
<td>This review article highlights that higher odds of caesarean delivery, LBW and preterm birth among pregnant patients with COVID-19 suggest a possible association between COVID-19 infection and pregnancy complications. Low risk of vertical transmission is present, and SARS-CoV-2 can be detected in all conception products, particularly placenta and breast milk.</td>
</tr>
<tr>
<td>112</td>
<td>Characterization of neonates born to mothers with SARS-CoV-2 infection: Review and meta-analysis</td>
<td>Author: Neef V et al Study Citation: Pediatr Neonatol. 2021 Jan;62(1):11-20. Study Type: Meta-analysis Patients No.: 261</td>
<td>This meta-analysis showed that neonates are mostly non-affected by the mother's SARS-CoV-2 infection, and the risk of vertical transmission is low.</td>
</tr>
<tr>
<td>113</td>
<td>Incidence of SARS-CoV-2 vertical transmission: a meta-analysis</td>
<td>Author: Goh XL et al Study Citation: Arch Dis Child Fetal Neonatal Ed. 2021 Jan;106(1):112-113 Study Type: Meta-analysis Patients No.: NA</td>
<td>This meta-analysis demonstrated that continued vigilance is needed as COVID-19 infection can potentially cause serious complications in the newborn.</td>
</tr>
<tr>
<td>114</td>
<td>A systematic review and meta-analysis of pregnancy and COVID-19: Signs and symptoms, laboratory tests, and perinatal outcomes</td>
<td>Author: Hassanipour S et al Study Citation: Int J Reprod Biomed. 2020 Dec 21;18(12):1005-1018 Study Type: Meta-analysis Patients No.: NA</td>
<td>In this systematic review, analysis of perinatal outcomes revealed that of the newborns of the corona-positive mothers, only one had a positive test result. Also, there was only one death due to disseminated intravascular coagulation.</td>
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<td>115</td>
<td>Can immunity during pregnancy influence SARS-CoV-2 infection? - A systematic review</td>
<td>Author: Areia AL et al Study Citation: J Reprod Immunol. 2020 Nov;142:103215. Study Type: Systematic review Patients No.: NA</td>
<td>This systematic review showed that pregnant women with COVID-19 in terms of immunity only differ from other pregnant women in their lower WBC count.</td>
</tr>
<tr>
<td>116</td>
<td>Exploring the emergence of vertical transmission of SARS-CoV-2: A Rapid Review</td>
<td>Author: Jain V et al Study Citation: Acta Biomed. 2020 Dec 22;91(4):e2020129. Study Type: Review Patients No.: NA</td>
<td>This systematic review suggested the possibility of vertical transmission of SARS-CoV-2.</td>
</tr>
<tr>
<td>117</td>
<td>The 2019 Novel Coronavirus Disease in Pregnancy: A Systematic Review</td>
<td>Author: Makvandi S et al Study Citation: Adv Exp Med Biol. 2021;1321:299-307. Study Type: Systematic review Patients No.: 68</td>
<td>This systematic review showed that the most common obstetrical complication was preterm labor (33.3%). No maternal deaths were reported. The Cesarean section rate was 83.3% and the vertical transition rate was 2.23%. The findings showed that the clinical symptoms and laboratory measures of pregnant women affected by COVID-19 did not differ from the general population.</td>
</tr>
<tr>
<td>118</td>
<td>Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review</td>
<td>Author: Oltean I et al Study Citation: Heliyon. 2021 Mar;7(3):e06393. Study Type: Review Patients No.: NA</td>
<td>This systematic review stated that intensive care unit (ICU) admission, gestational diabetes, preeclampsia, C-sections, pre-term birth, and C-reactive protein (CRP) were higher among pregnant women with COVID-19 infection compared to those without. Careful monitoring of pregnancies with SARS-CoV-2 is recommended.</td>
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<td>119</td>
<td>The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis</td>
<td>Author: Wei SQ et al Study Citation: CMAJ. 2021 Apr 19;193(16):E540-E548. Study Type: Meta-analysis Patients No.: 438 548</td>
<td>This systematic review and meta-analysis showed that COVID-19 may be associated with increased risks of preeclampsia, preterm birth and other adverse pregnancy outcomes.</td>
</tr>
<tr>
<td>120</td>
<td>The Profile of the Obstetric Patients with SARS-CoV-2 Infection According to Country of Origin of the Publication: A Systematic Review of the Literature</td>
<td>Author: Cuñarro-López Y et al Study Citation: J Clin Med. 2021 Jan 19;10(2):360 Study Type: systematic review Patients No.: 2670</td>
<td>This systematic review showed that proportion of C-sections are elevated together with prematurity, increasing maternal perinatal morbimortality in the obstetric patients with SARS-CoV-2 Infection.</td>
</tr>
<tr>
<td>121</td>
<td>Cesarean Section or Vaginal Delivery to Prevent Possible Vertical Transmission From a Pregnant Mother Confirmed With COVID-19 to a Neonate: A Systematic Review</td>
<td>Author: Cai J et al Study Citation: Med (Lausanne). 2021 Feb 17;8:634949. Study Type: systematic review Patients No.: 1019</td>
<td>This systematic review reported probable congenital SARS-CoV-2 infections in 3.29% neonates. Of babies born vaginally, 2.16%) were tested positive vs. 4.05% of those who were born by cesarean delivery. Of babies born vaginally, no neonatal deaths were reported vs. 6 out of 618 (0.97%) born by cesarean delivery. Based on the evidence available, there is no sufficient evidence supporting that the cesarean section is better than vaginal delivery in preventing possible vertical transmission from a pregnant mother confirmed with COVID-19 to a neonate.</td>
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<tr>
<td>122</td>
<td>Current trends and geographical differences in therapeutic profile and outcomes of COVID-19 among pregnant women - a systematic review and meta-analysis</td>
<td>Author: Dubey P et al Study Citation: BMC Pregnancy Childbirth. 2021 Mar 24;21(1):247. Study Type: Meta-analysis Patients No.: 1239</td>
<td>This systematic review and meta-analysis reported that highest preterm birth and the average length of hospital stay (35%, 11.9 days) were estimated in Asian studies compared to the US studies (13%, 9.4 days) and European studies (29%, 7.3 days), respectively in pregnant women with COVID-19 infection.</td>
</tr>
<tr>
<td>123</td>
<td>A Systematic Review of 571 Pregnancies Affected by COVID-19</td>
<td>Author: Karimi L et al Study Citation: Adv Exp Med Biol. 2021;1321:287-298. Study Type: systematic review Patients No.: 571</td>
<td>This systematic review showed that the vertical transmission rate was 7.9% out of total 571 pregnant women with COVID-19. Characteristics of COVID-19 was comparable to general population.</td>
</tr>
<tr>
<td>124</td>
<td>Clinical manifestation and maternal complications and neonatal outcomes in pregnant women with COVID-19: a comprehensive evidence synthesis and meta-analysis</td>
<td>Author: Sohelli M et al Study Citation: J Matern Fetal Neonatal Med. 2021 Feb 18:1-14. Study Type: systematic review Patients No.: 5560</td>
<td>This is a systemic review with 5560 pregnant women with COVID-19 including 43 retrospectives or cross-sectional studies, and 31 case report and case series studies. The results showed , pregnant women with COVID-19 with or without pneumonia, are at a higher risk of preeclampsia, preterm birth, miscarriage and cesarean delivery. Furthermore, the risk of LBW and intrauterine fetal distress seems to be increased in neonates.</td>
</tr>
<tr>
<td>125</td>
<td>A systematic review of clinical and laboratory parameters of 3,000 COVID-19 cases.</td>
<td>Author: Goel H et al Study Citation: Obstet Gynecol Sci. 2021 Mar;64(2):174-189 Study Type: systematic review Patients No.: 3000</td>
<td>Pregnant women were a part of the sub analysis of the study which demonstrated that preterm delivery was seen in 25% of the cases .</td>
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| 126 | Maternal, fetal and neonatal outcomes of large series of SARS-CoV-2 positive pregnancies in peripartum period: A single-center prospective comparative study | Author: Hcini N et al  
Study Citation: Eur J Obstet Gynecol Reprod Biol. 2021 Feb;257:11-18.  
Study Type: cohort  
Patients No.: 507 | This prospective cohort study enrolled all pregnant women admitted for delivery to compare maternal, fetal and neonatal outcomes of SARS-CoV-2 infected pregnant women with those of non-infected patients. There were no significant differences in spontaneous births as well as for iatrogenic preterm and caesarean sections. There were statistically significant differences between the two groups concerning fetal adverse outcomes. |
| 127 | Obstetric Outcomes of SARS-CoV-2 Infection in Asymptomatic Pregnant Women. | Author: Cruz-Lemini M et al  
Study Citation: Viruses. 2021 Jan 15;13(1):112.  
Study Type: Cohort  
Patients No.: 604 | This multicenter prospective study found no difference in maternal & neonatal outcomes were observed. |
| 128 | Impact of SARS-CoV-2 Infection on Pregnancy Outcomes: A Population-Based Study. | Author: Crovetto F et al  
Study Citation: Clin Infect Dis. 2021 Feb 8:ciab104.  
Study Type: Cohort  
Patients No.: 2225 | This population-based study to describe the impact of SARS-CoV-2 infection on pregnancy outcomes found women with symptomatic COVID-19 had increased rates of preterm delivery and intrapartum fetal distress. |
| 129 | COVID-19 in pregnancy: a systematic review of chest CT findings and associated clinical features in 427 patients | Author: Oshay RR et al  
Study Citation: Clin Imaging. 2021 Jul;75:75-82.  
Study Type: Review  
Patients No.: 427 | This systematic review suggested a low risk of vertical transmission from neonatal test findings. |
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<td>130</td>
<td>SARS-CoV-2 detection in human milk: a systematic review</td>
<td>Author: Kumar J et al Study Citation: J Matern Fetal Neonatal Med. 2021 Feb 8:1-8. Study Type: systematic review Patients No.: 116</td>
<td>This systematic review showed low quality evidence for SARS-CoV-2 RNA detection in human milk. No conclusion can be drawn about its infectivity and impact on the infants. In concordance with World Health Organization recommendations, exclusive breastfeeding should be considered in all cases unless any other contraindication exists.</td>
</tr>
<tr>
<td>131</td>
<td>SARS-CoV-2 genome and antibodies in breastmilk: a systematic review and meta-analysis</td>
<td>Author: Zhu F et al Study Citation: Arch Dis Child Fetal Neonatal Ed. 2021 Feb 10:fetalneonatal-2020-321074. Study Type: systematic review Patients No.: 183</td>
<td>This systematic review stated that low proportion of SARS-CoV-2 genome is reported in breast milk and has low virulent activity. Thus, based on these findings, mothers with COVID-19 should be supported to breastfeed.</td>
</tr>
<tr>
<td>132</td>
<td>Risk of pre-term births and major birth defects resulting from paternal intake of COVID-19 medications prior to conception</td>
<td>Author: Rizzi S et al Study Citation: BMC Res Notes. 2020 Nov 7;13(1):509. Study Type: cohort Patients No.: NA</td>
<td>This study suggested azithromycin and naproxen are safe with respect to pre-term birth and birth defects. For the other drugs investigated larger exposures are needed for conclusive statements.</td>
</tr>
<tr>
<td>133</td>
<td>Clinical presentation of coronavirus disease 2019 (COVID-19) in pregnant and recently pregnant people</td>
<td>Author: Afshar Y et al Study Citation: Obstet Gynecol. 2020 Dec;136(6):1117-1125. Study Type: Cohort Patients No.: 991</td>
<td>The PRIORITY (Pregnancy CoRonavIrus Outcomes RegIstTrY) study that is an ongoing nationwide prospective cohort study of people in the United States who are pregnant or up to 6 weeks postpregnancy with known or suspected SARS-CoV-2 infection concluded that COVID-19 has a prolonged and nonspecific disease course during pregnancy and in the 6 weeks after pregnancy.</td>
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| 134 | Excess maternal deaths associated with coronavirus disease 2019 (COVID-19) in Mexico | Author: Lumbreras-Marquez MI et al  
Study Citation: Obstet Gynecol. 2020 Dec;136(6):1114-1116.  
Study Type: Cohort  
Patients No.: NA | The results of this study, which aimed to analyse total number of excess deaths from all causes that could be directly or indirectly attributed to COVID-19, suggest higher mortality among pregnant women in Mexico during the COVID-19 pandemic. Similar to these findings, it is possible that other low- and middle-income countries have experienced a disproportionate burden of maternal mortality related to COVID-19. |
| 135 | Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) universal screening in gravids during labor and delivery | Author: Savirón-Cornudella R et al  
Study Citation: Eur J Obstet Gynecol Reprod Biol. 2021 Jan;256:400-404  
Study Type: Cohort  
Patients No.: 266 | This study that aimed to screen pregnant women at risk of SARS-CoV-2 infection during delivery found that the systematic RT-PCR assessment and serological studies of SARS-CoV-2 seem appropriated to identify women at risk during labor and delivery. |
| 136 | Clinical course of novel COVID-19 infection in pregnant women          | Author: Shmakov RG et al  
Study Citation: J Matern Fetal Neonatal Med. 2020 Nov 29:1-7  
Study Type: Cohort  
Patients No.: 66 | The study reported that the manifestations of COVID-19 were mild, yet 9% of cases were severe, and could contribute to preterm delivery, abortion or maternal and fetal morbidity. No evidence of vertical transmission during pregnancy and delivery was found. |
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| 137 | Maternal immune responses and obstetrical outcomes of pregnant women with COVID-19 and possible health risks of offspring | Author: Cavalcante MB et al  
Study Citation: J Reprod Immunol. 2021 Feb;143:103250  
Study Type: Review  
Patients No.: NA | This review suggests structural and systemic follow-up of offspring who are exposed to SARS-CoV-2 in-utero. Initial studies demonstrate a possible association between COVID-19 and preterm birth, intrauterine growth restriction, and low birth weight, which have been reported to increase risks for long-term non-communicable diseases in adulthood. |
| 138 | Special issue on COVID-19 and pregnancy: Consequences for maternal and neonatal health | Author: Sharma S et al  
Study Citation: Am J Reprod Immunol. 2020 Nov;84(5):e13354.  
Study Type: Review  
Patients No.: NA | This editorial states that the COVID-19 pandemic has demonstrated altered maternal immunity, and effect on gametogenesis and organogenesis as well as placental function. Long-term effects of in utero exposure to COVID-19 are not known. |
| 139 | Perinatal COVID-19 outcomes: evaluating the strength of current evidence | Author: Sulentic RO  
Study Citation: J Matern Fetal Neonatal Med. 2020 Nov 29:1-7.  
Study Type: Review  
Patients No.: 729 | This review reports that even though initial reports suggest limited risks of infection in pregnancy with SARS-CoV-2, subsequent findings have demonstrated pregnant women are at risk for severe morbidity and mortality. |
| 140 | Comparison of hematological parameters and perinatal outcomes between COVID-19 pregnancies and healthy pregnancy cohort | Author: Erol Koç EM et al  
Study Citation: J Perinat Med. 2020 Dec 1;49(2):141-147.  
Study Type: Cohort  
Patients No.: 108 | This study conducted in a high volume tertiary obstetrics center in Turkey revealed that pregnancies complicated by COVID-19 is not related with adverse perinatal outcomes. |
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<td>141</td>
<td>Maternal, Perinatal and Neonatal Outcomes With COVID-19: A Multicenter Study of 242 Pregnancies and Their 248 Infant Newborns During Their First Month of Life</td>
<td>Author: Marín Gabriel MA et al Study Citation: Pediatr Infect Dis J. 2020 Dec;39(12):e393-e397 Study Type: Cohort Patients No.: 242</td>
<td>This multicenter descriptive study involving 16 Spanish hospitals that reviewed the medical records of pregnant women did not detect COVID-19 transmission during delivery or throughout the first month of life in newborns.</td>
</tr>
<tr>
<td>142</td>
<td>Maternal and Perinatal Outcomes in Patients with Suspected COVID-19 and Their Relationship with a Negative RT-PCR Result.</td>
<td>Author: Cuñarro-López Y et al Study Citation: Clin Med. 2020 Nov 4;9(11):3552 Study Type: Cohort Patients No.: 111</td>
<td>This retrospective cohort study in obstetrics patients with suspected COVID-19 who underwent an RT-PCR test in a tertiary hospital in Madrid, Spain reported that patients with a positive RT-PCR result had a higher proportion of prematurity and C-section. Monocyte count, LDH level and a need for oxygen therapy were the variables related to a negative RT-PCR result.</td>
</tr>
<tr>
<td>143</td>
<td>Impact of the COVID-19 Pandemic on Excess Perinatal Mortality and Morbidity in Israel</td>
<td>Author: Mor M et al Study Citation: Am J Perinatol. 2021 Mar;38(4):398-403. Study Type: Cohort Patients No.: NA</td>
<td>This single center retrospective cohort study that aimed to evaluate the effect of the first wave of the COVID-19 pandemic on obstetrical emergency attendance in a low-risk population and the corresponding perinatal outcomes reported less obstetrical ER attendance and an increase in stillbirth rate, which can be attributed to the pandemic stay-at-home policy combined with patient fear of contracting the disease in hospital.</td>
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<td>144</td>
<td>Pregnancy outcomes among symptomatic and asymptomatic women infected with COVID-19 in the west of Iran: a case-control study</td>
<td>Author: Jenabi E et al Study Citation: J Matern Fetal Neonatal Med. 2020 Dec 15:1-3 Study Type: Case-control Patients No.: 90</td>
<td>This case-control study that aimed to investigate pregnancy outcomes among symptomatic and asymptomatic women infected with coronavirus disease 2019 (COVID-19) in the west of Iran showed that cesarean delivery and LBW were significantly higher in symptomatic women compared with asymptomatic women. Also, PCR test is recommended for all pregnant women upon admission for delivery in areas with high COVID-19 pandemics.</td>
</tr>
<tr>
<td>145</td>
<td>Comparison of VEGF-A values between pregnant women with COVID-19 and healthy pregnancies and its association with composite adverse outcomes</td>
<td>Author: Yazihan N et al Study Citation: J Med Virol. 2021 Apr;93(4):2204-2209 Study Type: Case-control Patients No.: 187</td>
<td>This prospective case-control study showed that the VEGF-A values were similar between pregnant women with COVID-19 and healthy controls. Also, VEGF-A was not associated with disease severity and obstetric complications.</td>
</tr>
<tr>
<td>146</td>
<td>Management of life-threatening acute respiratory syndrome and severe pneumonia secondary to COVID-19 in pregnancy: A case report and literature review</td>
<td>Author: Yaqoub S et al Study Citation: Clin Case Rep. 2020 Nov 11;9(1):137-143 Study Type: Case report Patients No.: 1</td>
<td>This case report presents the management of a critically ill pregnant women infected with SARS-CoV-2 that demonstrates the need of a multidisciplinary approach to treating and complete recovery of acute respiratory failure and severe pneumonia secondary to SARS-COV2 infection during pregnancy, as managing maternal complications as well as reassuring fetal well-being during such critical period is challenging.</td>
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| 147 | Systematic screening for SARS-CoV-2 in pregnant women admitted for delivery in a Portuguese maternity | Author: Figueiredo R et al  
Study Citation: J Perinat Med. 2020 Nov 26;48(9):977-980.  
Study Type: Cohort  
Patients No.: 184 | This observational study that intended to estimate the SARS-CoV-2 infection rate in an obstetric population admitted for delivery reported that the proportion of asymptomatic infection highlights the importance of universal laboratory screening for all women admitted for delivery as opposed to symptom-based screening. |
| 148 | Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls | Author: DeBolt CA et al  
Study Citation: Am J Obstet Gynecol. 2021 May;224(5):510.e1-510.e12.  
Study Type: Case-control  
Patients No.: 38 | This multicenter, retrospective, case-control study showed that pregnancy may be associated with a worse outcome in women with severe and critical cases of coronavirus disease 2019, and likely to demonstrated increased risk of morbidity and disease severity. |
| 149 | Maternal, neonatal and placental characteristics of SARS-CoV-2 positive mothers. | Author: Zhang P et al  
Study Citation: J Matern Fetal Neonatal Med. 2021 Feb 28;1-9.  
Study Type: Cohort  
Patients No.: 142 | The analysis of medical records demonstrate that there was no increase of pre-term labor and delivery or NICU admissions from SARS-CoV2 positive mothers. |

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<td>150</td>
<td>Maternal and neonatal outcomes of pregnant patients with COVID-19: A prospective cohort study.</td>
<td>Author: Abedzadeh-Kalahrudi M et al. Study Citation: Int J Gynaecol Obstet. 2021 Jun;153(3):449-456. Study Type: Cohort Patients No.: 56</td>
<td>This prospective cohort study compared pregnant women with COVID-19 and healthy pregnant women to determine the maternal and neonatal outcomes of pregnant women with COVID-19 infection. The rate of preterm labor in the exposed group was higher.</td>
</tr>
<tr>
<td>151</td>
<td>Pregnancy and neonatal outcomes of COVID-19: co-reporting of common outcomes from PAN-COVID and AAP SONPM registries</td>
<td>Author: Mullins E et al. Study Citation: Ultrasound Obstet Gynecol. 2021 Apr;57(4):573-581 Study Type: Cohort Patients No.: 4005</td>
<td>This analysis of data from the PAN-COVID registry included pregnancies with suspected or confirmed maternal SARS-CoV-2 infection at any stage in pregnancy, and the AAP SONPM National Perinatal COVID-19 registry</td>
</tr>
<tr>
<td>152</td>
<td>Obstetric Outcomes of SARS-CoV-2 Infection in Asymptomatic Pregnant Women.</td>
<td>Author: Cruz-Lemini M et al. Study Citation: Viruses. 2021 Jan 15;13(1):112. Study Type: cohort Patients No.: 604</td>
<td>This multicenter prospective study found no difference in maternal &amp; neonatal outcomes in groups that included pregnancies with suspected or confirmed maternal SARS-CoV-2 infection at any stage in pregnancy, and the AAP SONPM National Perinatal COVID-19 registry</td>
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| 153 | Disease Severity and Perinatal Outcomes of Pregnant Patients With Coronavirus Disease 2019 (COVID-19) | Author: Metz TD et al  
Study Citation: Obstet Gynecol. 2021 Apr 1;137(4):571-580.  
Study Type: Cohort  
Patients No.: 1219 | This is an observational cohort study of all pregnant patients with a singleton gestation and a positive test result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Frequency of perinatal death or a positive neonatal SARS-CoV-2 test result did not differ by severity. Adverse perinatal outcomes were more frequent among patients with more severe illness. |
| 154 | Neonates born to mothers with COVID-19: Data from the Spanish society of neonatology registry | Author: Sánchez-Luna M et al  
Study Citation: Pediatrics. 2021 Feb;147(2):e2020015065  
Study Type: cohort  
Patients No.: 503 | The nationwide registry of the Spanish Society of Neonatology of neonatal and maternal characteristics of the largest prospective cohort of newborns from mothers with coronavirus disease 2019 (COVID-19). |
| 155 | Disease Severity, Pregnancy Outcomes and Maternal Deaths among Pregnant Patients with SARS-CoV-2 Infection in Washington State | Author: Lokken EM et al  
Study Citation: Am J Obstet Gynecol. 2021 Jan 27:S0002-9378(21)00033-8  
Study Type: Cohort  
Patients No.: 240 | This is a multicenter retrospective cohort study of facilities covering 61% of annual births in Washington State. The 3 pregnant patients who died owing to COVID-19 disease, had significant comorbidities that included obesity, hypertension, autoimmune disease, or congenital heart disease. There were 2 stillbirths in this study; neither stillbirth was attributed to SARS-CoV-2 infection. An extensive investigation to determine the cause of death was performed in 1 case, as previously reported, and a genetic cause was attributed to the second death. Maternal and delivery characteristics were similar between women with SARS-CoV-2 infections in the second and third trimesters. |
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<td>156</td>
<td>564 Comparison of clinical outcomes in pregnant women with and without COVID-19 based on disease severity</td>
<td>Author: Gold S et al. Study Citation: Am J Obstet Gynecol. 2021;224(2):S357 Study Type: Cohort Patients No.: 2714</td>
<td>This is a multicenter retrospective cohort study which concluded that women with symptomatic or asymptomatic COVID-19 infection does not lead to increased odds of overall maternal morbidity compared to women without COVID-19 in pregnancy.</td>
</tr>
<tr>
<td>157</td>
<td>Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis</td>
<td>Author: Chmielewska B et al Study Citation: Lancet Glob Health. 2021 Jun;9(6):e759-e772 Study Type: systematic review Patients No.: NA</td>
<td>This is systematic review and meta-analysis of studies on the effects of the pandemic on maternal, fetal, and neonatal outcomes. Global maternal and fetal outcomes have worsened during the COVID-19 pandemic, with an increase in maternal deaths, stillbirth, ruptured ectopic pregnancies, and maternal depression.</td>
</tr>
<tr>
<td>158</td>
<td>Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis.</td>
<td>Author: Allotey J et al Study Citation: BMJ. 2020 Sep 1;370:m3320. Study Type: meta-analysis Patients No.: NA</td>
<td>This is systematic review and meta-analysis with 192 studies. Pregnant and recently pregnant women with covid-19 attending or admitted to the hospitals for any reason are less likely to manifest symptoms such as fever, dyspnoea, and myalgia, and are more likely to be admitted to the intensive care unit or needing invasive ventilation than non-pregnant women of reproductive age. Pre-existing comorbidities, non-white ethnicity, chronic hypertension, pre-existing diabetes, high maternal age, and high body mass index are risk factors for severe covid-19 in pregnancy. Pregnant women with covid-19 versus without covid-19 are more likely to deliver preterm and could have an increased risk of maternal death and of being admitted to the intensive care unit. Their babies are more likely to be admitted to the neonatal unit.</td>
</tr>
</tbody>
</table>

Last updated 12/08/2021
Literature Monitoring

Topic Covered

Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

Duration:

1st Nov 2020 to 12th Aug 2021
Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

| No. | Title                                                                 | Study Type & Citation                                                                 | Key Results                                                                                                                                                                                                                                                                                                                                 |
|-----|----------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1   | COVID-19 guidelines for pregnant women and new mothers: A systematic evidence review | Author: DiLorenzo MA et al Study Citation: Int J Gynaecol Obstet. 2021 Jun;153(3):373-382. Study Type: systematic review Patients No.: NA | This systematic review states that  
  • vertical transmission through breast milk remains unlikely  
  • shared decision making between patients and providers is advocated when considering separation of the mother and newborn in the immediate post-partum period.  
  • at least a two-meter distance to be maintained between the mother and child to prevent the spread of COVID-19  

| 2   | COVID-19 and pregnancy: An umbrella review of clinical presentation, vertical transmission, and maternal and perinatal outcomes | Author: Ciapponi A et al Study Citation: PLoS One. 2021 Jun 29;16(6):e0253974. Study Type: Systematic review Patients No.: NA | Findings from this systematic review supports that pregnant women with COVID-19 may be at increased risk of adverse pregnancy and birth outcomes and low risk of congenital transmission.  
  • Common clinical findings were fever (28-100%), mild respiratory symptoms (20-79%), raised C-reactive protein (28-96%), lymphopenia (34-80%), and pneumonia signs in diagnostic imaging (7-99%).  
  • Rates of C-section were 23-96% and preterm delivery 14-64%.  
  • Most babies were asymptomatic (16-93%)  
  • Fever presentation (0-50%), low birth weight (5-43%) or preterm delivery (2-69%)  
  • The risk of congenital transmission or via breast milk was estimated to be low  

DISCLAIMER: Because of the rapidly evolving events surrounding the COVID-19, the presented information may have changed since the date of search mentioned in this document.
### Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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<td>3</td>
<td>Vertical transmission and COVID-19: a scoping review</td>
<td>Author: Oliveira KF et al Study Citation: Rev Bras Enferm. 2021 May 21;74(suppl 1):e20200849. Study Type: Review Patients No.: NA</td>
<td>This review study analyzed evidences related to SARS-CoV-2 infection and vertical transmission. A small percentage of neonates tested positive for COVID-19, but these cases were not attributed to vertical transmission.</td>
</tr>
</tbody>
</table>
| 4   | Entry, egress and vertical transmission of SARS-CoV-2                  | Author: Zhang H et al Study Citation: J Mol Cell Biol. 2021 Jul 6;13(3):168-174. Study Type: Review Patients No.: NA | This review summarizes the molecular mechanism for entry of SARS-CoV-2 into host cells and the evidence for congenital transmission. Findings suggests that  
• Infection of neonates can occur via the transplacental or transcervical route or via environmental exposure.  
• Transplacental transmission may cause placental inflammation and neonatal viremia.                                                                                                                            |
Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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| 5   | Influence of SARS-CoV-2 during pregnancy: a placental view          | Author: da Costa MAS et al   
Study Citation: Biol Reprod. 2021 Jun 4;104(6):1189-1193.   
Study Type: Review   
Patients No.: NA | This study aimed to review placental changes in infected pregnant women and/or asymptomatic carriers of COVID-19 during pregnancy, and possibility of vertical transmission.   
• The virus presence was seen in the amniotic fluid, umbilical cord, and peripheral blood.   
• Study concludes that there is little evidence of transplacental vertical viral transmission and respective placental morphological changes. |
| 6   | The Immunological Role of the Placenta in SARS-CoV-2 Infection-Viral Transmission, Immune Regulation, and Lactoferrin Activity | Author: Bukowska-Ośko I et al   
Study Citation: Int J Mol Sci. 2021 May 28;22(11):5799.   
Study Type: Review   
Patients No.: NA | This review focused on the mother-fetal-placenta interface and its role in the potential transmission of SARS-CoV-2.   
• The presence of virus in the placenta does not determine the incidence of vertical transmission.   
• The vertical transmission of the virus in the third trimester is approximately 3.2%. The vertical transmission risk seems to be relatively low.   
• Lactoferrin through immunomodulatory and anti-inflammatory effects, may have some therapeutic value in COVID-19 pandemic. |

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Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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• the effect of infection with COVID-19 on the outcomes of pregnancy or health of the offspring is not well known.  
• Considering the risk of vertical transmission necessary precaution & measures to be adopted by infected mothers  
  |
| 8   | Severe Acute Respiratory Syndrome Coronavirus 2 Placental Infection and Inflammation Leading to Fetal Distress and Neonatal Multi-Organ Failure in an Asymptomatic Woman | Author : Schoenmakers S et al. Study Citation: J Pediatric Infect Dis Soc. 2021 May 28;10(5):556-561. Study Type : Case report Patients No. : 1 | This case report shows that a maternal SARS-CoV-2 infection during the third trimester of pregnancy may cause adverse neonatal outcome based on a placental inflammatory reaction and subsequent dysfunction of the placenta.  
• Study diagnosed placental inflammation caused by SARS-CoV-2 infection, based on the detection of virus infection in syncytiotrophoblasts, which led to placental failure, fetal distress, and perinatal asphyxia.  
• despite the massive placental infection, all neonatal samples were negative for SARS-CoV-2, and there was no evidence for vertical transmission.  
  |
# Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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| 9   | Being pregnant in the COVID-19 pandemic: Effects on the placenta in all aspects | Author: Seymen CM  
Study Citation: J Med Virol. 2021 May;93(5):2769-2773.  
Study Type: Review  
Patients No.: NA | This review showed that the placenta also carries a risk for SARS-COV-2 virus.  
Data suggest that the indirect effects of the virus can be seen on the fetus, from spontaneous miscarriage to intrauterine growth restriction.  
Cytokine storm, which occurs during pregnancy may adversely affect fetus. |
| 10  | Coronavirus Diseases in Pregnant Women, the Placenta, Fetus, and Neonate   | Author: Schwartz DA, Dhaliwal A.  
Study Type: Review  
Patients No.: NA | This review suggest Pregnant women with COVID-19 can develop critical illness.  
- Preterm birth is a frequent complication.  
- Vertical infection may leads to early onset of neonatal COVID-19.  
- Placental infection with SARS-CoV-2 leads to occurrence of intrauterine maternal-fetal transmission. |
| 11  | Vertical Transmission of SARS-CoV-2: A Systematic Review               | Author: Barcelos IDES et al  
Study Citation: Rev Bras Ginecol Obstet. 2021 Mar;43(3):207-215.  
Study Type: Systematic Review  
Patients No.: 9 | This systematic review evaluated 177 records and identified only 1 case with sufficient evidence of vertical transmission. It concludes that the risk of vertical transmission by SARS-CoV-2 is probably very low. |
Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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<td>12</td>
<td>Updates in neonatal coronavirus disease 2019: What can we learn from detailed case reports? (Review)</td>
<td>Author : Li X et al. Study Citation : Mol Med Rep. 2021 May;23(5):351. Study Type : Review Patients No. : 40</td>
<td>This review 40 case reports focusing mainly on demographic characteristics, transmission modes, clinical features, treatments and prognosis of neonatal COVID-19. • Horizontal transmission was the main mode of transmission along with vertical transmission possibility. • The earlier the onset of neonatal COVID-19, the more possibility of vertical transmission. • No deaths from neonatal COVID-19 was been reported</td>
</tr>
<tr>
<td>13</td>
<td>Vertical Transmission of COVID-19: A Case Report and Review of Literature</td>
<td>Author : Thapa B et al Study Citation : J Nepal Health Res Counc. 2021 Apr 23;19(1):203-205. Study Type : Review Patients No. : 1</td>
<td>This review reported a case of vertical transmission in a neonate born to asymptomatic COVID-19 infected mother. The neonate was immediately shifted to isolation nursery and formula fed. The neonatal outcome was good.</td>
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| 14  | COVID-19 during pregnancy should we really worry from vertical transmission or rather from fetal hypoxia and placental insufficiency? A systematic review | **Author**: AbdelMassih et al  
**Study Citation**: Egyptian Pediatric Association Gazette (2021) 69:1  
**Study Type**: Review  
**Patients No.**: 1787 | The findings from this review suggest that even though vertical transmission is unlikely, there appears to be an underlying risk of placental insufficiency due to the prothrombotic tendency seen in COVID-19 infection. Proper prophylactic anticoagulation in COVID-positive mothers need to be considered. |
| 15  | Perinatal outcome and possible vertical transmission of coronavirus disease 2019: Experience from North India | **Author**: Sharma R  
**Study Citation**: Clin Exp Pediatr.2021 May;64(5):239-246.  
**Study Type**: Cohort  
**Patients No.**: 44 | This study evaluated the effect of coronavirus disease 2019 (COVID-19) on neonatal outcomes and the scope of vertical transmission. 56% were delivered by cesarean section. 29.5% had low birth weight; 15.9% were preterm; and 13.6% required NICU admission. The possibility of vertical transmission was almost negligible. |
## Relationship of vertical or placental transmission in SARS-CoV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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| 16  | Chronic Histiocytic Intervillositis With Trophoblast Necrosis Is a Risk Factor Associated With Placental Infection From Coronavirus Disease 2019 (COVID-19) and Intrauterine Maternal-Fetal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Transmission in Live-Born and Stillborn Infants | **Author**: Schwartz D.A  
**Study Citation**: Archives of pathology & laboratory medicine (2021) 145:5 (517-528).  
**Study Type**: Cohort  
**Patients No.**: NA | This cohort study showed that chronic histiocytic intervillositis together with syncytiotrophoblast necrosis accompanies SARS-CoV-2 infection of syncytiotrophoblast in live-born and stillborn infants.  
The coexistence of these 2 findings in all placentas from live-born infants acquiring their infection prior to delivery indicates that they constitute a pathology risk factor for transplacental fetal infection. |
| 17  | Vertical transmission of SARS-CoV-2: consider the denominator        | **Author**: Shook L.L et al  
**Study Citation**: Am J Obstet Gynecol MFM. 2021 Apr 29;3(4):100386  
**Study Type**: Cohort  
**Patients No.**: 369 | In this observational study no case of SARS-CoV-2 infection identified in 369 newborns born to 354 women who tested positive for SARS-CoV-2 during pregnancy. |
## Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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| 18  | SARS-CoV-2 placentitis: An uncommon complication of maternal COVID-19 | **Author:** Linehan L. et al  
**Study Citation:** Placenta  . 2021 Jan 15;104:261-266  
**Study Type:** Case-report  
**Patients No.:** 1 | This case report is a case of third trimester pregnancy complicated by SARS-CoV-2 infection and subsequent reduced fetal movements, resulting in emergency Caesarean delivery with demonstrable placental SARS-CoV-2 placentitis. SARS-CoV-2 placentitis is an uncommon but readily recognisable complication of maternal SARS-CoV-2 infection that may be a marker of potential vertical transmission and that may have the capacity to cause fetal compromise through a direct injurious effect on the placenta. |
| 19  | Epidemiology, management and risk of SARS-CoV-2 transmission in a cohort of newborns born to mothers diagnosed with COVID-19 infection | **Author:** Solís-García G  
**Study Citation:** An Pediatr (Engl Ed)  . 2021 Mar;94(3):173-178.  
**Study Type:** Cohort  
**Patients No.:** 73 | The aim of this study was to describe characteristics and evolution of newborns born to mothers with SARS-CoV-2 infection. 95.9% of maternal infections were diagnosed during the third trimester of pregnancy, 43.8% were asymptomatic. No positive PCR results were observed in newborns at delivery. |
| 20  | Perinatal Transmission of 2019 Coronavirus Disease-Associated Severe Acute Respiratory Syndrome Coronavirus 2: Should We Worry?   | **Author:** Fan C et al.  
**Study Citation:** Clin Infect Dis  . 2021 Mar 1;72(5):862-864.  
**Study Type:** Case report  
**Patients No.:** 2 | This report provided evidence of low risk of intrauterine infection by vertical transmission of SARS-CoV-2. |

Last updated 12/08/2021
## Relationship of vertical or placental transmission in SARS-CoV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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| 21  | The immunological role of the placenta in sars-cov-2 infection—viral transmission, immune regulation, and lactoferrin activity | **Author**: Bukowska-Ośko I et al.  
**Study Citation**: Int J Mol Sci. 2021 May 28;22(11):5799  
**Study Type**: Review  
**Patients No.**: NA | This review summarizes the current knowledge on the anti-viral activity of lactoferrin during viral infection in pregnant women, analyzes its role in the pathogenicity of pandemic virus particles, and describes the potential evidence for placental blocking/limiting of the transmission of the virus. |
Relationship of vertical or placental transmission in SARS-CoV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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| 22  | Infection with SARS-CoV-2 in pregnancy. Update of Information and proposed care. CNGOF | Author: Peyronnet V et al  
Study Citation: Gynecol Obstet Fertil Senol. 2020 Dec;48(12):858-870.  
Study Type: Review  
Patients No.: NA | This study showed that intrauterine maternal-fetal transmission has been identified. Induced prematurity and cases of respiratory distress in newborns of infected mothers have been described.                                                                                                                                                        |
| 23  | Transmission of SARS-CoV-2 to premature twins from an asymptomatic mother | Author: Gaunt P et al  
Study Citation: Case Reports in Perinatal Medicine. 2020;9(1): 20200064  
Study Type: Case-report  
Patients No.: 2 | This case study showed potential for intrauterine transmission of SARS-CoV-2                                                                                                                                                                                                                                                                                                           |
| 24  | Detection of SARS-CoV-2 in placental but not fetal tissues in the second trimester | Author: Valk JE et al  
Study Citation: J Perinatol. 2021 May;41(5):1184-1186.  
Study Type: Case-report  
Patients No.: NA | This letter to the editor described SARS-CoV-2 involvement of placentas detectable by qRT-PCR in asymptomatic COVID-19-infected pregnant women in the second trimester. Also, low incidence of vertical transmission of the virus has been described.                                                                                     |
### Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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</table>
| 25  | COVID-19 Infection in Newborn Infants                              | Author: Mascarenhas D  
Study Citation: Indian J Pediatr. 2021 Apr;88(4):394.  
Study Type: Case-report  
Patients No.: NA | This article states that horizontal transmission from infected mothers is probable. Neonatal COVID-19 appears to have a varied presentation, with most reports describing a mild nature of disease. |
| 26  | Third-trimester placentas of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive women: histomorphology, including viral immunohistochemistry and in-situ hybridization | Author: Smithgall MC et al  
Study Citation: Histopathology. 2020 Dec;77(6):994-999.  
Study Type: Cohort  
Patients No.: NA | This study reported that third-trimester placentas from SARS-CoV-2-positive women were more likely to show evidence of maternal-fetal vascular malperfusion, but no evidence of direct viral involvement or vertical transmission was attained. |
| 27  | COVID-19 in third trimester may not be as scary as you think, it can be innocent: Evaluating vertical transmission from a COVID-19 positive asymptomatic pregnant woman with early membrane rupture | Author: Palalioglu RM et al  
Study Citation: J Obstet Gynaecol Res. 2021 Feb;47(2):838-842.  
Study Type: Case-report  
Patients No.: 1 | This case report involved a patient presenting to the emergency gynecology clinic with membrane rupture who was infected with SARS-CoV-2 but was not treated since the disease was asymptomatic. The infant had no clinical, radiological, hematological or biochemical evidence of SARS-CoV-2, indicating that SARS-CoV-2 does not cause perinatal complications in the third trimester and especially after 34 weeks of gestation, and there is no vertical transmission. |
# Relationship of vertical or placental transmission in SARS-COV-2 infected mothers on miscarriage, stillbirth, preterm delivery and perinatal death

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<td>28</td>
<td>COVID-19: neonatal-perinatal perspectives</td>
<td>Author: Barrero-Castillero A et al Study Citation: J Perinatol. 2021 May;41(5):940-951. Study Type: Review Patients No.: NA</td>
<td>This comprehensive review presenting an up-to-date summary of the literature on the management of the COVID-19 pandemic focusing on the care of pregnant women and newborns suggested that the risk of neonatal transmission is low and that neonatal disease most commonly ranges from asymptomatic to mildly symptomatic.</td>
</tr>
<tr>
<td>29</td>
<td>Is Vertical Transmission of SARS-CoV-2 Infection Possible in Preterm Triplet Pregnancy? A Case Series.</td>
<td>Author: Alwardi TH et al Study Citation: Pediatr Infect Dis J. 2020 Dec;39(12):e456-e458. Study Type: Case-report Patients No.: NA</td>
<td>This case series that reports the first case of vertical transmission in preterm triplet pregnancy, with all triplets positive for severe acute respiratory syndrome-coronavirus-2, demonstrates that vertical transmission of the infection is possible, rare, and often asymptomatic.</td>
</tr>
<tr>
<td>30</td>
<td>Congenital SARS-CoV-2 infection in a neonate with severe acute respiratory syndrome</td>
<td>Author: Correia CR et al Study Citation: Pediatr Infect Dis J. 2020 Dec;39(12):e439-e443. Study Type: Case report Patients No.: NA</td>
<td>This case report of vertical transmission of SARS-CoV-2 in a preterm born to an infected mother highlights the importance of pregnancy, labor and neonatal period surveillance of affected mothers and their newborns.</td>
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<td>31</td>
<td>Vertical transmission of SARS-CoV-2 infection</td>
<td>Author: Study Citation: Study Type: Patients No.:</td>
<td>This review stated uncertainty for fully implicate the diagnosis of vertical transmission of SARS-CoV-2 infection</td>
</tr>
<tr>
<td>32</td>
<td>Is there possibility of vertical transmission of COVID-19: a systematic review</td>
<td>Author: Yuan J et al Study Citation: Transl Pediatr. 2021 Feb;10(2):423-434. Study Type:Review Patients No.: 564</td>
<td>This systematic review and meta-analysis showed that the positive rate for COVID-19 infection was 3.8% which included a total of 564 pregnant women with COVID-19 and their 555 neonates, of which 549 neonates. Amniotic fluid of one woman was tested positive for SARS-CoV-2. No sufficient evidence to exclude the possibility of vertical transmission for COVID-19 based on the current available data.</td>
</tr>
<tr>
<td>33</td>
<td>Possible vertical transmission and antibodies against SARS-CoV-2 among infants born to mothers with COVID-19: A living systematic review</td>
<td>Author: Bwire GM et al Study Citation: J Med Virol. 2021 Mar;93(3):1361-1369. Study Type: Systematic review Patients No.: 205</td>
<td>This systematic review showed that IgG/IgM were detected in 90% infants who were tested negative for COVID-19 virus. There is low possibility of vertical transmission of COVID-19 and antibodies against SARS-CoV-2 were detected among vertically exposed but negative infants.</td>
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| 34  | Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review   | Author: Centeno-Tablante E et al  
Study Citation: Ann N Y Acad Sci. 2021 Jan;1484(1):32-54.  
Study Type: systematic review  
Patients No.: 77 | This systematic review analyzed breast milk samples, and reported that 9 of the 68 analyzed breast milk samples from mothers with COVID-19 were positive for SARS-CoV-2 RNA, and out of exposed infants 4 were positive and two were negative for COVID-19. More number of studies are needed to confirm the viral presence in breast milk. |
| 35  | Pregnancy and Breastfeeding During COVID-19 Pandemic: A Systematic Review of Published Pregnancy Cases | Author: Rodrigues C et al  
Study Citation: Front Public Health. 2020 Nov 23;8:558144.  
Study Type: systematic review  
Patients No.: 3985 | This systematic review showed that there is likelihood of vertical transmission of SARS-CoV-2; however, there were few cases reported with intrapartum samples. Adequate counselling and monitoring will help prevent and manage consequences associated with COVID-19 infection. |
| 36  | Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis       | Author: Kotlyar AM et al  
Study Citation: Am J Obstet Gynecol. 2021 Jan;224(1):35-53.e3  
Study Type: Meta-analysis  
Patients No.: 936 | This systematic review and meta-analysis showed that there is a likelihood of vertical transmission among severe acute respiratory syndrome coronavirus 2 in minority of cases of maternal coronavirus disease 2019 infection in the third trimester. The rates of infection are similar to those of other pathogens that cause congenital infections. |
Literature Monitoring

Topic Covered

Effects of COVID-19 vaccination on pregnancy

Duration:

1st Nov 2020 to 12th Aug 2021
# Effects of COVID-19 vaccination on pregnancy

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| 1   | Methodologic approaches in studies using real-world data (RWD) to measure pediatric safety and effectiveness of vaccines administered to pregnant women: A scoping review | Author: Lasky T et al  
Study Citation: Vaccine. 2021 Jun 29;39(29):3814-3824.  
Study Type: Review  
Patients No.: NA | This scoping review mapping studies using RWD/RWE to measure pediatric safety and effectiveness of vaccines administered to the mother during pregnancy will help clarify approaches to key methodologic issues such as documentation of the vaccine administered, linkage of maternal and infant data, estimation of gestational age, and definition of safety and effectiveness endpoints. |
| 2   | Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine | Author: Bookstein Peretz S et al  
Study Citation: Ultrasound Obstet Gynecol. 2021 Jul 1. Epub ahead of print  
Study Type: Case control  
Patients No.: 539 | • The adverse-effect profile and short-term obstetric and neonatal outcomes among pregnant women who were vaccinated with the BNT162b2 vaccine at any stage of pregnancy do not indicate any safety concerns.  
• The vaccine is effective in generating a humoral immune response in pregnant women, although SARS-CoV-2 IgG levels were lower than those observed in non-pregnant vaccinated women. |

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Last updated 12/08/2021
# Effects of COVID-19 vaccination on pregnancy

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| 3   | Vaccination against COVID-19 infection: the need of evidence for diabetic and obese pregnant women | Author: Lapolla A et al  
Study Type: Review  
Patients No.:  | This review highlights the need of systematic and proactive data on the effect of COVID-19 vaccination, in terms of maternal and fetal outcomes and vaccine related symptoms in high risk women during pregnancy and breastfeeding. |
| 4   | The Israeli study of Pfizer BNT162b2 vaccine in pregnancy: Considering maternal and neonatal benefits | Author: Burd I et al  
Study Citation: J Clin Invest. 2021 Jul 1;131(13):e150790.  
Study Type: Review  
Patients No.:  | This study provides evidence to support the safety and efficacy of COVID-19 vaccination in pregnancy with protection to the neonate against infection, outlining clear vaccine benefits for both maternal and child health. |

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</table>
| 5   | Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine | Author: Beharier O et al  
Study Citation: J Clin Invest. 2021 Jul 1;131(13):e150319.  
Study Type: Cohort  
Patients No.: | This study demonstrated robust maternal humoral immune response coupled to a rise in protective antibodies in the fetal circulation as early as 15 days after the first BNT162b2 mRNA vaccination supporting the role of vaccination during pregnancy.  
also, mid-pregnancy SARS-CoV-2 infection results in prolonged maternal and fetal humoral immunity presented at delivery time. |
| 6   | COVID-19 vaccine acceptance in pregnant women                          | Author:Sule Goncu Ayhan et al  
Study Citation: Int J Gynaecol Obstet. 2021 Aug;154(2):291-296.  
Study type:Survey  
Patient No:300 | The present study reported low acceptance of COVID-19 vaccination in a sample of pregnant women. Concern about vaccine safety was the major reason for hesitancy. Identifying attitudes among priority groups will be useful for creating vaccination strategies that increase uptake during the current pandemic. |

**DISCLAIMER:** Because of the rapidly evolving events surrounding the COVID-19, the presented information may have changed since the date of search mentioned in this document.
## Effects of COVID-19 vaccination on pregnancy

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| 7   | Appropriateness for SARS-CoV-2 vaccination for otolaryngologist and head and neck surgeons in case of pregnancy, breastfeeding, or childbearing potential: Yo-IFOS and CEORL-HNS joint clinical consensus statement | **Author**: Saibene AM et al  
**Study Citation**: Eur Arch Otorhinolaryngol. 2021 Apr 15:1-9  
**Study Type**: Clinical consensus statement  
**Patients No.**: NA | Of the 13 statements, 7 reached consensus or strong consensus, 2 reached no consensus, and 2 reached near-consensus. According to the statements with strong consensus otolaryngologists—head and neck surgeons who are pregnant, breastfeeding, or with childbearing potential should have the opportunity to receive SARS-Cov-2 vaccination. Moreover, personal protective equipment (PPE) should still be used even after the vaccination. |
| 8   | Are COVID-19 vaccines safe in pregnancy?                             | **Author**: Male V.  
**Study Citation**: Nat Rev Immunol. 2021 Apr;21(4):200-201  
**Study Type**: Review  
**Patients No.**: NA | Although the data are sparse, they are so far reassuring. For this reason, regulatory bodies in the UK, EU and US have recommended that pregnant people should be offered the vaccine where the benefits outweigh the potential risks.  
The work is underway to determine the extent to which vaccine-elicited antibodies to spike protein enter breast milk and whether this has any protective effect for breast-fed infants. |
# Effects of COVID-19 vaccination on pregnancy

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| 9   | Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine | **Author:** Beharier O et al.  
**Study Citation:** J Clin Invest. 2021 May 20;150319  
**Study Type:** Cohort  
**Patients No.:** 213 | Antenatal BNT162b2 mRNA vaccination induces a robust maternal humoral response that effectively transfers to the fetus within 15 days following the first dose., supporting the role of vaccination during pregnancy. |
| 10  | Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy | **Author:** Gill L  
**Study Citation:** Obstet Gynecol. 2021 May 1;137(5):894-896  
**Study Type:** Case-report  
**Patients No.:** 1 | A 34-year-old multigravid patient received the Pfizer-BioNTech (BNT162b2) mRNA vaccine for SARS-CoV-2 in the third trimester of pregnancy. Both the patient and the neonate were positive for antibodies at a titer of 1:25,600. |
| 11  | COVID-19 vaccination in pregnancy and postpartum                      | **Author:** Brillo E et al.  
**Study Citation:** J Matern Fetal Neonatal Med. 2021 May 16;1-20  
**Study Type:** Review  
**Patients No.:** NA | This review aimed to identify whether COVID-19 vaccines should be administered in pregnant and breastfeeding women. It summarizes that COVID-19 vaccines administered in pregnancy can reduce the risk of severe COVID-19 and their serious consequences for mothers and their offspring. |
### Effects of COVID-19 vaccination on pregnancy

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</table>
| 12  | Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women | **Author:** Collier A.-R.Y et al.  
**Study Citation:** JAMA. 2021 May 13;e217563  
**Study Type:** Cohort  
**Patients No.:** 103 | This cohort study aimed to evaluate the immunogenicity of COVID-19 messenger RNA (mRNA) vaccines in pregnant and lactating women. Binding, neutralizing, and functional non-neutralizing antibody responses as well as CD4 and CD8 T-cell responses were present in pregnant, lactating, and non-pregnant women following vaccination. Binding and neutralizing antibodies were also observed in infant cord blood and breast milk. |
| 13  | Joint IFFS/ESHRE statement on COVID-19 vaccination for pregnant women and those considering pregnancy | **Author:** Ory S., et al.  
**Study Citation:** Hum Reprod Open. 2021 Apr 16;2021(2):hoab016.  
**Study Type:** Systematic review  
**Patients No.:** NA | This joint statement shares overview on vaccination recommendations, recommendations for women who plan to conceive and those who are pregnant. |
| 14  | Cord blood antibodies following maternal coronavirus disease 2019 vaccination during pregnancy | **Author:** Mithal L.B., et al.  
**Study Citation:** Am J Obstet Gynecol. 2021 Apr 1;S0002-9378(21)00215-5  
**Study Type:** Case series  
**Patients No.:** NA | This review showed that most pregnant women who received a COVID-19 mRNA vaccine during the third trimester had transplacental transfer of IgG to the infant. The results show promising evidence for passive immunity against SARS-CoV-2 in newborns after maternal receipt of COVID-19 mRNA vaccinations. |
# Effects of COVID-19 vaccination on pregnancy

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| 15  | COVID-19 Vaccine Considerations during Pregnancy and Lactation        | **Author**: Blumberg D et al.  
**Study Citation**: Am J Perinatol. 2021 May;38(6):523-528.  
**Study Type**: Editorial  
**Patients No.**: NA | This review summarizes that available evidence, theoretical considerations, FDA evaluation, CDC and professional medical society guidance point towards the benefits of COVID-19 immunization outweighing the scant theoretical safety concerns in pregnancy and lactation. Thus, recommends consideration of COVID-19 immunization during pregnancy and lactation. |
| 16  | Covid-19: Pregnant women should be offered Pfizer or Moderna vaccine, says UK advisory committee | **Author**: Mahase E et al  
**Study Citation**: BMJ. 2021 Apr 19;373:n1013  
**Study Type**: Review  
**Patients No.**: NA | This article projects the government’s vaccine advisory committees recommendation to offer the Pfizer BioNTech or Moderna covid-19 vaccine in pregnant women. |
| 17  | Compromised SARS-CoV-2 neutralizing antibody response in cord blood versus mothers | **Author**: Govindaraj S et al.  
**Study Citation**: Topics in Antiviral Medicine (2021) 29:1 (223)  
**Study Type**: Cohort  
**Patients No.**: 69 | This study demonstrated that although both maternal and cord blood has receptor-binding domain (RBD) binding antibodies, there is no neutralization seen in any of the cord blood tested compared to respective maternal blood. Our findings suggests that maternally-derived SARS-CoV-2 specific antibodies lack neutralization potential to provide neonatal protection from COVID-19. |
# Effects of COVID-19 vaccination on pregnancy

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| 18  | COVID-19 vaccination in pregnant and lactating diabetic women        | **Author:** Sculli M et al.  
**Study Citation**: Nutrition, Metabolism and Cardiovascular Diseases (2021).  
**Study Type**: Editorial  
**Patients No.**: NA                                                                 | This review summarizes discusses available information on the opportunity for pregnant women affected by diabetes/obesity to receive COVID-19 vaccine. The review concluded that after an individual risk/benefit evaluation pregnant and lactating women should be counselled to receive COVID-19 vaccines. |
| 19  | EBCOG position statement on COVID-19 vaccination for pregnant and breastfeeding women | **Author:** Martins I et al  
**Study Citation**: EJOG  
https://doi.org/10.1016/j.ejogrb.2021.05.021  
**Study Type**: Clinical consensus statement  
**Patients No.**: NA | EBCOG acknowledges that there is limited evidence on the long-term safety of COVID-19 vaccination during pregnancy, and that there is a need for more robust data before it can be recommended to all pregnant women. EBCOG supports that COVID-19 vaccination be recommended to all breastfeeding women, in the absence of a specific contraindication. |

Last updated 12/08/2021
# Effects of COVID-19 vaccination on pregnancy

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| 20  | Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons | **Author:** Shimabukuro T et al  
**Study Citation:** N Engl J Med. 2021 Apr 21;NEJMoa2104983.  
**Study Type:** Surveillance review  
**Patients No.:** 3958 | This covid-19 vaccination surveillance study showed that COVID-19 vaccine did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. The most commonly reported event was spontaneous abortion. Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%) among 3958 participants enrolled in the v-safe pregnancy registry. |
| 21  | The coronavirus disease 2019 vaccine in pregnancy: risks, benefits, and recommendations | **Author:** Stafford I et al  
**Study Citation:** Am J Obstet Gynecol. 2021 May;224(5):484-495.  
**Study Type:** Review  
**Patients No.:** NA | This review article suggested that covid-19 vaccine should be given to pregnant women after discussing the lack of safety data, with preferential administration for those at highest risk of severe infection, until safety and efficacy of these novel vaccines are confirmed. |
| 22  | Newborn antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination – a case report | **Author:** Paul G., Chad R. et al  
**Study Citation:** BMC Pediatr. 2021 Mar 22;21(1):138.  
**Study Type:** case report  
**Patients No.:** 1 | A vigorous, healthy, full-term female was born to a COVID-19 naïve mother who had received a single dose of messenger RNA (mRNA) vaccine for SARS-CoV-2 3 weeks prior to delivery. IgG cord blood antibodies were detected to SARS-CoV-2 at the time of birth. Here, we report the first known case of an infant with SARS-CoV-2 IgG antibodies detectable in cord blood after maternal vaccination. |
| 23  | Professionally responsible coronavirus disease 2019 vaccination counseling of obstetrical and gynecologic patients | **Author:** Chervenak F et al  
**Study Citation:** Am J Obstet Gynecol. 2021 May;224(5):470-478.  
**Study Type:** review  
**Patients No.:** NA | This review article stated that physicians should recommend coronavirus disease 2019 vaccination to patients who are pregnant, planning to become pregnant, and breastfeeding or planning to breastfeed. |
# Effects of COVID-19 vaccination on pregnancy

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| 24  | Longitudinal analysis of antibody response following SARS-CoV-2 infection in pregnancy: From the first trimester to delivery | **Author:** Cosma S et al  
**Study Citation:** J Reprod Immunol. 2021 Apr;144:103285  
**Study Type:** Cohort  
**Patients No.:** 164 | This longitudinal analysis study showed that all the newborns of women who developed IgG antibodies demonstrated the presence of the same antibodies in arterial cord blood. It is important to understand the longevity and type of SARS-CoV-2 antibody response for developing important vaccination strategies in pregnancy. |
| 25  | COVID-19 vaccine response in pregnant and lactating women: a cohort study | **Author:** Gray K et al  
**Study Citation:** medRxiv. 2021 Mar 8;2021.03.07.21253094.  
**Study Type:** Cohort  
**Patients No.:** 131 | This prospective cohort study showed that COVID-19 mRNA vaccines developed robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity compared to that seen in non-pregnant women. Vaccine-induced immune responses were significantly greater than the response to natural infection. Immune transfer to neonates occurred via placenta and breastmilk. |
# Effects of COVID-19 vaccination on pregnancy

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**Study Citation:** Obstet Gynecol. 2021 Apr 28.  
**Study Type:** Observational  
**Patients No.:** 122 | Between January 28, 2021, and March 31, 2021, we studied 122 pregnant women with cord blood available at the time of birth at a single academic medical center. Women who self-reported receipt of one or both doses of a messenger RNA (mRNA)–based COVID-19 vaccine and gave birth to a singleton neonate (gestational age between 35 0/7 and 41 2/7 weeks) were included in the study. Only women who tested negative for antibodies against the nucleocapsid protein antigen were included to ensure antibodies were not the result of past severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.  
By the time of delivery, 55 pregnant women had received one dose of an mRNA vaccine and 67 had received both vaccine doses. Eighty-five women received the Pfizer-BioNTech vaccine, and 37 women received the Moderna vaccine. All women tested negative for SARS-CoV-2 infection using reverse-transcriptase polymerase chain reaction on nasopharyngeal swabs, and all women and neonates were asymptomatic at birth and until time of discharge. Forty-four percent (24/55) of cord blood samples from women who received only one vaccine dose had detectable IgG, whereas 99% (65/67) of cord blood samples from women who received both vaccine doses had detectable IgG. |
| 27  | Are COVID-19 vaccines safe in pregnancy?                               | **Author:** Male V et al.  
**Study Citation:** Nat Rev Immunol. 2021 Apr;21(4):200-201.  
**Study Type:** Review  
**Patients No.:** NA | There was no significant difference in the rate of accidental pregnancies in the vaccinated groups compared with the control groups, which indicates that the vaccines do not prevent pregnancy in humans. Similarly, the miscarriage rates are comparable between the groups, indicating no detrimental effect of vaccination on early pregnancy. |
Literature Monitoring

Topic Covered

Effect of SARS-COV-2 infection on male fertility

Duration:

1st Nov 2020 to 12th Aug 2021

* No study published on female fertility in this duration
## Effect of SARS-COV-2 infection on male fertility

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| 1   | Early effects of the COVID-19 pandemic on fertility preferences in the United States: an exploratory study | Author: Christine H Naya et al  
Study Citation: Fertil Steril. 2021 Jul 26;S0015-0282(21)00445-3  
Study Type: Exploratory  
Patients No.: 440 | This exploratory study highlights how the fertility preferences of racial and ethnic minorities, sexual minorities, and those experiencing mental health issues may be disparately influenced by the pandemic.  
Approximately 1 in 3 participants reported changing their fertility preferences because of the COVID-19 pandemic.  
Every 1 unit increase in state anxiety and depressive symptoms was associated with a 26% or 17% increase in odds of pushing back TTC, respectively |
| 2   | Air Pollution and COVID-19: A Possible Dangerous Synergy for Male Fertility | Author: Luigi Montano et al  
Study Type: Review  
Patients No.: | Study demonstrated that altered environmental conditions, together with the direct and indirect short- and long-term effects of viral infection could cause a worsening of semen quality with important consequences for male fertility, especially in those areas with higher environmental impact. |
| 3   | Guidelines and best practice recommendations on reproductive health services provision amid COVID-19 pandemic: scoping review | Author: Lemi Belay Tolu et al  
Study Citation: BMC Public Health. 2021 Feb 3;21(1):276.  
Study Type: Review  
Patients No.: NA | The practice recommendations focus on innovative ways of service provision to minimize patient and staff exposure to COVID-19 as well as alleviate the burden on the health care system. These include utilizing telemedicine and community/home-based care or self-care. |

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## Effect of SARS-COV-2 infection on male fertility

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| 4   | COVID-19 and human reproduction: A pandemic that packs a serious punch  | Author: George Anifandis et al  
Study Citation: Syst Biol Reprod Med  
2021 Feb;67(1):3-23  
Study Type: Review  
Patients No. | This review aims to provide an overview of critical research and ethics issues that have been continuously emerging in the field of reproductive medicine as the COVID-19 pandemic tragically unfolds. |
| 5   | Effect of COVID-19 on Male Reproductive System - A Systematic Review   | Author: Yanfei He et al  
Study Citation: Front Endocrinol (Lausanne). 2021 May 27;12:677701  
Study Type: Review  
Patients No. | Study highlights impact of COVID-19 on male reproduction, as it may induce orchitis via immune or inflammatory reactions, potentially damage spermatogenesis, decrease sperm quality in moderately infected patients, and further adversely affect male reproduction. |
| 6   | Editorial: It was the best of times; it was the worst of times: the impact of the SARS-CoV2 (COVID-19) pandemic on reproductive endocrinology | Author: Ruben Alvero et al  
Study Citation: Curr Opin Obstet Gynecol  
2021 Aug 1;33(4):324-326  
Study Type: Editorial  
Patients No. | Editorial reviews the impact that COVID-19 has had on the practice of reproductive endocrinology and infertility. |

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# Current evidence on the effect of SARS-COV-2 infection on male fertility

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Study Citation: Hormones (Athens). 2021 Jun;20(2):259-268  
Study Type: Review  
Patients No.: NA | - Data concerning the effect of SARS-CoV-2 on the gonads, especially in males, are increasing. Both reproduction and sex steroid synthesis of males are found to be diminished by SARS-CoV-2 infection in some studies.  
- Therefore, follow-up of patients to monitor for gonad function and even fertility should be encouraged after COVID-19.  
- Sex steroids, mainly estrogen, can modulate inflammation and may therefore be effective in the prevention and treatment of COVID-19.  
- Even androgen-modulating drugs could be evaluated as a potential treatment for COVID-19. |
| 8   | COVID-19 Pandemic and Male Fertility: Clinical Manifestations and Pathogenic Mechanisms | Author: Abdel-Moneim A.  
Study Citation: Biochemistry (Mosc). 2021 Apr;86(4):389-396.  
Study Type: Review  
Patients No.: NA | - COVID-19 could have various effects on male reproductive health  
- SARS-CoV-2 infection might be responsible for impairment of testicular function.  
- ACE2 is primarily expressed in spermatogonia and Leydig and Sertoli cells of the human testes, which may lead to a testicular dysfunction in patients infected with SARS-CoV-2  
- Moreover, testicular damage may be attributed to the inflammatory responses and fever-associated inflammation, as well as medications used in the severe cases |
| 9   | Physiological implications of COVID-19 in reproduction: angiotensin-converting enzyme 2 a key player | Author: Sharma GT et al.  
Study Citation: Reprod Fertil Dev. 2021 Apr;33(6):381-391  
Study Type: Review  
Patients No.: NA | - This review focuses on the interaction between SARS-CoV-2 and the ACE2 receptor and speculates on the mechanistic interplay in association with male and female reproductive physiology.  
- Higher ACE2 expression in the human placenta and reports of vertical transmission of SARS-CoV-2 among clinical cases have increased the relevance of further studies in this area |
## Current evidence on the effect of SARS-COV-2 infection on male fertility

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| 10  | The impact of SARS-CoV-2 and COVID-19 on male reproduction and men’s health | **Author**: Patel DP et al  
**Study Citation**: Fertil Steril. 2021 Apr;115(4):813-823.  
**Study Type**: Review  
**Patients No.**: NA |  
- Based on the current evidence, the likelihood of SARS-CoV-2 transmission through the seminal fluid is very low.  
- Although there have been many reports regarding viral tropism for the male reproductive tract, an important consideration for viral entry is coexpression of both ACE2 and TMPRSS2 at sufficient levels.  
- There are very limited data to characterize the impact of SARS-CoV-2 infection on male reproductive hormones and semen parameters. |
| 11  | Potential mechanisms of SARS-CoV-2 action on male gonadal function and fertility: Current status and future prospects | **Author**: Haghpanah A et al  
**Study Citation**: Andrologia. 2021 Feb;53(1):e13883.  
**Study Type**: Review  
**Patients No.**: NA |  
- Review studies  
- Potential mechanisms of SARS-CoV-2 action on male gonadal function and fertility: Current status and future prospects  
- Possible inflammatory and oxidative stress related mechanisms induced by SARS-CoV-2 in male reproductive system.  
- Hormonal alterations in infected patients with SARS-CoV-2.  
- Potential formation of anti-sperm antibodies due to SARS-CoV-2 infection.  
- Sperm DFI as a promising determiner of male infertility |
| 12  | Review of COVID-19 and male genital tract | **Author**: Sheikhzadeh Hesari F et al  
**Study Citation**: Andrologia. 2021 Feb;53(1):e13914.  
**Study Type**: Review  
**Patients No.**: NA |  
Expression of ACE2 and TMPRSS2 at RNA or protein level has been reported across various investigations indicates that the male genitalia potentially is vulnerable to SARS-CoV-2 infection.  
Presence of SARS-CoV-2 within semen samples and following direct viral damage, secondary inflammatory response causing orchitis or testicular discomfort and finally the amount of viral load leading testicular damage and immune response activation are among probable underlying mechanisms that have been discussed in this review. |
## Current evidence on the effect of SARS-COV-2 infection on male fertility

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| 13  | Addressing male sexual and reproductive health in the wake of COVID-19 outbreak | Author: Sansone A et al  
Study Citation: J Endocrinol Invest. 2021 Feb;44(2):223-231  
Study Type: Review  
Patients No.: NA | - Male sexual and reproductive health are affected in the survivors, by the sequelae of the COVID-19, both in the short and long terms.  
- Erectile function, as a surrogate marker of cardiovascular/pulmonary health, could also become extremely valuable as a quick and inexpensive first-line assessment of the pulmonary and cardiovascular complications for COVID-19 survivors.  
- Penile color-doppler ultrasound and hypothalamic-pituitary–testicular axis evaluation, will be necessary to assess the extent to which COVID-19 has been able to impair erectile, and finally vascular, function, the former being an efficient predictor of complete restitutio ad integrum.  
- Tailored psychological interventions would be necessary to adequately support patients who develop sexual dysfunction |
| 14  | COVID-19 and human spermatozoa-Potential risks for infertility and sexual transmission? | Author: Aitken RJ.  
Study Citation: Andrology. 2021 Jan;9(1):48-52.  
Study Type: Review  
Patients No.: NA | - This article reviews the roles played by various cellular constituents in maintaining the vitality of human spermatozoa and their competence for fertilization.  
- The reproductive consequences of a viral attack on these systems, in terms of fertility and the risk of sexual transmission, are currently unknown.  
- The evident importance of the renin-angiotensin and TMPRSS-family proteases in sperm cell biology, as well as the clear capacity of these cells to fuse with viruses, suggests that we should at least be open to the possibility |
| 15  | The probable destructive mechanisms behind COVID-19 on male reproduction system and fertility | Author: Moshrefi M et al  
Study Citation: J Assist Reprod Genet. 2021 May 11;1-18  
Study Type: Review  
Patients No.: NA | - The study aimed to summarize the current understanding of probable mechanisms and claims of adverse effects of SARS-CoV-2 on male fertility potential  
- Data showed coronavirus affects men more than women because of more expression of 2019 nCoV receptors (ACE2 and TMPRSS2) in testicular cells.  
- SARS-COV-2 mRNA and protein were detected in the semen of patients that had recovered from SARS-CoV-2 infection. Therefore, the probable disruption of blood-testis barrier (BTB) in febrile diseases is suspected in the acute phase of the disease enabling viral entry into the testes |
## Current evidence on the effect of SARS-COV-2 infection on male fertility

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| 16  | COVID-19 and male fertility: Taking stock of one year after the outbreak began | Author: Delle Fave RF et al  
Study Citation: Arch Ital Urol Androl  
Study Type: Review  
Patients No: NA | This systematic review highlighted insufficient evidence on the effect of COVID-19 on male reproductive system and transmission of virus through sperm. Certain mechanisms of testicular damage are still to be assessed, as any risk categories like age, ethnicity, or others. |
| 17  | A Systematic Review of the Assessment of the Presence of SARS-CoV-2 in Human Semen | Author: Vahedian-Azimi A et al  
Study Citation: Adv Exp Med Biol  
2021;1321:335-342  
Study Type: Review  
Patients No. :NA | This systematic review suggested that long-term effects of COVID-19 on the semen is unclear.                                                                                                                            |
| 18  | SARS-CoV-2 infection affects the lower urinary tract and male genital system: A systematic review | Author: Creta M et al  
Study Citation: J Med Virol  
2021 May;93(5):3133-3142.  
Study Type: Review  
Patients No. :575 | This systematic review analyzed a case-control study which showed significant reduction in sperm concentration, the total number of sperms per ejaculate, progressive motility, and complete motility in patients with moderate COVID-19. |
### Current evidence on the effect of SARS-COV-2 infection on male fertility

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<td>19</td>
<td>A Systematic Review on the Investigation of SARS-CoV-2 in Semen</td>
<td>Gonzalez DC et al</td>
<td>Study Citation: Res Rep Urol. 2020 Dec 1;12:615-621</td>
<td>This systematic review has highlighted the presence of SARS-CoV-2 in semen in one out of 8 studies. Moreover, findings have also stated that the risk of the presence of SARS-CoV-2 in semen appears to be extremely low and likely negligible in recovered men.</td>
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<tr>
<td>20</td>
<td>Effects of COVID-19 on male sex function and its potential sexual transmission</td>
<td>Rodriguez B et al</td>
<td>Study Citation: Arch Ital Urol Androl. 2021 Mar 18;93(1):48-52</td>
<td>This systematic review showed that the male reproductive system would be highly vulnerable and susceptible to infection by SARS-CoV-2 given the expression of the ACE2 receptor in somatic and germ cells. The seminal fluid would remain free of viral presence in patients with COVID-19. In addition, all necessary tests must be carried out to ensure the donor is free of the virus at the time of collection and handling of the seminal sample for all the ART procedures.</td>
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<tr>
<td>21</td>
<td>Effect of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) on reproductive system</td>
<td>Wang N et al</td>
<td>Study Citation: Stem Cell Res. 2021 Apr;52:102189.</td>
<td>This review suggested that severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection might damage male reproductive system via its effect on ACE2 receptors. Also, male patients were reported to be more affected by SARS-CoV-2 infection compared to female patients.</td>
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<tr>
<td>22</td>
<td>SARS-COV-2 (Covid-19) and male fertility: Where are we?</td>
<td>Omolaoye T et al</td>
<td>Study Citation: Reprod Toxicol. 2021 Jan;99:65-70.</td>
<td>This review article analyzed findings of several studies and demonstrated that SARS-COV-2 infection can lead to testicular injury and inflammatory infiltration, viral orchitis causing scrotal discomfort, and increase in the number of spermatozoa with DNA fragmentation, which correlated with the potential effect of causing fertility issues in these patients.</td>
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## Current evidence on the effect of SARS-COV-2 infection on male fertility

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| 23  | Pathological and molecular examinations of postmortem testis biopsies reveal SARS-CoV-2 infection in the testis and spermatogenesis damage in COVID-19 patients | **Author:** Ma X et al.  
**Study Citation:** Cell Mol Immunol. 2021 Feb;18(2):487-489  
**Study Type:** Cohort  
**Patients No.:** 5 | This review showed that SARS-CoV-2 can infect the testis and germ cells, implicating the potential effect of the COVID-19 infection on spermatogenesis and male fertility. |
| 24  | Viral pathogenesis of SARS-CoV-2 infection and male reproductive health | **Author:** Roychoudhury S et al  
**Study Citation:** Open Biol. 2021 Jan;11(1):200347.  
**Study Type:** Review  
**Patients No.:** NA | This review suggested the possibility of both direct and indirect infection of SARS-CoV-2 in the reproductive system of males and possible impact on general health and well-being, which can potentially lead to infertility. |
| 25  | COVID-19 impact on reproduction and fertility                          | **Author:** Mali AS et al  
**Study Citation:** JBRA Assist Reprod. 2021 Apr 27;25(2):310-313  
**Study Type:** Review  
**Patients No.:** NA | This review suggested that further evaluation on the effect of the direct impact of SARS-CoV-2 on the urogenital organs of males and females is still to be assessed. |
| 26  | Impact of SARS-CoV-2 on Male Reproductive Health: A Review of the Literature on Male Reproductive Involvement in COVID-19 | **Author:** He W et al.  
**Study Citation:** Front Med (Lausanne).2020 Nov 19;7:594364  
**Study Type:** Review  
**Patients No.:** NA | This review proposed the likely mechanism of orchitis caused by SARS-CoV-2 and the potential transmission route of the virus. |
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| 27  | It is currently unknown whether SARS-CoV-2 is viable in semen or whether COVID-19 damages spermatozoa | **Author:** Perry M et al  
**Study Citation:** Andrology.2021 Jan;9(1):30-32  
**Study Type:** Review  
**Patients No.:** NA | This review stated that the virus transmission may be facilitated by ART, especially intracytoplasmic sperm injection (ICSI). Although most ART involves washing and repeated dilution of the semen sample, virus particles could theoretically be transmitted directly via ICSI. Therefore, possible effects on early embryogenesis and development must also be considered. Semen and sperm studies are needed going forward for proper care and guidance of men and women at risk of COVID-19 infections and to those recovering from illness. |
| 28  | COVID-19 pandemic: what about the gonads? | **Author:** Selek A, Güçlü M, Bolu ŞE.  
**Study Citation:** Hormones (Athens). 2021 Jun;20(2):259-268  
**Study Type:** Review  
**Patients No.:** NA | This review showed increasing evidence on the effect of SARS-CoV-2 on the gonads, especially in males. Few studies also suggested decrease in the reproduction and sex steroid synthesis of males are found to be diminished by SARS-CoV-2 infection. |
| 29  | Evaluating the impact of COVID-19 on male reproduction | **Author:** Tian Y et al  
**Study Citation:** Reproduction. 2021 Feb;161(2):R37-R44  
**Study Type:** Review  
**Patients No.:** NA | This review studies highlighted that impact of SARS-CoV-2 on male reproduction in preliminary studies. It also showed that severe inflammation secondary to viral infection could disrupt the BTB and cause orchitis. The subsequent damage of germ cells and interstitium would adversely impact spermatogenesis and hormone production within the testes. |
| 20  | Can COVID-19 be transmitted sexually by semen? | **Author:** Taha A et al  
**Study Citation:** Journal of Pure and Applied Microbiology 14(4):2287-2293  
**Study Type:** Review  
**Patients No.:** NA | This review suggests an increasing number of asymptomatic and reactivated SARS-cov-2 cases, and thus, attention to semen safety and SARS-cov-2 transmission should be considered particularly in high-risk areas, to ensure the safety of male gametes for artificial reproduction and the general public. Avoiding cryopreservation of male gametes, condom use or even abstinence might be of paramount importance for these persons. |
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<td>31</td>
<td>COVID-19 and male fertility: Taking stock of one year after the outbreak began</td>
<td>Author: Delle Fave RF et al. Study Citation: Arch Ital Urol Androl. 2021 Mar 22;93(1):115-119. Study Type: Review. Patients No.: NA.</td>
<td>This review showed that the data demonstrating effects of COVID-19 infection on the male reproductive system are currently insufficient as they are based on a small number of patients and therefore are often contradictory. Certain mechanisms of testicular damage are still to be assessed, as any risk categories like age, ethnicity, or others. As for the transmission of the virus through sperm, there is insufficient evidence to ensure that this cannot happen.</td>
</tr>
<tr>
<td>32</td>
<td>Does SARS-CoV-2 Threaten Male Fertility?</td>
<td>Author: Vahedian-Azimi A et al. Study Citation: Adv Exp Med Biol. 2021;1321:139-14. Study Type: Review. Patients No.: NA.</td>
<td>This review suggested that the orchitis caused by the SARS-CoV-2 virus may have an important impact on fertility. Prolonged and high fever may lead to changes in testicular temperature and destroy germ cells. It is recommended to evaluate the presence of virus in semen and fertility-related item in men of reproductive age.</td>
</tr>
<tr>
<td>33</td>
<td>Histopathology and Ultrastructural Findings of Fatal COVID-19 Infections on Testis</td>
<td>Author: Achua J et al. Study Citation: World J Mens Health. 2021 Jan;39(1):65-74. Study Type: Cohort. Patients No.: 6.</td>
<td>This study suggested that the male reproductive tract, specifically the testes, may be targets of COVID-19 infection. Authors also reported an inverse association between ACE-2 receptor levels and spermatogenesis, suggesting a possible mechanism of how COVID-19 can cause infertility.</td>
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<tr>
<td>34</td>
<td>COVID-19 in men: With or without virus in semen, spermatogenesis may be impaired</td>
<td>Author: Bendayan M et al. Study Citation: Andrologia. 2021 Feb;53(1):e13878. Study Type: review. Patients No.: NA.</td>
<td>This study highlighted that precautionary measure, clinical, hormonal and semen parameter evaluations of patients diagnosed with COVID-19 are recommended at the time of infection and during follow-up appointments (3 and 6 months), especially in severe forms. For infertile men, a postponement of ART activities to three months post-infection is advisable.</td>
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| 35  | COVID-19 and human spermatozoa—Potential risks for infertility and sexual transmission? | **Author**: Aitken R et al.  
**Study Citation**: Andrology. 2021 Jan;9(1):48-52.  
**Study Type**: Review  
**Patients No.**: NA | This study showed that there is a possibility that there may be reproductive consequences of COVID-19 infection in young males that go beyond their capacity to survive a viral attack.                                                                                                                                                                                                                                                                                      |
| 36  | Radiological patterns of incidental epididymitis in mild-to-moderate COVID-19 patients revealed by colour Doppler ultrasound | **Author**: Carneiro F et al  
**Study Citation**: Andrologia. 2021 May;53(4):e13973.  
**Study Type**: Cohort  
**Patients No.**: 26 | This study showed that the use of colour Doppler ultrasound in mild-to-moderate COVID-19 men, even in the absence of testicular complaints, might be useful to diagnose epididymitis that could elicit fertility complications.                                                                                                                                                                                                                                                                                                    |
| 37  | ACE2 Expression in Kidney and Testis May Cause Kidney and Testis Infection in COVID-19 Patients | **Author**: Fan C et al  
**Study Citation**: Front Med (Lausanne). 2020; 7: 563893.  
**Study Type**: Review  
**Patients No.**: NA | The study results showed that ACE2 expression could contribute to testis infection after COVID-19 infection. Clinicians should pay attention to the risk of testicular lesions in patients during hospitalization and later clinical follow-up, especially the assessment and appropriate treatment measures in young patients' fertility.                                                                                                                                                                           |
| 38  | Potential mechanisms of SARS-CoV-2 action on male gonadal function and fertility: Current status and future prospects | **Author**: Haghpanah A et al  
**Study Citation**: Andrologia. 2021 Feb;53(1):e13883.  
**Study Type**: Review  
**Patients No.**: NA | This study showed that invasion of SARS-CoV-2 to the spermatogonia, Leydig cells and Sertoli cells can lead to sex hormonal alteration and impaired gonadal function. Measuring the sperm DNA fragmentation index (DFI) can be used as a determinant of male fertility impairment in patients with COVID-19 along with other options such as sex-related hormones and semen analysis.                                                                                                                                                     |
## Current evidence on the effect of SARS-COV-2 infection on male fertility

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| 39  | Ultrasound imaging findings of acute testicular infection in patients with coronavirus disease 2019: A single-center-based study in Wuhan, China | **Author**: Chen L et al  
**Study Citation**: J Ultrasound Med. 2020 Nov 11  
**Study Type**: Cohort  
**Patients No.**: 132 | A study that aimed to evaluate if SARS-CoV-2 can cause testicular infection in male hospitalized patients with COVID-19 in Wuhan demonstrated ultrasound imaging evidence that SARS-CoV-2 may cause infection of the testis or epididymis. |
| 40  | Coronavirus disease-19 infection: Implications on male fertility and reproduction | **Author**: Navarra A et al  
**Study Citation**: Front Physiol. 2020 Nov 17;11:574761  
**Study Type**: Review  
**Patients No.**: NA | This review that aimed to investigate about the effect of COVID-19 disease on male fertility and reproduction reported that SARS-CoV-2 could indirectly compromise male gametes, testicular cells, and therefore fertility because the fever and the cytokine storm associated with COVID-19 induce a sperm DNA fragmentation and reduce the male reproductive potential. |
| 41  | Coronavirus: A possible cause of reduced male fertility               | **Author**: Huang C et al  
**Study Citation**: Andrology. 2021 Jan;9(1):80-87.  
**Study Type**: Review  
**Patients No.**: NA | This review that intended to describe the impaired fertility of humans with coronaviruses to deduce the impact of the new coronavirus on male fertility showed that male fertility might be highly vulnerable to SARS-CoV-2 infection, and it can lead to male infertility. |
| 42  | The impact of SARS-CoV-2 and COVID-19 on male reproduction and men’s health | **Author**: Patel DP et al  
**Study Citation**: Fertil Steril. 2021 Apr;115(4):813-823  
**Study Type**: Review  
**Patients No.**: NA | This review highlighted limited definitive evidence regarding impact of COVID-19 on male reproductive health, creating a challenging landscape for both patients and physicians to obtain and provide the best clinical care. |
### Current evidence on the effect of SARS-COV-2 infection on male fertility

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| 43  | Evaluation of SARS-CoV-2 in Human Semen and Effect on Total Sperm Number: A Prospective Observational Study | **Author**: Best J et al  
**Study Citation**: World J Mens Health 2021 Feb 24.  
**Study Type**: Observational  
**Patients No.**: 30 | This prospective observational study showed that SARS-CoV-2 infection, though not detected in semen of recovered men, can affect total sperm number in ejaculate in the acute setting. Long-term effect of SARS-COV-2 on the spermatogenic function requires more number of studies for its validation. |
| 44  | Impaired spermatogenesis in COVID-19 patients                           | **Author**: Li H et al  
**Study Citation**: EClinicalMedicine 2020 Nov;28:100604.  
**Study Type**: Cohort  
**Patients No.**: 29 | This observational study showed impairment of spermatogenesis in COVID-19 patients, which may be due to an elevated immune response in testis. In addition, autoimmune orchitis were also reported in some COVID-19 patients. |
| 45  | Relationship between COVID-19 and the male reproductive system          | **Author**: Meng T et al  
**Study Citation**: Eur Rev Med Pharmacol Sci 2021 Jan;25(2):1109-1113  
**Study Type**: Review  
**Patients No.**: NA | This mini-review suggested that COVID-19 infection can affect male reproductive function, and standard treatment strategies should be established in time to help male patients infected with COVID-19. |
| 46  | Absence of SARS-CoV-2 in semen of a COVID-19 patient cohort             | **Author**: Guo L et al.  
**Study Citation**: Andrology 2021 Jan;9(1):42-47.  
**Study Type**: Cohort  
**Patients No.**: 23 | This cohort study showed no SARS-CoV-2 RNA detected in semen samples in patients with a recent infection or recovering from COVID-19, which indicated unlikely possibility of sexual transmission through semen at about 1 month after first detection. |
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| 47  | No detection of SARS-CoV-2 from urine, expressed prostatic secretions, and semen in 74 recovered COVID-19 male patients: A perspective and urogenital evaluation | **Author:** Ruan Y et al.  
**Study Citation:** Andrology. 2021 Jan;9(1):99-106  
**Study Type:** Cohort  
**Patients No.:** 74 | This cohort study showed that there was no direct urogenital involvement in the recovered COVID-19 male patients. SARS-CoV-2 RNA was undetectable in the urogenital secretions, and semen quality declined slightly, while hormonal profiles remained normal. Moreover, patients with a long time (≥90 days) since recovery had lower total sperm count. |
| 48  | COVID-19 and male reproductive function: a prospective, longitudinal cohort study | **Author:** Hajizadeh Maleki B et al.  
**Study Citation:** Reproduction. 2021 Mar;161(3):319-331.  
**Study Type:** Cohort  
**Patients No.:** 84 | This prospective, longitudinal cohort study reported that the reproductive function of the patients recovering from the disease should be precisely followed and evaluated to detect and avoid more serious reproductive problems in the future, as they may develop a transient state of male subfertility like those with oligoasthenoteratozoospermia. |
| 49  | Testicular pain as an unusual presentation of COVID-19: a brief review of SARS-CoV-2 and the testis | **Author:** La Marca A et al  
**Study Citation:** Reprod Biomed Online.2020 Nov;41(5):903-906  
**Study Type:** Review  
**Patients No.:** NA | This case study showed no evidence of sexual transmission of SARS-CoV-2; however, the possibility of virus-induced testis damage and dysfunction cannot be excluded. |
| 50  | Post-COVID-19-associated decline in long-term male fertility and embryo quality during assisted reproductive technology | **Author:** Mannur S et al.  
**Study Citation:** QJM. 2021 Jan 28;hcab019  
**Study Type:** Case report  
**Patients No.:** | This case profile findings suggested that Coronavirus disease 2019 (COVID-19) can impair male fertility with alterations in sperm morphology and DNA integrity could be a major post-COVID-19 complication in men. All the clinicians should suggest periodic andrological assessment for COVID-19 ‘infected’ and ‘recovered’ patients. Further, all the men for ART should be tested for COVID-19 before the procedure. |
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| 51  | Does COVID-19 affect male fertility?                                 | **Author:** Abobaker A et al  
**Study Citation:** World J Urol. 2020 Apr 21 : 1–2.  
**Study Type:** letter to the editor  
**Patients No.:** |
| 52  | Investigation of SARS-CoV-2 in semen samples and the effects of COVID-19 on male sexual health by using semen analysis and serum male hormone profile: A cross-sectional, pilot study | **Author:** Temiz M et al  
**Study Citation:** Andrologia. 2021 Mar;53(2):e13912.  
**Study Type:** Cohort  
**Patients No.:** 55 |
| 53  | Risks associated with cryopreserved semen in a human sperm bank during and after the COVID-19 pandemic | **Author:** Huang C et al  
**Study Citation:** Reprod Biomed Online. 2021 Mar;42(3):589-594  
**Study Type:** Retrospective cohort  
**Patients No.:** 100 |

This letter to the editor highlights theoretical possibility of testicular damage and subsequent infertility following COVID-19 infection. The possibility of testicular damage is caused by either direct viral invasion through binding of SARS-COV2 virus to ACE2 receptors or secondary to immunological and inflammatory response.

This cross-sectional pilot study showed that COVID-19 and its treatment had no specific deteriorative effect on male sexual health at a short-time period. In the patients before treatment, decreased serum of T, FSH and LH levels was consistent with acute patient stress due to COVID-19. Similarly, it seems that decreased sperm morphology was associated with the acute fever.

This retrospective study showed that cryopreserved semen at the Hunan Province Human Sperm Bank during and after the COVID-19 pandemic wave was free of SARS-CoV-2 and was considered to be safe for external use.
Literature Monitoring

Topic Covered

Effect of SARS-COV-2 infection on female fertility

Duration:

1\textsuperscript{st} Nov 2020 to 12\textsuperscript{th} Aug 2021

* No study published on female fertility in this duration
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<td>1</td>
<td>Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age</td>
<td>Kezhen Li, et al.</td>
<td>Reprod Biomed Online. 2021 Jan; 42(1): 260–267.</td>
<td>- Average sex hormone concentrations and ovarian reserve did not change significantly in COVID-19 women of child-bearing age. Nearly one-fifth of patients exhibited a menstrual volume decrease or cycle prolongation. The menstruation changes of these patients might be the consequence of transient sex hormone changes caused by suppression of ovarian function that quickly resume after recovery.</td>
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| 2   | COVID-19 in Africa: an ovarian victory?                                | Osman A Dufailu et al           | J Ovarian Res. 2021 May 21;14(1):70       | - Women of African descent have elevated levels of estrogen compared with Caucasians hence we anticipate that estrogen might offer some protection against the SARS-CoV-2 infections.  
- This articles provide insight on how the high levels of estrogen in African women might contribute to the lower cases and fatalities in Africa. |
| 3   | Effects of SARS-CoV-2 infection on human reproduction                  | Yang M et al.                   | J Mol Cell Biol. 2021 May 18;mjab025.      | This review summarizes the basic and clinical research of SARS-CoV-2 on reproduction up to date, hoping to offer guidance and advice to people at reproductive age and provide clues for the prevention and treatment of associated diseases.  
At present, there is no direct evidence to indicate that SARS-CoV-2 negatively influences human reproduction. |
| 4   | The Impact of Epidemiology on Fertility and Prenatal Care During the COVID-19 Pandemic | Dionne-Odom J, Klipstein S.     | Am J Epidemiol. 2021 May 4;190(5):701-706   | - A review of epidemiologic studies published between March and December 2020 that have directly informed prenatal and fertility care during the COVID-19 pandemic. In future , a commitment toward inclusion of pregnant persons and those attempting pregnancy in the design of observational and interventional trials is necessary to gain earlier insights about outcomes and assist providers and patients in making data-driven decisions. |
# Effect of SARS-COV-2 infection on fertility

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| 4   | Potential effects of COVID-19 on reproductive systems and fertility; assisted reproductive technology guidelines and considerations: a review | **Author**: Lee WY, Mok A, Chung JPW.  
**Study Citation**: Hong Kong Med J. 2021 Apr;27(2):118-126  
**Study Type**: Review  
**Patients No.**: NA | The ART guidelines from different fertility societies for the management of patients treated with ART are provided. The importance of prioritising ‘time-sensitive’ patients for ART, counselling patients about the uncertainty and risks of ART, and pregnancy during the pandemic is discussed. Recommendations are also provided for infection control and safe regulation of ART centres and laboratories. |
| 5   | Key Points in Fertility Preservation Treatment Strategies during COVID-19 Pandemic. An Update on Pharmacological Therapies | **Author**: Varlas V  
**Study Citation**: Farmacia (2021) 69:2 (189-199)  
**Study Type**: Review  
**Patients No.**: NA | • Access to fertility conservation services decreased during the analysed period due to the medical services restrictions and the reorientation of medical resources on patients with COVID-19, without major changes in the current therapeutic protocols.  
• In terms of pharmacotherapy in ovarian stimulation (OS) procedures, letrozole is first line therapy, superior to CC for OS. Similar ovulation and pregnancy rate can be obtained in letrozole - induced ovulation compared to gonadotropin protocol.  
• Adjuvant therapies may be used for OS but lack proven efficacy. Further studies on adjuvant therapies and complementary support are needed, to ensure optimal condition in assisted reproductive interventions for fertility preservation, especially in gonadotoxic therapies. |
| 6   | How to manage the IVF during COVID-19 pandemic among diabetic females: a scientific perspective | **Author**: Bukhari M et al  
**Study Citation**: Clinical Diabetology 2020;9(6):372-377.  
**Study Type**: Review  
**Patients No.**: NA | • There is no evidence yet on the effect of COVID-19 on the fetus during the first or second trimesters of pregnancy |

Last updated 12/08/2021
## Current evidence on the effect of SARS-COV-2 infection on female fertility

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| 7   | Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its effect on gametogenesis and early pregnancy | Author: Singh B et al  
Study Citation: Am J Reprod Immunol.2020 Nov;84(5):e13351.  
Study Type: Meta-analysis  
Patients No.: | This review showed that SARS-CoV-2 infection could lead to functional abnormalities leading to spermatogenic failure and male infertility in males. Also, an alteration of the ACE2 cascade via SARS-CoV-2 infection could lead to impairment in important follicular and luteal processes in females. |
| 8   | Human Oocytes Express Both ACE2 and BSG Genes and Corresponding Proteins: Is SARS-CoV-2 Infection Possible? | Author: Virant-Klun I et al  
Study Citation: Stem Cell Rev Rep.2021 Feb;17(1):278-284.  
Study Type: Review  
Patients No.: | This review stated that the human oocytes from the in vitro fertilization program expressed both the ACE2 and BSG genes and the corresponding ACE2 and BSG proteins, and thus these oocytes posses the molecular 'machinery' to facilitate SARS-CoV-2 entrance and infection. |
| 9   | A comprehensive review of the impact of COVID-19 on human reproductive biology, assisted reproduction care and pregnancy: a Canadian perspective | Author: Madjunkov M et al  
Study Citation: J Ovarian Res. 2020 Nov 27;13(1):140.  
Study Type: review  
Patients No.: | This review stated Canadian perspective on severity of COVID-19 and its effect on pregnant women, and it showed that the data is limited and similar to non-pregnant women. In addition, Human reproduction societies have issued guidelines on implementation of mitigation practices and infection control protocols in fertility care units for practice during COVID-19 pandemic. Canada has also dedicated funds to support COVID-19 research including a surveillance study to monitor outcomes of COVID-19 during pregnancy and assisted reproduction. |
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| 10  | Cryopreservation in reproductive medicine during the COVID-19 pandemic: rethinking policies and European safety regulations | **Author**: Alteri A et al  
**Study Citation**: Hum Reprod. 2020 Dec 1;35(12):2650-2657.  
**Study Type**: review  
**Patients No.**: | This review highlighted the advise to postpone pregnancy in order to avoid a severe infectious disease during gestation while concomitantly counteracting the possible detrimental effect of time. Critical threats, at present still undefined, are represented by potential adverse events for the mother and offspring due to infected gametes or embryos after thawing and, subsequently, the re-spreading of the virus. |
| 11  | Suggestions on cleavage embryo and blastocyst vitrification/transfer based on expression profile of ACE2 and TMPRSS2 in current COVID-19 pandemic | **Author**: Cheng G et al  
**Study Citation**: Mol Reprod Dev. 2021 Mar;88(3):211-216.  
**Study Type**: review  
**Patients No.**: | In this review, authors suggested that fertility preservation for COVID-19 patients is relatively safe and rational. They also recommend embryo cryopreservation and embryo transfer into healthy recipient mother at cleavage stage instead of blastocyst stage. |
| 12  | Increased COVID-19 infections in women with polycystic ovary syndrome: a population-based study | **Author**: Subramanian A et al  
**Study Citation**: Eur J Endocrinol. 2021 May;184(5):637-645.  
**Study Type**: Cohort  
**Patients No.**: 21 292 | This population-based study showed that women with PCOS are at an increased risk of COVID-19 infection and should be specifically encouraged to adhere to infection control measures during the COVID-19 pandemic. |
| 13  | SARS-CoV-2 and the reproductive system: known and the unknown..!!     | **Author**: Sharma I et al  
**Study Citation**: Middle East Fertil Soc J. 2021;26(1):1  
**Study Type**: Review  
**Patients No.**: | This review highlighted that SARS-CoV-2 may potentially affect both male and female reproductive tracts. Researchers recommend close monitoring of young and pregnant COVID-19 patients concerning reproductive health with utmost priority. |
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| 14  | Undetectable viral RNA in oocytes from SARS-CoV-2 positive women                                    | **Author**: Barragan M et al  
Study Citation: Hum Reprod. 2021 Jan 25;36(2):390-394  
**Study Type**: Case report  
**Patients No.**:  
**Study Type**: Case report  
**Patients No.**: | This case study described findings of two women who underwent controlled ovarian stimulation and tested positive to SARS-CoV-2 infection by PCR on the day of oocyte collection. The viral RNA for gene N was undetectable in all the oocytes analyzed from the two women. |
| 15  | High-security closed devices are efficient and safe to protect human oocytes from potential risk of viral contamination during vitrification and storage especially in the COVID-19 pandemic | **Author**: Porcu E et al  
Study Citation: J Assist Reprod Genet. 2021 Mar;38(3):681-688.  
**Study Type**: Cohort  
**Patients No.**: 737  
**Study Type**: Cohort  
**Patients No.**:  | This prospective randomized study showed that replacement of the open vitrification system by a closed one has no impact on in vitro and in vivo survival, development, pregnancy and implantation rate. Furthermore, to ensure safety, especially during the current COVID-19 pandemic, the use of the closed device can help eliminate the potential contamination of the samples’ during vitrification and storage process. |
| 16  | To treat or not to treat: perceptions of the initial American Society for Reproductive Medicine COVID-19 recommendations among women’s health providers | **Author**: Wiltshire A et al  
Study Citation: J Assist Reprod Genet. 2021 Mar;38(3):621-626.  
**Study Type**: Cohort  
**Patients No.**: 278  
**Study Type**: Cohort  
**Patients No.**: | This study that aimed to evaluate the perception of the initial ASRM COVID-19 recommendations for infertility treatment held by women’s health providers within varying subspecialties showed a generalized agreement with the restrictions initially recommended by ASRM on infertility care during the pandemic. |
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| 17  | Failure to detect viral RNA in follicular fluid aspirates from a SARS-CoV-2-positive woman | **Author:** Demirel C et al  
**Study Citation:** Reprod Sci. 2021 Feb 22;1-3.  
**Study Type:** case report  
**Patients No.:** | A case report of oocyte retrieval from a SARS-CoV-2-positive woman and the search for viral RNA by polymerase chain reaction in the follicular fluid aspirates highlighted that the handling of oocytes, sperm, seminal fluid, or follicular fluid in IVF laboratory may not constitute a significant threat for the healthcare professionals and laboratory setup, if the patient is SARS-CoV-2 positive. |
| 18  | Female reproductive tract has low concentration of SARS-CoV2 receptors | **Author:** Goad J et al  
**Study Citation:** PLoS One. 2020 Dec 14;15(12):e0243959  
**Study Type:** Review  
**Patients No.:** | This review that aimed to investigate the prevalence of SARS-CoV2 receptors among reproductive tissues suggested that myometrium, uterus, ovaries, fallopian tube, and breast are unlikely to be susceptible to infection by SARS-CoV2. |
| 19  | Novel targets of SARS-CoV-2 spike protein in human fetal brain development suggest early pregnancy vulnerability | **Author:** Varma P et al  
**Study Citation:** Front Neurosci. 2021 Jan 21;14:614680.  
**Study Type:** Cohort  
**Patients No.:** | This study that aimed to analyse the expression of known and novel S protein interactors of SARS-CoV-2 in fetal brain development suggested that even though two of the known S protein interactors are present at low levels in fetal brain, novel S protein interactors are abundantly present and could play a direct or indirect role in SARS-CoV-2 fetal brain pathogenesis, especially during the 2nd and 3rd trimesters of pregnancy. |
Literature Monitoring

Topic Covered

Effect of COVID-19 on ART

Duration:

1st Nov 2020 to 12th Aug 2021
## Effect of SARS-COV-2 infection on ART

<table>
<thead>
<tr>
<th>No.</th>
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</table>
| 1   | The COVID-19 pandemic and reproductive health                        | Author: Richard S. Legro et al  
Study Citation: Fertility and Sterility® Vol. 115, No. 4, April 2021 0015-0282  
Study Type: Review  
Patients No.: | This review summarizes the guide to patient counseling and the safest practices into the ART laboratory.  
It also reviews the effects of COVID-19 on pregnancy and implications for female and male reproductive health.  
It also talks about the assessment of the risk for transmitting as well as best practices to prevent infection in an ART practice and laboratory. |
| 2   | SARS-CoV-2 vs. human gametes, embryos and cryopreservation          | Author: George Anifandis et al  
Study Citation: Syst Biol Reprod Med.2021 Aug;67(4):260-269  
Study Type: review  
Patients No.: | This communication aims to provide some aspects of the possible impact of the virus on gametes and embryos and how it may affect the cryopreservation procedures. |
| 3   | Willingness of Women with Endometriosis Planning to Undergo IVF to Participate in a Randomized Clinical Trial and the Effects of the COVID-19 Pandemic on Potential Participation | Author: Shannon Pretzel et al  
Study Citation: Reprod Sci. 2021 Aug 6. doi: 10.1007/s43032-021-00705-0  
Study Type: Cohort  
Patients No. 212 | Study demonstrate ability of the EMR to serve as a source for participant recruitment for clinical trials in women with endometriosis.  
None reported that they would not consider participation because of COVID-19. EMR-based recruitment for an endometriosis clinical trial is feasible although the overall yield of participants is low. Delays in treatment due to COVID-19 did not appear to overly influence potential recruitment. |
| 4   | Investigating the impact of asymptomatic or mild SARS-CoV-2 infection on female fertility and in vitro fertilization outcomes: A retrospective cohort study | Author: Meng Wang et al  
Study Citation: EClinicalMedicine. 2021 Aug;38:101013  
Study Type: Cohort  
Patients No. 70 | The documented no evidence that a history of asymptomatic or mild SARS-CoV-2 infection in females may negatively affect female fertility, embryo laboratory outcomes, or clinical outcomes in ART treatments. |

**DISCLAIMER:** Because of the rapidly evolving events surrounding the COVID-19, the presented information may have changed since the date of search mentioned in this document.
## Effect of SARS-COV-2 infection on ART

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<td>5</td>
<td>Should women undergoing in vitro fertilization treatment or who are in the first trimester of pregnancy be vaccinated immediately against COVID-19?</td>
<td>Author: Meredith L. Snook et al.</td>
<td>Study Citation: Fertil Steril. 2021 Jul; 116(1): 16–24. Study Type: editorial</td>
<td>The editorial suggests that patients undergoing IVF treatment or in early pregnancy, it is in their best interests to strongly consider vaccination once eligible, and sooner rather than later, as they may incur the risk of severe COVID-related illness and associated morbidity and mortality the longer they wait.</td>
</tr>
<tr>
<td>6</td>
<td>Infection precautions for severe acute respiratory syndrome coronavirus 2 in assisted reproduction centers: dodging an invisible bullet</td>
<td>Author: Amy E T Sparks et al.</td>
<td>Study Citation: Fertil Steril. 2021 Apr;115(4):831-839. Study Type: Review Patients No.</td>
<td>This review discusses what is currently known about SARS-CoV-2 infection risks in assisted reproductive centers and recommends the implementation of specific mitigation strategies.</td>
</tr>
<tr>
<td>7</td>
<td>SARS-CoV-2 spike protein seropositivity from vaccination or infection does not cause sterility</td>
<td>Author: Morris RS.</td>
<td>Study Citation: F S Rep. 2021 Jun 2. Epub ahead of print. Study Type: Cohort Patients No. 171</td>
<td>This cohort study used frozen embryo transfer (FET) as a model to compare implantation rates between SARS-CoV-2 vaccine seropositive, infection seropositive and seronegative women. Findings from the study suggests that seropositivity to the SARS-CoV-2 spike protein, whether from vaccination or infection, does not prevent embryo implantation or early pregnancy development.</td>
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<td>8</td>
<td>Sperm Parameters Before and After COVID-19 mRNA Vaccination</td>
<td>Author: Daniel C. Gonzalez et al.</td>
<td>Study Citation: JAMA. 2021;326(3):273-274. Study Type: Cohort Patients No. 45 men</td>
<td>Study assessed sperm parameters before and after mRNA vaccine administration there and found that were no significant decreases in any sperm parameter among this small cohort of healthy men.</td>
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## Effect of COVID-19 infection on ART

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| 8   | Perinatal outcomes of pregnancies resulting from assisted reproduction technology in SARS-CoV-2-infected women: a prospective observational study | **Author**: Engels Calvo V et al  
**Study Citation**: Fertil Steril. 2021 Apr 12;S0015-0282(21)00290-9.  
**Study Type**: Cohort  
**Patients No.**: 1347 | This cohort study aimed to evaluate the perinatal and maternal outcomes of pregnancies in women infected with SARS-CoV-2, comparing spontaneous and in vitro fertilization (IVF) pregnancies.  
The operative delivery rate was high in all patients, especially in the IVF group.  
The reason for cesarean section was induction failure in 56.1% of the IVF patients.  
High rate of ICU admission seen in IVF group attributed to pre-eclampsia. |
| 9   | How to provide fertility treatment during COVID-19 pandemic            | **Author**: Cruz M, Requena A.  
**Study Citation**: Curr Opin Obstet Gynecol. 2021 Jun 1;33(3):159-163  
**Study Type**: Review  
**Patients No.**: NA | • SARS-CoV-2 infection is unlikely to have long-term effects on male and female reproductive function, suggesting that the risk of undergoing an Assisted Reproductive treatment is not altered by the pandemic.  
• Knowing how the virus biologically behaves during pregnancy is essential for defining proper obstetric management of pregnant women with the disease.  
• Detecting asymptomatic patients is of great importance, so Reproductive Medicine centers must take special care with screening and testing procedures.  
• There is no reason to delay pregnancy attempt or defer treatment because of vaccination administration. |
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<td>10</td>
<td>Navigating assisted reproduction treatment in the time of COVID-19: concerns and considerations</td>
<td>Author: Simopoulou M et al&lt;br&gt;Study Citation: J Assist Reprod Genet. 2020 Nov;37(11):2663-2668&lt;br&gt;Study Type: Commentary&lt;br&gt;Patients No.:</td>
<td>This review showed that SARS-CoV-2 infection could lead to functional abnormalities leading to spermatogenic failure and male infertility in males. Also, an alteration of the ACE2 cascade via SARS-CoV-2 infection could lead to impairment in important follicular and luteal processes in females.</td>
</tr>
<tr>
<td>11</td>
<td>Resuming Assisted Reproduction Services during COVID-19 Pandemic: An Initial Indian Experience</td>
<td>Author: Jirge P et al&lt;br&gt;Study Citation: J Hum Reprod Sci. Oct-Dec 2020;13(4):323-332&lt;br&gt;Study Type: Cohort&lt;br&gt;Patients No.: 169</td>
<td>This review stated that the human oocytes from the in vitro fertilization program expressed both the ACE2 and BSG genes and the corresponding ACE2 and BSG proteins, and thus these oocytes possess the molecular 'machinery' to facilitate SARS-CoV-2 entrance and infection.</td>
</tr>
<tr>
<td>12</td>
<td>COVID-19 risk assessment and safety management operational guidelines for IVF center reopening</td>
<td>Author: Alaluf M et al&lt;br&gt;Study Citation: J Assist Reprod Genet. 2020 Nov;37(11):2669-2686.&lt;br&gt;Study Type: Commentary&lt;br&gt;Patients No.:</td>
<td>This review stated Canadian perspective on severity of COVID-19 and its effect on pregnant women, and it showed that the data is limited and similar to non-pregnant women. In addition, human reproduction societies have issued guidelines on implementation of mitigation practices and infection control protocols in fertility care units for practice during COVID-19 pandemic. Canada has also dedicated funds to support COVID-19 research including a surveillance study to monitor outcomes of COVID-19 during pregnancy and assisted reproduction.</td>
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<tr>
<td>13</td>
<td>COVID-19: A review and considerations for the resumption of activities in an IVF laboratory and clinic in Brazil</td>
<td>Author: Ceschin I et al&lt;br&gt;Study Citation: J BRA Assist Reprod. 2021 Apr 27;25(2):293-302&lt;br&gt;Study Type: Review&lt;br&gt;Patients No.:</td>
<td>This review highlighted the advise to postpone pregnancy in order to avoid a severe infectious disease during gestation while concomitantly counteracting the possible detrimental effect of time. Critical threats, at present still undefined, are represented by potential adverse events for the mother and offspring due to infected gametes or embryos after thawing and, subsequently, the re-spreading of the virus.</td>
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| 14  | Prioritizing IVF treatment in the post-COVID 19 era: a predictive modelling study based on UK national data | Author: Bhattacharya S et al  
Study Citation: Hum Reprod. 2021 Feb 18;36(3):666-675.  
Study Type: Cohort  
Patients No.: 5989 | In this review, authors suggested that fertility preservation for COVID-19 patients is relatively safe and rational. They also recommend embryo cryopreservation and embryo transfer into healthy recipient mother at cleavage stage instead of blastocyst stage. |
| 15  | IVF during coronavirus pandemic: Who comes first? the poseidon viewpoint | Author: Demirel C et al  
Study Citation: J. Gynaecol. Obstet. 2020, 32, N.4  
Study Type: Review  
Patients No: | This review by the POSEIDON group proposes the use of a specific algorithm that could help clinicians to most optimally manage who need immediate IVF treatment during COVID-19 pandemic. |
| 16  | Considerations on the restriction of Assisted Reproductive Technology (ART) due to COVID-19 | Author: Goad J et al  
Study Citation: Semin Perinatol. 2020 Nov;44(7):151288.  
Study Type: Review  
Patients No.: | This review showed that the rapid rise of novel coronavirus disease 2019 (COVID-19) cases led the American Society for Reproductive Medicine (ASRM) to recommend immediate cessation of all new fertility treatment cycles on March 17, 2020. |
Literature Monitoring

Topic Covered

Effects of COVID-19 vaccination on fertility

Duration:

1st Nov 2020 to 12th Aug 2021
# Effects of COVID-19 vaccination on fertility

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Study Citation: JAMA. 2021;326(3):273-274.  
Study Type: Cohort  
Patients No. 45 men. | Study assessed sperm parameters before and after mRNA vaccine administration there and found that there were no significant decreases in any sperm parameter among this small cohort of healthy men. |
| 2   | Does mRNA SARS-CoV-2 vaccine influence patients’ performance during IVF-ET cycle? | Author: Orvieto R et al  
Study Citation: Reprod Biol Endocrinol. 2021 May 13;19(1):69  
Study Type: observational  
Patients No. 36 couples | • Thirty-six couples resumed IVF treatment 7–85 days after receiving mRNA SARS-CoV-2 vaccine.  
• mRNA SARS-CoV-2 vaccine showed no detrimental effect on patients’ total motile count.  
• mRNA SARS-CoV-2 vaccine did not affect patients’ performance or ovarian reserve in their immediate subsequent IVF cycle. |