



INTERNATIONAL FEDERATION OF FERTILITY SOCIETIES
Fédération internationale des sociétés de fertilité
Federación internacional de sociedades de fertilidad

IFFS SARS-COV-2 LITERATURE MONITORING REPORT

December 2020 update



Contents

Section	Slide number
Report objectives	3
Literature monitoring	4
• Effects on human reproductive system: male and female gametes and tissues	5-12
• SARS-CoV-2 and Medically Assisted Reproduction (MAR)	13-19
• Pregnancy, maternal-fetal and new-born related outcomes	20-55
✓ Pregnancy outcomes and management	20-36
✓ Vertical transmission and management	37-46
✓ New-born child and management	47-52
✓ Summary of SARS-CoV-2 and early pregnancy	53
✓ SARS-CoV-2 and early pregnancy risk for fetus (new section!)	54-55



Report Objectives

- **This quarterly 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 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 1, 2019 to November 27, 2020.
- As from July 2020, a new section has been introduced to track the reports of early pregnancy risk for embryo
- **Highlighted articles are new to the collection (not present in the previous edition, September 2020).**
- This collection adds 53 new articles:
 - 3 new articles in the human gametes and tissues section
 - 4 new articles in the Medically Assisted Reproduction (MAR) section
 - 22 new articles in the pregnancy outcomes and management section
 - 7 new articles in the vertical transmission and management section
 - 13 new articles in the new-born child and management section
 - 4 new articles in the early pregnancy risk for the embryo section.



SARS-CoV-2 taskforce – literature monitoring – Key search terms

Date of Search: 01 November 2019 – 27 November 2020

- **Key search terms** used: ('SARS-CoV-2' or 'COVID-19' or 'Coronavirus' or 'Coronavirus-2019' or 'Covid 19' or 'coronavirus 2019') AND ('Fertility' or 'pregnancy' or 'follicular stimulation' or 'follicular development' or 'follicular maturation' or 'follicular growth' or 'ovulation trigger' or 'ovulation induction' or 'ovarian stimulation' or 'controlled ovarian stimulation' or 'mild stimulation' or 'Reproductive medicine' or 'IVF' or 'in-vitro fertilisation' or 'in vitro fertilization' or 'IUI' or 'intrauterine insemination' or 'ICSI' or 'intracytoplasmic sperm injection' or 'reproduction' or 'assisted reproduction' or 'assisted reproduction technology' or 'infertility therapy' or 'reproductive technologies' or 'embryo transfer' or 'ET' or 'time to pregnancy' or 'time to live birth' or 'cumulative live birth rate' or 'cumulative pregnancy rate' or 'miscarriage' or 'maternal health' or 'maternal safety' or 'mother' or 'new-born' or 'baby' or 'new-born baby' or 'reproductive outcome' or 'birth'). Due to a large amount of published information, only search results with the above-mentioned search hedge have been included.
- **Each publication title is hyperlinked to the abstract (if available) on PubMed**/relevant data source for further reference.
- **Highlighted articles are new to the collection.** If an article was highlighted as an Epub in previous versions of this report, it will not be included in a subsequent report when it is published in print.
- **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.



Effects on Human Reproductive system

No.	Publication	Notes
1	A review of severe acute respiratory syndrome coronavirus 2 infection in the reproductive system. Huang H-H, et al. J Chin Med Assoc. 2020 Oct;83(10):895-897.	SARS-CoV-2's target, ACE2 has a dominant role in fertility function. In this review, writers saw that men are at risk of orchitis and elevated LH levels. Evidence of the virus has also been seen in semen, although this is still debated. Male fertility must be observed carefully through the COVID-19 pandemic.
2	Renin Angiotensin System, COVID-19 and Male Fertility: Any Risk for Conceiving? Pascolo L, et al. Microorganisms. 2020 Sep 28;8(10):1492.	The abundance of ACE2 in reproduction systems may affect reproduction and fertility. The potential infectivity of SARS-CoV-2 in reproductive male tissues should be strongly considered and further investigated for proper management of IVF procedures.
3	The hypothesis that SARS-CoV-2 affects male reproductive ability by regulating autophagy. Sun J, et al. Med Hypotheses. 2020 Oct;143:110083	ACE2 is highly expressed in Leydig cells and seminiferous tubules cells. Evidence has shown the virus can be found in semen. SARS-CoV-2 may influence autophagy and affect the reproductive system, meaning staff must be aware of this and monitor male fertility.
4	SARS-CoV-2 and its relationship with the genitourinary tract: implications for male reproductive health in the context of COVID-19 pandemic. Hallak J, et al. Andrology. 2020; https://doi.org/10.1111/andr.12896	During the COVID-19 pandemic, an international coordinated scientific effort must arise to understand the role of the urogenital system in the SARS-CoV-2 infection in the clinical setting. SARS-CoV-2 has potential implications across the male genitourinary system, with potential risks to testis' function and fertility, as well as a risk of kidney injury.
5	The jury is still out: COVID-19 and male reproduction. Patel DP, et al. Fertil Steril. 2020 Aug; 114(2): 257–258.	While there has been evidence on the effect of SARS-CoV-2 on male reproduction, data is conflicting. Data suggests the testis are susceptible to infection which may cause injury, and some reports have reported altered semen parameters among infected men. There is also conflicting data about whether the virus can be transmitted in semen. Such confusion must be considered during ART, procedures, particularly ICSI.



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Last updated
27/11/2020

Effects on Human Reproductive system

No.	Publication	Notes
6	<u>Does severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) cause orchitis in patients with coronavirus disease 2019 (COVID-19)?</u> Alkhatatbeh H, et al. Arab J Urol. 2020;18(3):129–133.	253 males with COVID-19 were followed throughout their recovery. Although no patients with COVID-19 has symptoms of signs of orchitis, such an association cannot be excluded, and further studies are needed.
7	<u>SARS-CoV-2 and the testis: similarity with other viruses and routes of infection.</u> Cardona Maya WD, et al. Reprod Biomed Online. 2020 Jun; 40(6): 763–764.	Evidence exists supporting the link of SARS-CoV-2 infection and orchitis, although there is debate around whether the virus is present in testicular epithelium, despite clear damage. Precautionary measurements should be practiced by candidates who have not yet been tested positive for SARS-CoV-2, and also by those previously infected. It is recommended to avoid possible transfection by refraining from sexual relations without protection, as the virus could persist for a longer period of time in the male reproductive system compared with other body fluids, rendering the testis a potential viral reservoir.
9	<u>SARS-COV-2 and Male Reproductive Health.</u> Fραιetta R, et al. JBRA Assist Reprod. 2020 Jul-Sep; 24(3): 347–350.	There is the theoretical possibility that testicular damage and subsequent infertility may result following COVID-19 infection, and also the possibility of sexual transmission. However, available data are recent, based on small sample sizes, and present conflicting information. Further research is needed to understand the long-term impacts of SARS-CoV-2 on male reproductive function, including its potential effects on fertility and testicular endocrine function.
9	<u>SARS-CoV-2 and Male Infertility: Possible Multifaceted Pathology.</u> Dutta S, Sengupta P. Reprod Sci. 2020 Jul 10 : 1–4. doi: 10.1007/s43032-020-00261-z [Epub ahead of print]	The testis remain a potential target for SARS-CoV-19, with evidence of infection, inflammation and damage. This article aims to precisely present the possible impact of COVID-19 on male reproductive functions, and to highlight the speculations that need in-depth research for the exact underlying mechanisms how COVID-19 is associated with men’s health and fertility.
10	<u>Evaluation of sex-related hormones and semen characteristics in reproductive-aged male COVID-19 patients.</u> Ma L, et al. J Med Virol. 2020 Jul 4 : 10.1002/jmv.26259. doi: 10.1002/jmv.26259 [Epub ahead of print]	12 patients’ semen parameters were tested, with 4 showing poor semen quality, and 2 showed slight variation compared to previous records. No virus was found in semen. Infected patients had higher LH levels compared to non-infected patients. SARS-CoV-2 infection affect men’s reproductive parameters, which must be considered on patients’ evaluation.



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27/11/2020

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11	<p><u>COVID-19 and human spermatozoa – potential risks for infertility and sexual transmission.</u> Aitken RJ. Andrology. 2020 Jul 10 : 10.1111/andr.12859. doi: 10.1111/andr.12859 [Epub ahead of print]</p>	While there is evidence that SARS-CoV-2 can infect various tissues, the risk of infection on male spermatozoa is still being debated. The presence of ACE2 receptors and TMPRSS proteins, suggest this is likely, and that there is therefore the potential that the virus could affect male fertility.
12	<p><u>The interference of COVID-19 in the male reproductive system: Important questions and the future of assisted reproduction techniques.</u> de Carvalho RC, et al. Clinics (Sao Paulo). 2020; 75: e2183. Published online 2020 Aug 21. doi: 10.6061/clinics/2020/e2183</p>	With evidence of receptor proteins needed for virus replication found in testicular tissue, there remains important questions to be answered to determine the risk to male fertility and how this may affect ART. These are: can SARS-Cov-2 be found in semen? Is the seminal sample a means of transmission for this virus? Can this viral infection lead to loss of gonadal function or changes in male fertility potential? If this loss or change is proven, is it a reversible or permanent? In relation to assisted reproduction techniques (ART), will future conduct in this area need to be reprogrammed?
13	<p><u>Is there an impact of the COVID-19 pandemic on male fertility? The ACE2 connection.</u> Younis JS, et al. Am J Physiol Endocrinol Metab 318: E878–E880, 2020.</p>	ACE2 is common in the testes, showing a risk of infection by SARS-CoV-2. This is of particular concern for men already known to have sperm problems, As ART facilities may not be fully open, sperm banking and other procedures should be discussed as needed.
14	<p><u>Assessment of SARS-CoV-2 in human semen-a cohort study</u> Holtmann N, et al. Fertil Steril 2020 Aug;114(2):233-238. doi: 10.1016/j.fertnstert.2020.05.028. Epub 2020 May 29.</p>	34 men who are either recovering, COVID free or with acute infection gave semen samples and parameters were analysed. No RNA was detected in semen of any sample. There was evidence of impaired sperm quality in patients with a moderate infection, suggestion mild infection is not likely to affect function.
15	<p><u>Male Fertility and the COVID-19 Pandemic: Systematic Review of the Literature</u> Khalili MA, et al. World J Mens Health. 2020 Oct;38(4):506-520. doi: 10.5534/wjmh.200134. Epub 2020 Aug 14.</p>	Review including 24 articles. Viral nRNA identified in semen of infected men, with evidence of altered parameters. Evidence also of low testosterone and dihydrotestosterone and raised LH in men, with some reports of preterm delivery in women. Male gonads may be vulnerable to SARS-CoV-2 virus.



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27/11/2020

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16	<p><u>Testicular pain as an unusual presentation of COVID-19: a brief review of SARS-CoV-2 and the testis</u> La Marca A, et al. Reprod Biomed Online. 2020 Jul 23;S1472-6483(20)30388-6. doi: 10.1016/j.rbmo.2020.07.017. Online ahead of print.</p>	ACE2 allows entry of SARS-CoV-2, which is widely expressed in testicular cell types. While there is the possibility of testicular damage and dysfunction cannot be excluded, evidence of sexual transmission has not been shown.
17	<p><u>ACE2 receptor expression in testes: implications in coronavirus disease 2019 pathogenesis</u> Verma S, et al. Biol Reprod. 2020 Aug 21;103(3):449-451. doi: 10.1093/biolre/ioaa080.</p>	Expression of angiotensin-converting enzyme 2, receptor of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is high in the testes, therefore SARS-CoV-2 infection and its association with male reproductive health should be investigated in male coronavirus disease 2019 patients.
18	<p><u>Pathological Findings in the Testes of COVID-19 Patients: Clinical Implications</u> Yang M, et al. Eur Urol Focus. 2020 Sep 15;6(5):1124-1129. doi: 10.1016/j.euf.2020.05.009. Epub 2020 May 31.</p>	In postmortem examination of testes of 12 COVID-19 patients, significant seminiferous tubular injury, reduced Leydig cells, and mild lymphomatic inflammation was found. 90% of cases did not show evidence of SARS-CoV-2 in the testes by RT-PCR, and none by electron microscopy.
19	<p><u>SARS-CoV-2 and the next generations: which impact on reproductive tissues?</u> Zupin L, et al. J Assist Reprod Genet. 2020 Aug 11;1-5. doi: 10.1007/s10815-020-01917-0. Online ahead of print.</p>	ACE2 expression demonstrated in human testis through protein expression database analysis, highlighting their potential as a possible target for viral entry, with potential impact on semen, which should be considered during IVF procedures. For older women with a shorter window of opportunity, ART should be considered alongside available therapy.
20	<p><u>Absence of SARS-CoV-2 in Semen of a COVID-19 Patient Cohort.</u> Guo L, et al. Andrology. 2020 Jun 29;10.1111/andr.12848. doi: 10.1111/andr.12848. Online ahead of print.</p>	23 male patients with COVID-19 were recruited. Semen characteristics and the viral RNA load in semen from these patients in the acute and recovery phases of SARS-CoV-2 infection were assessed. All patients tested negative for SARS-CoV-2 RNA in semen specimens. Among them, the virus had been cleared in 11 patients, as they tested negative. The remaining 12 patients tested negative for SARS-CoV-2 RNA in semen samples, but were positive in sputum and fecal specimens.



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27/11/2020

Effects on Human Reproductive system

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21	<p>Assessment of SARS-CoV-2 in human semen-a cohort study. Holtmann N, et al. Fertil Steril. 2020 May 29;S0015-0282(20)30519-7. doi: 10.1016/j.fertnstert.2020.05.028. Online ahead of print.</p>	<p>18 semen samples from recovered men were obtained 8-54 days after absence of symptoms, 14 from control subjects, and 2 from patients with an active COVID-19 infection. No RNA was detected in the semen, including semen samples from two patients with an acute COVID-19 infection. Subjects with a moderate infection showed an impairment of sperm quality. Mild COVID-19 infection is not likely to affect testis and epididymis function. Semen parameters seemed impaired after a moderate infection. SARS-CoV-2 RNA could not be detected in semen of recovered and acute COVID-19-positive men. This suggests no viral transmission during sexual contact and assisted reproductive techniques.</p>
22	<p>Coronavirus disease-19 and fertility: viral host entry protein expression in male and female reproductive tissues. Stanley KE, et al. Fertil Steril. 2020 Jul;114(1):33-43. doi: 10.1016/j.fertnstert.2020.05.001. Epub 2020 May 8.</p>	<p>Coexpression of ACE2 and TMPRSS2 was not detected in testicular cells, including sperm. A subpopulation of oocytes in nonhuman primate ovarian tissue was found to express ACE2 and TMPRSS2, but coexpression was not observed in ovarian somatic cells. RNA expression of TMPRSS2 in 18 samples of human cumulus cells was shown to be low or absent. These analyses suggest that SARS-CoV-2 infection is unlikely to have long-term effects on male and female reproductive function. Results imply that procedures in which oocytes are collected and fertilized in vitro are associated with very little risk of viral transmission from gametes to embryos.</p>
23	<p>Could SARS-CoV-2 affect male fertility? Vishvkarma R, Rajender S. Andrologia. 2020 Jun 23;e13712. doi: 10.1111/and.13712. Online ahead of print.</p>	<p>Systematic review looking at expression studies of ACE2 in testicular tissue and semen samples. The presence of ACE2 on almost all testicular cells and the report of a significant impact of previous SARS coronavirus on testes suggest that SARS-CoV-2 is highly likely to affect testicular tissue, semen parameters and male fertility.</p>
24	<p>No evidence of severe acute respiratory syndrome-coronavirus 2 in semen of males recovering from coronavirus disease 2019. Pan F, et al. Fertil Steril. 2020 Jun;113(6):1135-1139. doi: 10.1016/j.fertnstert.2020.04.024. Epub 2020 Apr 17.</p>	<p>In 34 adult males, 6 patients (19%) demonstrated scrotal discomfort suggestive of viral orchitis around the time of COVID-19 confirmation. SARS-CoV-2 was not detected in semen after a median of 31 days from COVID-19 diagnosis. Single-cell transcriptome analysis demonstrates sparse expression of ACE2 and TMPRSS2, with almost no overlapping gene expression. SARS-CoV-2 was not detected in the semen of patients recovering from COVID-19 1 month after COVID-19 diagnosis. ACE-2-mediated viral entry of SARS-CoV-2 into target host cells is unlikely to occur within the human testicle based on ACE2 and TMPRSS2 expression.</p>



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27/11/2020

Effects on Human Reproductive system

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25	<p><u>The ACE2 expression in Sertoli cells and germ cells may cause male reproductive disorder after SARS-CoV-2 infection.</u> Shen Q, et al. J Cell Mol Med . 2020 Jun 28;10.1111/jcmm.15541. doi: 10.1111/jcmm.15541. Online ahead of print.</p>	<p>mRNA expression of ACE2 analysed in germ and somatic cells. Rates of positive ACE2 expression was higher in testes infertile men than fertile men, which indicates that SARS-CoV-2 may cause reproductive disorders through pathway activated by ACE2 and the men with reproductive disorder may more easily be infected by SARS-CoV-2. The expression level of ACE2 was related to the age, and the mid-aged with higher positive rate than young men testicular cells. Taken together, this research provides a biological background of the potential route for infection of SARS-CoV-2 and may enable rapid deciphering male-related reproductive disorders induced by COVID-19.</p>
26	<p><u>Potential influence of COVID-19/ACE2 on the female reproductive system.</u> Jing Y, et al. Mol Hum Reprod. 2020 May 4 : gaaa030. Published online 2020 May 4. doi: 10.1093/molehr/gaaa030</p>	<p>Evidence suggests that ACE2 is widely expressed in the ovary, uterus, vagina and placenta. Therefore, the possibility of mother-to-child and sexual transmission also exists. Ang II, ACE2 and Ang-(1-7) regulate follicle development and ovulation, modulate luteal angiogenesis and degeneration, and also influence the regular changes in endometrial tissue and embryo development. Taking these functions into account, 2019-nCoV may disturb the female reproductive functions through regulating ACE2.</p>
27	<p><u>Potential risks of SARS-CoV-2 infection on reproductive health.</u> Li R, et al. Reprod Biomed Online. 2020 Jul; 41(1): 89–95.</p>	<p>The potential pathogenicity of COVID-19 may influence testicular and ovarian function, and sperm and oocyte quality. Contraception is recommended not only during the antiviral treatment, but also after treatment (for not less than 8 months). However, there is no evidence to support the termination of pregnancy without medical indicators.</p>
28	<p><u>Could COVID-19 have an impact on male fertility?</u> Illiano E, Trama F, Costantini E. Andrologia. 2020 Jul;52(6):e13654. doi: 10.1111/and.13654. Epub 2020 May 21.</p>	<p>ACE2 is expressed in the testes, particularly in Leydig and Sertoli cells. This could give the potential for targeting by SARS-CoV-2 and an inflammatory response. This must be studied and evaluated to ensure proper management of fertility in COVID-19 patients.</p>
29	<p><u>ACE2 Receptor Expression in Testes: Implications in COVID-19 Pathogenesis.</u> Verma S, Saksena S, Sadri-Ardekan H. Biology of Reproduction, , ioaa080, https://doi.org/10.1093/biolre/ioaa080</p>	<p>Expression of ACE2, receptor of SARS-CoV-2 is high in the testes, therefore SARS-CoV-2 infection and its association with male reproductive health should be investigated in male COVID-19 patients</p>



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27/11/2020

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30	<p><u>Prior and Novel Coronaviruses, COVID-19, and Human Reproduction: What Is Known?</u> Segars J, Katler Q, McQueen DB, et al. Fertil Steril. 2020 Apr 16 doi: 10.1016/j.fertnstert.2020.04.025 [Epub ahead of print]</p>	<p>This is a review on reproductive outcomes, effect on gametes and pregnancy outcomes. The authors stated that, "There are limited data regarding the impact of SARS-CoV-2 on human reproduction as the virus is novel and has only recently infected humans. To date, there have been no reports of the virus in the female reproductive tract, in vaginal secretions, in amniotic fluid or in peritoneal fluid. Although there is nothing to suggest that female or male gametes would be impacted directly by infection with SARS-CoV-2 or other coronaviruses, there is evidence that fever can impact spermatogenesis. Therefore, male fertility may be diminished for 72-90 days following COVID-19 due to decreased sperm concentration and motility." Additional studies are needed to assess effects of SARS-CoV-2 infection on male and female fertility.</p>
31	<p><u>Does COVID-19 affect male fertility?</u> Abobaker A, Raba AA. World J Urol. 2020 Apr 21. doi: 10.1007/s00345-020-03208-w. [Epub ahead of print]</p>	<p>The testis express ACE2, the receptor of SARS-CoV-2, presenting a possible target of infection. Damage is theoretically possible through direct viral infection or secondary inflammation, and males may be at risk of testicular damage.</p>
32	<p><u>Potential influence of COVID-19/ACE2 on the female reproductive system</u> Yan Jing, Li RunQian, Wang HaoRan et al Molecular Human Reproduction, gaaa030, https://doi.org/10.1093/molehr/gaaa030</p>	<p>The available evidence suggests that ACE2 is widely expressed in the ovary, uterus, vagina and placenta. Therefore, authors stated, " we believe that apart from droplets and contact transmission, the possibility of mother-to-child and sexual transmission also exists. Ang II, ACE2 and Ang-(1-7) regulate follicle development and ovulation, modulate luteal angiogenesis and degeneration, and also influence the regular changes in endometrial tissue and embryo development. Taking these functions into account, 2019-nCoV may disturb the female reproductive functions through regulating ACE2."</p>
33	<p><u>Coronavirus Disease 2019 (COVID-19) and men's reproductive health</u> Eisenberg ML. Fertility and Sterility. 2020 Apr 13. doi://doi.org/10.1016/j.fertnstert.2020.04.039</p>	<p>Addressed potential for testicular manifestations. No SARS-CoV-2 was detected in semen of the 34 men tested. Scrotal discomfort was reported in 17.6% of subjects. Semen quality appeared unaffected, but more data needed to confirm.</p>



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27/11/2020

Effects on Human Reproductive system

No.	Publication	Notes
34	<p><u>Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019</u> Diangeng Li, Meiling Jin, Pengtao Bao et al JAMA Netw Open. 2020;3(5):e208292. doi:10.1001/jamanetworkopen.2020.8292</p>	<p>Study in patients from China evaluated the semen of 38 COVID-19 patients; 15.8% of these patients had results positive for SARS-CoV-2 in the semen. The six patients with SARS-CoV-2-positive semen collected their samples 6-16 days after the onset of symptoms. Four of 15 patients (26.7%) were categorized in the “acute stage of infection,” while two of 23 patients (8.7%) were categorized to be in the “recovery” phase</p>
35	<p><u>No evidence of SARS-CoV-2 in semen of males recovering from COVID-19</u> Pan F, Xiao X, Guo J, Song Y, Li H, Patel DP, et al. Fertility and Sterility (2020), doi: https://doi.org/10.1016/j.fertnstert.2020.04.024</p>	<p>SARS-CoV-2 virus does not appear to be present in the semen of SARS-CoV-2 positive men (N=34) when tested a mean/median 31 days (range 8-75 days) after serum positive testing. ACE2-mediated viral entry of SARS-CoV-2 into target host cells is unlikely to occur within the human testicle based on ACE2 and TMPRSS2 expression. The long-term effects of SARS-CoV-2 on male reproductive function remain unknown.</p>
36	<p><u>SMRU Statement Regarding Male Reproductive Health and COVID-19</u> ASRM. Prepared in conjunction with the Society for the Study of Male Reproduction (SSMR)</p>	<p>There are differing reports on whether the virus is found in semen. Ongoing studies are needed to confirm these findings before specific recommendations can be made. There is no clear data to support or refute the effects of hydroxychloroquine or antivirals on semen quality in men. Male reproductive consultations should continue via telehealth or other forms of remote two-way consultation. Cryopreservation should be continued for patients with cancer or other malignant diseases. Other situations should be addressed on a case-by-case basis.</p>
37	<p><u>Study of SARS-CoV-2 in semen and urine samples of a volunteer with positive naso-pharyngeal swab.</u> Paoli D, Pallotti F, Colangelo S, et al. Journal of Endocrinological Investigation. https://doi.org/10.1007/s40618-020-01261-1</p>	<p>A patient who tested positive for the virus was tested. Eight days after diagnosis he provided semen and urine samples. Both were negative, although was a mild case and the test was several days after diagnosis.</p>
38	<p><u>Absence of 2019 Novel Coronavirus in Semen and Testes of COVID-19 Patients</u> Song C, Wang Y, Li W, et al. Biol Reprod. 2020 Jun 23;103(1):4-6. doi: 10.1093/biolre/ioaa050.</p>	<p>Letter to editor. Study of 13 men diagnosed with COVID-19. Semen tests on all patients were negative for the virus. It appears unlikely that the virus is found in semen or the testes, although more data is needed to confirm.</p>



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27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
1	COVID-19 and ART outcomes. Chamani IJ, et al. Fertil Steril. 2020 Sep; 114(3): e556.	In the months after the end of COVID-19 treatment suspension, there were no apparent differences in patient characteristics or the quantitative responses to stimulation. However, there was a significant difference in the number of euploid embryos. It remains unclear if or how the pandemic is related to this.
2	Delay in IVF treatment up to 180 days does not affect pregnancy outcomes in women with diminished ovarian reserve. Romanski PA, et al. Hum Reprod. 2020 Jul 1;35(7):1630-1636.	The COVID-19 pandemic has affected clinics worldwide, raising concerns over its impact on patient's chances of success. This retrospective cohort study of 1790 patients with diminished ovarian reserve, delaying IVF treatment up to 180 days from the initial visit did not affect pregnancy outcomes, including for patients at high-categories for poor response.
3	First follow-up of art pregnancies in the context of the COVID-19 outbreak. Mayeur A, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Oct;253:71-75.	In this study, women were surveyed on their experiences during the pandemic, pregnant women (n = 88) did not change their physician visits. COVID-19 created no or few additional stresses for 77% of pregnant women. Miscarriage rate was reported at 14.4 % (n = 15). Ten patients (11.3 %) had symptoms related to COVID-19. No severe symptoms and no hospitalization in intensive care unit were identified. Pregnant women were psychologically able to experience the lockdown.
4	Undetectable viral RNA in oocytes from SARS-CoV-2 positive women. Barragan M, et al. Hum Reprod. 2020 Sep 30;deaa284	Two women undergoing controlled ovarian stimulation who tested positive for SARS-CoV-2 on the day of oocyte collection, had undetectable viral RNA in all oocytes retrieved.
5	Assisted reproduction and COVID-19: A joint statement of ASRM, ESHRE and IFFS. Veiga A, et al. Fertility and Sterility (2020) 114:3 (484-485).	Reproductive care is essential and reproductive medicine professionals are in a unique position to promote health and wellbeing. ASRM, ESHRE and IFFS are collaborating to advocate for patients and to gather data and resources to enhance the understanding of COVID-19 in relation to reproduction, pregnancy, and the impact on the fetus and neonate.
6	Non-essential treatment? Sub-fertility in the time of COVID-19 (and beyond). Cavaliere G. Reprod Biomed Online. 2020 Sep; 41(3): 543–545.	COVID-19 has created a set of uncertainties and stress for fertility patients, with ART initially classed as non-essential treatment across Europe and the USA. While facilities are reopening, the value of ART in society must be considered. This article argues that fertility treatment should be considered essential, and that closing facilities has severe impacts on patients in need of treatment.



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Last updated
27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
7	<p><u>Patient experiences of fertility clinic closure during the COVID-19 pandemic: appraisals, coping and emotions.</u> Boivin J, et al. Hum Reprod. 2020 Aug 6;deaa218. doi: 10.1093/humrep/deaa218. Online ahead of print.</p>	81.6% of patients had their treatment postponed, and reported this being extremely stressful. While patients understood reasons for closure, their perceived it to be unfair and a threat to future parenthood. Patients were able to cope using strategies that fit the uncertainty of the situation.
8	<p><u>Managing the IVF laboratory during a pandemic: international perspectives from laboratory managers.</u> Hickman C, et al. Reproductive BioMedicine Online 2020;41(2):141–150.</p>	To date, laboratory managers have had to make decisions and take action with a lack of scientific evidence. Steps are discussed for managing a laboratory effectively and safely during this period, including the use of PPE, air ventilation and managing staff through this period.
9	<p><u>The COVID-19 pandemic and human fertility.</u> Aassve A, et al. Science 2020;369(6502):370–371. doi: 10.1126/science.abc9520</p>	In addition to economic and health impact, COVID-19 will also likely have significant impacts on fertility, with significant impacts on ART facilities. Through changes in economies and lifestyles, birthrates are likely to be significantly affected globally, which must be addressed in future policy making.
10	<p><u>COVID-19: New adaptation for IVF laboratory protocols.</u> Andrabi SA, et al. JBRA Assist Reprod. 2020 Jul-Sep; 24(3): 358–361.</p>	Before resuming ART treatments, it is very important to consider local and national regulations. Change is necessary to return to ART without risking the spread of COVID-19 or compromising quality. Steps are given to recommend how to safely reopen clinics.
11	<p><u>Assisted reproduction and Coronavirus in Italy.</u> Pasquale C, et al. Eur Rev Med Pharmacol Sci. 2020 Jul;24(13):7512-7515. doi: 10.26355/eurrev_202007_21924.</p>	Other than the US, Italy is the country with the highest number of cases (197675 positives, 26644 deaths) (updated on April 26). The Italian National Transplant Centre and the Higher Institute of Health advised on March 17 to complete the cycles already started and not to start new cycles. Phase 2 will begin on 4 May with an increase in freedom of action and fertilization treatments will start again. The Society that brings together embryologists (SIERR) has issued the guidelines to be followed when this happens.



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Last updated
27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
12	<p><u>Assessment and management of the risk of SARS-CoV-2 infection in an IVF laboratory.</u> Maggiulli R, et al. Reprod Biomed Online. 2020 Sep; 41(3): 385–394. Published online 2020 Jun 27. doi: 10.1016/j.rbmo.2020.06.017</p>	<p>Standard laboratory protocols are insufficient to face a virus whose transmission is aerosol mediated. The measures outlined in this FMEA should thus be considered not only for facing this pandemic, but also for the future to promptly manage any aerosol-mediated virus infection, whose impact on the management of an IVF laboratory might be less severe than COVID-19 although not completely negligible.</p>
13	<p><u>COVID-19 and Assisted Reproduction: A Point of View on the Brazilian Scenario.</u> de Carvalho BR, et al. Rev Bras Ginecol Obstet 2020;42(6):305–309.</p>	<p>There is no data to say the COVID-19 is more harmful during pregnancy or that it can cross the placenta to affect the fetus. The effect of infection is also not fully known for pregnant women. The presence of the virus in semen cannot be ruled out. ART cycles are recommended to be postponed for the time being.</p>
14	<p><u>Fertility patients under COVID-19: Attitudes, Perceptions, and Psychological Reactions.</u> Ben-Kimhy R, et al. Human Reproduction, deaa248, https://doi.org/10.1093/humrep/deaa248.</p>	<p>In 168 patients who responded to the survey, many patients felt helpless following treatment suspension, associated with higher distress.. Most patients (72%) preferred to resume treatment given the chance regardless of background characteristics; higher self-mastery and greater perceived social support were associated with lower distress, while feeling helpless was associated with higher distress.</p>
15	<p><u>A picture of medically assisted reproduction activities during the COVID-19 pandemic in Europe</u> ESHRE Working Group, et al. Human Reproduction Open, Volume 2020, Issue 3, 2020, hoaa035, https://doi.org/10.1093/hropen/hoaa035</p>	<p>The coronavirus disease 2019 (COVID-19) pandemic had a large impact on infertile couples. A survey was sent to ESHRE members, investigating the status of ART activity. Most countries recommended stopping ART, with some variation across Europe in terms of duration of interruption. COVID-19 has had a significant and dramatic impact on ART resources across Europe.</p>
16	<p><u>Cryopreservation in reproductive medicine during the COVID-19 pandemic: rethinking policies and European safety regulations</u> Alteri A, et al. Hum Reprod. 2020 Aug 3;deaa210. doi: 10.1093/humrep/deaa210. Online ahead of print.</p>	<p>A SWOT analysis to identify challenges for ART during COVID-19. While Europe has robust availability of resources, uncertainties in management may undermine efforts. Cryopreservation offers a chance to delay pregnancy to attempt to avoid infection, while a clear threat is the potential of adverse outcomes of mother or neonate following infection.</p>



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Last updated
27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
17	<p><u>SARS-CoV-2 infection, male fertility and sperm cryopreservation: a position statement of the Italian Society of Andrology and Sexual Medicine (SIAMS) (Società Italiana di Andrologia e Medicina della Sessualità)</u> Corona G, et al. J Endocrinol Invest. 2020 Aug;43(8):1153-1157. doi: 10.1007/s40618-020-01290-w. Epub 2020 May 27.</p>	A review to justify the SIAMS position statement was conducted on available literature. Evidence suggest that in recovered patients, especially those in reproductive age, andrological consultation and evaluation of gonadal function including semen analysis should be suggested. Further studies are needed to confirm the effect in male gametes destined for cryopreservation for ART.
18	<p><u>First follow-up of art pregnancies in the context of the COVID-19 outbreak</u> Mayeur A, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Oct;253:71-75. doi: 10.1016/j.ejogrb.2020.07.050. Epub 2020 Jul 31.</p>	The epidemic context did not disrupt the medical monitoring of pregnancies and we did not recover an increased rate of miscarriage after ART. None of the patients who had COVID-related symptoms presented with severe clinical manifestations. Surprisingly, pregnant women were psychologically able to experience the lockdown.
19	<p><u>Cryopreservation and IVF in the time of Covid-19: what is the best good tissue practice (GTP)?</u> Pomeroy KO, Schiewe MC. J Assist Reprod Genet. 2020 Aug 3;1-6. doi: 10.1007/s10815-020-01904-5. Online ahead of print.</p>	Additionally, high security storage containers have proven to be resilient to potential cross-contamination and reliable for routine human sperm freezing and embryo vitrification. Several options to current IVF practices are presented that can effectively mitigate the risks of cross-contamination and infection due to the current Covid-19 pandemic or other viral exposures.
20	<p><u>Navigating assisted reproduction treatment in the time of COVID-19: concerns and considerations</u> Simopoulou M, et al. J Assist Reprod Genet. 2020 Sep 16. doi: 10.1007/s10815-020-01942-z. Online ahead of print.</p>	This article highlights matters of bioethical nature to be considered in the ART world at the time of COVID-19 while presenting an all-inclusive critique of the current status. When pursuing pregnancy through IVF treatment during the pandemic, distancing and caution have the lead role in an effort to defend the health of the intended parents and future children. To promote patient autonomy along with our ethical, moral, and legal duty towards our patients, emphasis should be given on ascertaining shared decision-making, and ensuring that an appropriate all-inclusive informed consent is signed prior to initiating any IVF treatment.
21	<p><u>Population implications of cessation of IVF during the COVID-19 pandemic</u> Smith ADAC, et al. Reprod Biomed Online. 2020 Sep;41(3):428-430. doi: 10.1016/j.rbmo.2020.07.002. Epub 2020 Jul 6.</p>	The study demonstrated that the discontinuation of fertility treatment for even 1 month in the USA could result in 369 fewer women having a live birth, due to the increase in patients' age during the shutdown. As a result of reductions in cumulative live birth rate, more cycles may be required to overcome infertility at individual and population levels.



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Last updated
27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
22	<p><u>Assisted reproduction and thromboembolic risk in the COVID-19 pandemic.</u> Fabreguesa F, Peñarrubiab J. Reprod Biomed Online. 2020 Jun 25. doi: 10.1016/j.rbmo.2020.06.013 [Epub ahead of print]</p>	<p>One of the main determining factors of the poor prognosis in COVID-19 infected patients is the development of coagulopathy. Moreover, it is well known that assisted reproductive technology procedures confer a risk of thromboembolic complications. In the present context, any risk of hyperstimulation should be avoided. GnRH agonist triggering should be mandatory in high-responder patients and/or those with COVID-19 infection. In addition, endometrial preparation for frozen-thawed embryo transfers should use the transdermal route in order to minimize the higher thrombotic risk associated with the oral route.</p>
23	<p><u>COVID-19 and ART: the view of the Italian Society of Fertility and Sterility and Reproductive Medicine.</u> Vaiarelli A, et al. Reprod Biomed Online. 2020 Jun;40(6):755-759. doi: 10.1016/j.rbmo.2020.04.003. Epub 2020 Apr 8.</p>	<p>Article outlining the position of the Italian Society of Fertility and Sterility and Reproductive Medicine (SIFES-MR) in outlining ART priorities during and after this emergency. Time to egg collection and drop-out rates are critical parameters for scheduling treatments once the curve of infections has peaked and plateaued in each country. Urgent oocyte collection for oncology patients must be guaranteed, and oocyte retrievals for women of advanced maternal age and/or reduced ovarian reserve cannot be postponed indefinitely.</p>
24	<p><u>COVID-19 should be a novel indication for fertility preservation.</u> Gerber S, et al. JBRA Assisted Reproduction 2020;24(3): DOI: 10.5935/1518-0557.20200048</p>	<p>While there is a lack of evidence around COVID-19 and reproductive outcomes and vertical transmission, recommendations have generally advised to avoid pregnancy and stop fertility treatment. Due to uncertainty around the duration of the pandemic, we cannot say when clinics will be able to offer routine basis treatment for infertile couples looking for treatment. Delaying ART may mean those with reduced ovarian reserve, older patients or those with financial problems are unable to conceive after the end of the pandemic. The authors recommend that COVID-19 could be a new indication for fertility preservation for a determined deadline, until complete return of assisted reproduction treatments in regular basis.</p>



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Last updated
27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
25	<p><u>COVID-19 and assisted reproductive technology services: repercussions for patients and proposal for individualized clinical management.</u> Alviggi C, Esteves SC, Orvieto R, et al. Reprod Biol Endocrinol. 2020; 18: 45.</p>	A prolonged suspension of ART services would be detrimental to patients, although care must be taken when reopening services. Recommendations are given, including excluding infected patients and allowing ART for eligible patients. Treatment should be considered depending on patients Poseidon group to identify the most suitable patients.
26	<p><u>Management of ART and COVID-19: Infertility in times of pandemic. What now?</u> Souza MDCB, Nakagawa H, Taitson PF, et al. JBRA Assist Reprod. 2020 Jul 14;24(3):231-232. doi: 10.5935/1518-0557.20200031</p>	Summary of the recommendations from several guidelines and organisations. Most generally advise pausing or suspending treatment where possible until new research is available.
27	<p><u>COVID-19 and ART: the view of the Italian Society of Fertility and Sterility and Reproductive Medicine</u> Vaiarelli A, Bulletti C, Cimadomo D, et al. Reproductive BioMedicine Online 2020 Apr 8; doi: https://doi.org/10.1016/j.rbmo.2020.04.003</p>	Article from the Italian Society of Fertility and Sterility and Reproductive Medicine outlining their recommendations. It generally recommends delaying pregnancy during the outbreak where possible, but in patients where this will affect their chances of conception, cryopreservation is recommended for soon after the peak of infections.
28	<p><u>COVID-19: lessons from the Italian reproductive medical experience</u> La Marca A, Niederberger C, Pellicer A, et al. Fertil Steril. 2020 Mar 25. pii: S0015-0282(20)30297-1. doi: 10.1016/j.fertnstert.2020.03.021. [Epub ahead of print]</p>	Summary of experiences in reproductive medicine in Italy. Treatment should be postponed in those who have been in contact with infected patients. Those suspected to be infected should be isolated.



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Last updated
27/11/2020

SARS-CoV-2 and ART (incl. IVF, ICSI, IUI, ET etc.)

No.	Publication	Notes
29	<u>A global recommendation for restrictive provision of fertility treatments during the COVID-19 pandemic</u> Rodriguez-Wallberg K.A., Wikander I Acta Obstetrica et Gynecologica Scandinavica 2020 99:5 (569-570)	An editorial discussing the recommendations of different organizations
30	<u>Joint Statement on Re-introduction of Hospital and Office-based Procedures in the COVID-19 Climate for the Practicing Gynecologist</u> International Gynecologic Cancer Society	Society of Gynaecologic Oncology adapted American College of Surgeons (ACS) tiered ranking list to develop guidance for urogynecologic and benign gynecologic surgeons. The system is meant to help surgeons and their health care systems decide who should undergo surgeries and does not list all elective surgeries in each tier.
31	<u>SARS-CoV-2 pandemic and repercussions for male infertility patients: a proposal for the individualized provision of andrological services</u> Esteves S.C., Lombardo F., Garrido N., Alvarez J., Zini A., Colpi G.M., Kirkman-Brown J., Lewis S.E., Björndahl L., Majzoub A., Cho C.-L., Vendeira P., Hallak J., Amar E., Cocuzza M., Bento F.C., Figueira R.C., Sciorio R., Laursen R.J., Metwalley A.M., Jindal S.K., Parekattil S., Ramasamy R., Alviggi C., Humaidan P., Yovich J.L., Agarwal A. [Article in Press] Andrology 2020	An opinion paper proposing to modify the current recommendations regarding sperm banking to be expanded to other groups of vulnerable male infertility patients (e.g., azoospermic men and cryptozoospermic) undergoing medical or surgical treatment to improve sperm quantity and quality, as well as males of reproductive age affected by inflammatory and systemic auto-immune diseases who are about to start treatment with gonadotoxic drugs or who are under remission.
32	<u>After corona: there is life after the pandemic</u> Tesarik J. [Article in Press] Reproductive BioMedicine Online 2020 Cited by: 0	Author discusses the impact of COVID-19 on pregnancy and vertical transmission on the basis of available data and strategy for ART. The author stated, "Assisted reproductive technology (ART) makes it possible to separate fertilization and pregnancy in time. Whereas pregnant women infected with coronavirus may have an increased risk of adverse neonatal outcomes, gametes do not transmit COVID-19. Thus, performing ovarian stimulation and fertilization without delay, freezing the resulting embryos and delaying embryo transfer until the end of the pandemic appears to be the best strategy at present."
33	<u>SMRU Statement Regarding Male Reproductive Health and COVID-19</u> ASRM. Prepared in conjunction with the Society for the Study of Male Reproduction (SSMR)	There are differing reports on whether the virus is found in semen. Ongoing studies are needed to confirm these findings before specific recommendations can be made. Male reproductive consultations should continue via telehealth or other forms of remote two-way consultation. Cryopreservation should be continued for patients with cancer or other malignant diseases. Other situations should be addressed on a case-by-case basis.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
1	COVID-19 (coronavirus disease) - Fertility and Pregnancy Perinatal outcomes in COVID-19 infection. Cochrane Gynaecology and Fertility	Excel sheet Perinatal outcomes in COVID-19 infection.* Document from the Cochrane institute, collating data from various institutes on perinatal and maternal outcomes including the detection of SAR-CoV-2 in various swabs and body fluids like urine, breast milk etc.
2	A systematic review and meta-analysis of the reported symptoms of Covid 19 in pregnancy. Abduljabbar HSO, Abduljabar H. Clinical and Experimental Obstetrics & Gynecology. 2020. 47(5):632-637	In a meta-analysis of reported symptoms of COVID-19 during pregnancy, sore throat was the only symptom reported to be more common in pregnant than non-pregnant women. For pregnant women showing this symptoms, care should be taken to exclude COVID-19 infection.
3	Can immunity during pregnancy influence SARS-CoV-2 infection? - A systematic review. Areia AL, et al. J Reprod Immunol. 2020 Oct 16;142:103215. doi: 10.1016/j.jri.2020.103215. Online ahead of print.	From this systematic review, in line with previous coronavirus infections, severe maternal morbidity and perinatal death with COVID-19 infection were more likely to be expected in pregnancy. Their research showed that pregnant women with COVID-19 in terms of immunity only differ from other pregnant women in their lower WBC count.
4	Characteristics and Maternal and Birth Outcomes of Hospitalized Pregnant Women with Laboratory-Confirmed COVID-19 - COVID-NET, 13 States, March 1-August 22, 2020. Delahoy MJ, et al. MMWR Morb Mortal Wkly Rep. 2020 Sep 25;69(38):1347-1354. doi: 10.15585/mmwr.mm6938e1.	Among 272 pregnant women with COVID-19 who were symptomatic at admission, 16.2% were admitted to ICU, and 8.5% required invasive mechanical ventilation. During hospitalisations, 97.8% completed pregnancies resulted in a live birth and 2.2% resulted in a pregnancy loss.
5	Clinical characteristics and risk factors for mortality in obstetric patients with severe COVID-19 in Brazil: a surveillance database analysis. Takemoto M, et al. BJOG. 2020 Dec;127(13):1618-1626. doi: 10.1111/1471-0528.16470. Epub 2020 Sep 14.	Out of 978 pregnant or postpartum women identified with COVID-19 acute respiratory distress syndrome, there were 134 deaths (12.7%). 48.4% of deaths also had at least one comorbidity. The main risk factors for death by COVID-19 were being postpartum at onset of ARDS, obesity, diabetes and cardiovascular disease, whereas white ethnicity had a protective effect.

*Individual publications presented in the excel sheet by Cochrane are not included in this report to avoid duplication. However, reviews discussed in this report may include some individual cases or cases series discussed in Cochrane sheet.



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Last updated
27/11/2020

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Pregnancy outcomes and management

No.	Publication	Notes
6	Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. Yee J, et al. Sci Rep. 2020 Oct 22;10(1):18126. doi: 10.1038/s41598-020-75096-4.	Pregnant women with COVID-19 have relatively mild symptoms. However, abnormal proportions of laboratory parameters were similar or even increased, compared to general population. ~30% of pregnant women with COVID-19 experienced preterm delivery, whereas the mean birth weight was 2855.9 g. Fetal death and detection of SARS-CoV-2 were observed in about 2%; neonatal death was 0.4%.
7	Clinical Presentation of Coronavirus Disease 2019 (COVID-19) in Pregnant and Recently Pregnant People. Afshar Y, et al. Obstet Gynecol. 2020 Dec;136(6):1117-1125.	Of 991 participants, 736 had symptoms of COVID-19 at the time of testing; 594 tested positive for SARS-CoV-2 infection and 142 tested negative in this symptomatic group. Ninety-five percent were outpatients. The most prevalent first symptoms were cough (20%), sore throat (16%), body aches (12%), and fever (12%). Median time to symptom resolution was 37 days (95% CI 35-39). One quarter of participants who tested positive for SARS-CoV-2 infection had persistent symptoms 8 or more weeks after symptom onset.
8	Clinical Properties and Diagnostic Methods of COVID-19 Infection in Pregnancies: Meta-Analysis. Uygun-Can B, Acar-Bolat B. Biomed Res Int. 2020 Sep 29;2020:1708267. doi: 10.1155/2020/1708267.	Out of 12 articles covering 181 pregnant cases, fever and cough were the most common symptoms in pregnant cases with SARS-CoV-2 infection, and 91.8% (95% CI: 76.7-99.9%) of RT-PCR results are positive. No deaths were reported.
9	COVID-19 and Adverse Pregnancy Outcome: A Systematic Review of 104 Cases. Ghayda RA, et al. J Clin Med. 2020 Oct 26;9(11):E3441. doi: 10.3390/jcm9113441.	In 11 studies comprising 104 pregnant women with COVID-19, fever (58.6%) and cough (30.7%) were the most common symptoms. Fifty-two patients (50.0%) demonstrated abnormal chest CT. The most common treatment for COVID-19 was administration of antibiotics (25.9%) followed by antivirals (17.3%). Half of women had a caesarean). Fetal distress (13.5%), pre-labour rupture of membranes (9.6%), prematurity (8.7%), fetal death (4.8%), and abortion (2.9%) were reported.
10	COVID-19 during pregnancy: An overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries. Figueiro-Filho EA, et al. J Perinat Med. 2020 Nov 26;48(9):900-911.	In this study including 10,966 cases, pregnant women were not shown to be more affected by respiratory complications compared to the general population. The Th1-Th2 immune response shift during gestation is countered by the increased ACE2-Ang axis. The downregulation of ACE2 induced by SARS-CoV2 may adversely affect patients with preexisting ACE2 deficiency, which could explain their worse perinatal outcomes.



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Last updated
27/11/2020

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Pregnancy outcomes and management

No.	Publication	Notes
11	COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. Pettirosso E, et al. Aust N Z J Obstet Gynaecol. 2020 Oct;60(5):640-659.	Where universal screening was conducted, SARS-CoV-2 infection in pregnancy was often asymptomatic. Severe and critical disease rates approximate those in the general population. Vertical transmission is possible; however, it is unclear whether SARS-CoV-2 positive neonates were infected in utero, intrapartum or postpartum.
12	Effects of Severe Acute Respiratory Syndrome Coronavirus 2 Infection on Pregnant Women and Their Infants. Yang H, et al. Arch Pathol Lab Med . 2020 Oct 1;144(10):1217-1222.	In 27 pregnant women with confirmed SARS-CoV-2, 46.2% of patients were symptomatic, with fever and cough being the most common symptoms. 81.5% had lymphopenia. Twenty-six patients had viral pneumonia by chest CT. No maternal or neonatal deaths or major complications were recorded.
13	Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. Di Toro et al. Clin Microbiol Infect. 2020 Nov 1;S1198-743X(20)30618-2.	In this meta-analysis of 24 articles with 1100 pregnancies, the prevalence of pneumonia was 89%, while 8% of women were admitted to ICU. Three stillbirths and five maternal deaths were reported. A pooled prevalence of 85% was observed for caesarean deliveries. There were three neonatal deaths. While there was a high caesarean rate, COVID-19 should not be considered an indication for elective caesarean section.
14	Maternal mortality among women with coronavirus disease 2019 admitted to the intensive care unit. Blitz MJ. Am J Obstet Gynecol. 2020 Oct; 223(4): 595–599.e5.	Maternal death occurred in 15% of patients admitted to the ICUs for COVID-19 and in 25% of those who required invasive ventilation. Hispanic women constituted the largest racial or ethnic group in the study, which may reflect a disproportionate burden of disease among minority groups.
15	Maternal outcome of pregnant women admitted to intensive care units for coronavirus disease 2019. Kim CNH, et al. Am J Obstet Gynecol. 2020 Nov;223(5):773-774.	In 15 included articles following 85 pregnancies with COVID-19, 11 were admitted to ICU and later died, giving a fatality rate of 12.9%. While previous reports have not reported pregnant women as being at a higher risk of critical compared to the general population, the cumulative fatality rate among critically ill pregnant women remains concerning.
16	Outcomes of Maternal-Newborn Dyads After Maternal SARS-CoV-2. Verma S, et al. Pediatrics. 2020 Oct;146(4):e2020005637.	Of 149 mothers with SARS-CoV-2 infection and 149 newborns, 15% of symptomatic mothers required respiratory support, and 8% required intubation. Fifteen (10%) were born preterm, and 5 (3%) required mechanical ventilation. Symptomatic mothers had more premature deliveries (16% vs 3%), and their newborns were more likely to require intensive care than asymptomatic mothers.
17	Pregnancy and Neonatal Outcomes in SARS-CoV-2 Infection: A Systematic Review. Chamseddine RS, et al. J Pregnancy. 2020 Oct 7;2020:4592450.	Of 245 pregnancies complicated by SARS-CoV-2 infection, the most common symptoms were fever (55.9%), cough (36.3%), fatigue (11.4%), and dyspnea (12.7%). 89% delivered via cesarean section, with a 33.3% rate of gestational complications, a 35.3% rate of preterm delivery, and a concerning 2.5% rate of stillbirth delivery or neonatal death. 6.45% of newborns were positive for SARS-CoV-2.

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Last updated
27/11/2020



Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
18	Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study. Prabhu M, et al. BJOG. 2020 Nov;127(12):1548-1556.	In this study of 675 women admitted for delivery, 10.4% were positive for SARS-CoV-2. 46.7% of symptomatic patients delivered by caesarean, and 12.9% of experienced postpartum complications, vs 4.5% of women without COVID-19. Among pregnant women with COVID-19 at delivery, there were increased caesarean delivery rates and increased frequency of maternal complications in the postpartum period. Additionally, intraplacental thrombi may have maternal and fetal implications for COVID-19 remote from delivery.
19	Pregnant women with COVID-19 and risk of adverse birth outcomes and maternal-fetal vertical transmission: a population-based cohort study in Wuhan, China. Yang R, et al. BMC Med. 2020 Oct 19;18(1):330.	This population-based cohort study suggests that COVID-19 during late pregnancy is associated with an increased risk of adverse birth outcomes, including preterm birth and caesarean section delivery. In this study, no deaths were reported and little evidence for vertical transmission of SARS-CoV-2 was found.
20	Racial-ethnic disparities and pregnancy outcomes in SARS-CoV-2 infection in a universally-tested cohort in Houston, Texas. Pineles BL, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Nov;254:329-330.	Of 936 patients recorded at a community hospital during this study, positive pregnant patients were more likely to be Hispanic and to have public insurance. Most pregnant patients diagnosed on admission for delivery were asymptomatic, consistent with other universally-tested cohorts.
21	Third-trimester placentas of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive women: histomorphology, including viral immunohistochemistry and in-situ hybridization. Smithgall MC, et al. Histopathology. 2020 Dec;77(6):994-999.	In this study of 51 trimester placentas, evidence of maternal-fetal vascular malperfusion was seen, although no evidence of direct viral involvement or vertical transmission was seen.
22	Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. Zambrano LD, et al. MMWR Morb Mortal Wkly Rep. 2020 Nov 6;69(44):1641-1647.	In a report from CDC surveillance including 23,434 pregnant women with COVID-19, pregnant women were significantly more likely to be admitted to intensive care and receive invasive ventilation. There was also greater risk for severe illness in pregnant than non-pregnant women.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
23	<u>COVID Triggers Premature Births in Infected Moms.</u> Ellis R. MedScape 2020. Published September 21. Available at: https://www.medscape.com/viewarticle/937773?src=wnl_edit_tpal&uac=294497MV&impID=2580650&faf=1	A report from the US CDC suggests a higher risk of premature births in women who have COVID-19. Of 598 pregnant women hospitalised with COVID-19, there were 445 live birth reported, of which 12.6% were premature, 25% higher than the rate for the general population. 23.1% of symptomatic women and 8% of asymptomatic women has premature births.
24	<u>COVID-19 (SARS-CoV-2) Infection in Pregnancy: A Systematic Review.</u> Akhtar H, et al. Gynecol Obstet Invest. 2020 Jul 30;1-12. doi: 10.1159/000509290. Online ahead of print.	COVID-19 infection in pregnancy leads to increased risk in pregnancy complications such as preterm birth, PPRM, and may possibly lead to maternal death in rare cases. There is no evidence to support vertical transmission of SARS-CoV-2 infection to the unborn child.
25	<u>Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis.</u> Allotey J, et al. BMJ. 2020 Sep 1;370:m3320. doi: 10.1136/bmj.m3320.	Pregnant women are less likely show symptoms of fever and myalgia than non-pregnant women of reproductive age and are more likely to need intensive care for COVID-19. Pre-existing comorbidities, high maternal age, and high body mass index seem to be risk factors for severe covid-19. Preterm birth rates are high in pregnant women with covid-19 than in pregnant women without the disease.
26	<u>COVID-19 in pregnant women: A systematic review and meta-analysis.</u> Capobianco G, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Sep;252:543-558.	There appears to be a a high rate of maternal (45%) and neonatal complications in infected individuals, with 23% of cases being preterm. However, evidence highlights a low risk of neonatal infection (6% of cases).
27	<u>Perinatal transmission with SARS-CoV-2 and route of pregnancy termination: a narrative review.</u> Vigil-De Gracia P, et al. J Matern Fetal Neonatal Med. 2020 Jul 26;1-5. doi: 10.1080/14767058.2020.1788533.	This review shows that there is perinatal or neonatal infection with SARS-CoV-2 by finding a positive PCR in the first days of birth. In addition, that there is more possibility of neonatal infection if the birth is vaginal or if there is premature rupture of the membranes before cesarean section. Vaginal delivery and premature rupture of membranes should be considered as risk factors for perinatal infection.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
28	Clinical features and outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. Gao, Y-J, et al. BMC Infect Dis. 2020 Aug 3;20(1):564. doi: 10.1186/s12879-020-05274-2.	The incidences of fever, cough and positive CT findings in pregnant women with COVID-19 are less than those in the normal population with COVID-19, but the rate of preterm labor is higher among pregnant with COVID-19 than among normal pregnant women. There is currently no evidence that COVID-19 can spread through vertical transmission.
29	SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. Khalil A, et al. EClinicalMedicine. 2020 Aug;25:100446. doi: 10.1016/j.eclinm.2020.100446. Epub 2020 Jul 3.	The risk of iatrogenic preterm birth and caesarean delivery was increased with COVID-19. The available evidence is reassuring, suggesting that maternal morbidity is similar to that of women of reproductive age. Vertical transmission of the virus probably occurs, albeit in a small proportion of cases.
30	Maternal COVID-19 infection, clinical characteristics, pregnancy, and neonatal outcome: A prospective cohort study. Antoun L, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Sep;252:559-562. doi: 10.1016/j.ejogrb.2020.07.008. Epub 2020 Jul 15.	COVID-19 is associated with high prevalence of preterm birth, preeclampsia, and caesarean section compared to non-COVID pregnancies. COVID-19 infection was not found in the newborns and none developed severe neonatal complications
31	Maternal and neonatal characteristics and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis. Dubey P, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Sep;252:490-501. doi: 10.1016/j.ejogrb.2020.07.034. Epub 2020 Jul 22.	Adverse pregnancy outcomes were prevalent in COVID-19 infected females and varied by location, type, and size of the studies. Regular screening and early detection of COVID-19 in pregnant women may provide more favorable outcomes.
32	Late miscarriage as a presenting manifestation of COVID-19. Hachem R, et al. Eur J Obstet Gynecol Reprod Biol. 2020 Sep;252:614.	In our patient, the subclinical inflammation may have led to the miscarriage. Lymphocytopenia and high levels of C-reactive protein and ferritin could be predictive findings in suspected cases of COVID-19. Further reports on pregnancy outcomes in patients with COVID-19 are mandatory, and medical teams should participate in international registries of emergent pathogens in pregnancy, such as COVI-PREG



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
33	<p>Increased rate of ruptured ectopic pregnancy in COVID-19 pandemic: analysis from the North of Italy. Casadio P, et al. Ultrasound Obstet Gynecol. 2020 Aug;56(2):289. doi: 10.1002/uog.22126.</p>	<p>The proportion of ruptured ectopic pregnancies were significantly higher during the lockdown in comparison with the pre-lockdown period (6/9; 66.7% vs. 52/201; 25.9%, Fisher's Exact Test P = 0.02). Our data raise serious concerns regarding the potential deleterious consequences of the COVID-19 pandemic in women of reproductive age</p>
34	<p>Coronavirus Disease 2019 (COVID-19): A Systematic Review of Pregnancy and the Possibility of Vertical Transmission. Ashraf AA, et al. J Reprod Infertil . Jul-Sep 2020;21(3):157-168.</p>	<p>Systematic review of 21 articles with 90 pregnant patients and 92 neonates born to mothers infected with COVID-19. 3 mothers were admitted to ICU and required mechanical ventilation; among them, one died, and one was on extracorporeal membrane oxygenation. 86 neonates were tested for the possibility of vertical transmission; 4 were positive. Out of 92 neonates, one died, and one was born dead. 19 patients reported having no symptoms, while breathing problems and pneumonia were reported as the most common neonatal complications. There were no differences in the clinical characteristics of pregnant women and non-pregnant COVID-19 patients. COVID-19 infection caused higher incidence of fetal distress and premature labour in pregnant women.</p>
35	<p>Coronavirus disease 2019 during pregnancy: a systematic review of reported cases. Gatta AND, et al. Am J Obstet Gynecol. 2020 Jul;223(1):36-41. doi: 10.1016/j.ajog.2020.04.013. Epub 2020 Apr 18.</p>	<p>6 studies involving 51 pregnant women were eligible for the systematic review. 3 pregnancies were ongoing; of the remaining 48 pregnant women, 46 gave birth by caesarean delivery, and 2 gave birth vaginally, 1 stillbirth and 1 neonatal death were reported. Although vertical transmission of severe acute respiratory syndrome coronavirus 2 infection has been excluded thus far and the outcome for mothers and neonates has been generally good, the high rate of preterm delivery by caesarean delivery is a reason for concern. Caesarean delivery was typically an elective surgical intervention, and it is reasonable to question whether caesarean delivery for pregnant patients with coronavirus disease 2019 was warranted. COVID-19 associated with respiratory insufficiency in late pregnancies certainly creates a complex clinical scenario.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
36	<u>Coronavirus disease 2019 in pregnant women: a report based on 116 cases.</u> Yan J, et al. Am J Obstet Gynecol. 2020 Jul;223(1):111.e1-111.e14. doi: 10.1016/j.ajog.2020.04.014. Epub 2020 Apr 23.	Clinical records retrospectively reviewed for 116 pregnant women with COVID-19 from 25 hospitals in China. SARS-CoV-2 infection during pregnancy is not associated with an increased risk of spontaneous abortion and spontaneous preterm birth. No evidence of vertical transmission when the infection manifests during the third trimester of pregnancy.
37	<u>COVID-19 and pregnancy: a review of current knowledge.</u> Dana PM, et al. Infez Med. 2020 Jun 1;28(suppl 1):46-51.	Clinical findings in pregnant women with COVID-19 are not significantly different compared to other patients. Pregnant women with COVID-19 are not at a higher risk of developing critical pneumonia compared to non-pregnant women. There has been no sign of vertical infection in infants, but maternal infection can cause serious problems such as preterm labour and fetal distress.
38	<u>COVID-19 in pregnancy was associated with maternal morbidity and preterm birth.</u> Sentilhes L, et al. Am J Obstet Gynecol. 2020 Jun 15;S0002-9378(20)30639-6. doi: 10.1016/j.ajog.2020.06.022.	Outcomes of 54 pregnant women with confirmed (n=38) and suspected (n=16) COVID-19 infection were studied. 32 had an ongoing pregnancy, one a miscarriage, and 21 live births. Preterm deliveries were medically indicated for their COVID-19-related condition for 23.8% of patients who gave birth. Oxygen support was required for 24.1%. Of these, three, aged 35 years or older with positive COVID-19 RT-PCR, had respiratory failure requiring indicated delivery before 29 weeks' gestation. COVID-19 in pregnancy was associated with maternal morbidity and preterm birth.
39	<u>COVID-19 in Pregnant Women and Neonates: A Systematic Review of the Literature with Quality Assessment of the Studies.</u> Trippella G, et al. Pathogens . 2020 Jun 18;9(6):485. doi: 10.3390/pathogens9060485.	A review of the literature was performed. 37 studies involving 275 pregnant women with COVID-19 and 248 neonates were included. Only 10 were admitted in the ICU, and one died. Two stillbirths were reported; the incidence of prematurity was 28%. 16 tested positive for SARS-CoV-2 by RT-PCR, and 9 of them were born from mothers infected during pregnancy. All the affected neonates recovered. SARS-CoV-2 was not detected in amniotic fluid, vaginal/cervical fluids, placenta tissue, and breast milk samples. SARS-CoV-2 infection in pregnant women appeared associated with a low morbidity and mortality rate. The outcomes of neonates born from infected women were mainly favourable, although neonates at risk should be closely monitored.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
40	<p><u>Effects of COVID-19 Infection during Pregnancy and Neonatal Prognosis: What Is the Evidence?</u> De Sousa AFL, et al. Int J Environ Res Public Health. 2020 Jun 11;17(11):4176. doi: 10.3390/ijerph17114176.</p>	<p>Systematic literature review to study the effects of COVID-19 infection during pregnancy, and the neonatal prognosis. 755 pregnant women and 598 infants were assessed. 65% of pregnant women had C-sections. 82% of infants were tested for SARS-CoV-2, of which 2% tested positive. Potential worsening of the clinical conditions of pregnant women infected with SARS-CoV-2, whether the infection is associated with comorbidities or not cannot be excluded. We recommend relentless monitoring of all pregnant women in addition to testing them before delivery or the first contact with newborns.</p>
41	<p><u>First COVID-19 maternal mortality in the UK associated with thrombotic complications.</u> Ahmed I, et al. Br J Haematol. 2020 Jul;190(1):e37-e38. doi: 10.1111/bjh.16849. Epub 2020 Jun 8.</p>	<p>Report of the first maternal death of a 29-year woman of Pakistani origin at Birmingham Heartlands Hospital (BHH), UK on the 8 April 2020. She had a BMI of 35, type 2 diabetes mellitus (T2DM) on metformin and insulin, renal tubular acidosis, asthma and vitamin D deficiency. In her first pregnancy, she had a stillborn baby. At her first antenatal visit, her HbA1c was 9.7%. She also had a high albumin creatinine ratio but with normal kidney function. Both pregnancy and COVID-19 increases the risk of thrombosis. This case has highlighted the synergy of these factors in increasing the risk of thrombotic complications in pregnant women with COVID-19.</p>
42	<p><u>Pregnancy and COVID-19: a systematic review of maternal, obstetric and neonatal outcomes.</u> Trocado V, et al. J Matern Fetal Neonatal Med. 2020 Jul 7;1-13. doi: 10.1080/14767058.2020.1781809.</p>	<p>Systematic review of 8 studies involving 95 pregnant women and 51 neonates. 26% of women had a history of epidemiological exposure to SARS-CoV-2. The most common symptoms presented were fever (55%), cough (38%) and fatigue (11%). In 50 deliveries, 94% were caesarean sections and 35% were preterm births. Of the 51 neonates, 20% had low birth weight and 1 tested positive for Sars-CoV-2. There was 1 neonatal death, not related to the viral infection, and no cases of severe neonatal asphyxia.</p>
43	<p><u>Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Co-V-2) Infection: A Systematic Review.</u> Juntley BJF, et al. Obstet Gynecol. 2020 Jun 9. doi: 10.1097/AOG.0000000000004010. Online ahead of print.</p>	<p>Systematic review of 99 articles. 13 included 538 pregnancies complicated by SARS-CoV-2 infection, with reported outcomes on 435 (80.9%) deliveries. ICU admission occurred in 3.0% of cases (8/263). No maternal deaths were reported. The preterm birth rate was 20.1%, the caesarean delivery rate was 84.7%. No vertical transmission was reported and the neonatal death rate was 0.3%. The preterm birth rate of 20% and the caesarean delivery rate exceeding 80% seems related to geographic practice patterns.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
44	<p><u>COVID-19 Pneumonia and Pregnancy; A Systematic Review and Meta-Analysis.</u> Kasraeian M, Zare M, Vafaei H, et al. The Journal of Maternal-Fetal & Neonatal Medicine. 2020. DOI: https://doi.org/10.1080/14767058.2020.1763952</p>	<p>Meta-analysis on 87 pregnant women. Almost 65% of the patients reported a history of exposure to an infected person, 78% suffered from mild or moderate COVID-19, 99.9% had successful termination, 86% had cough, and 68% had fever. The overall proportions of vertical transmission, still birth, and neonatal death were zero. No evidence of vertical transmission has been suggested at least in late pregnancy. No hazards have been detected for fetuses or neonates. Most patients suffered from mild or moderate COVID-19 pneumonia with no pregnancy loss, proposing a similar pattern of the clinical characteristics of COVID-19 pneumonia to that of other adult populations.</p>
45		
46	<p><u>Effects of Coronavirus Disease 2019 (COVID-19) on Maternal, Perinatal and Neonatal Outcomes: A Systematic Review.</u> Juan J, Gil MM, Rong Z, et al. Ultrasound Obstet Gynecol . 2020 May 19. doi: 10.1002/uog.22088.</p>	<p>A total of 20 pregnant patients with laboratory-confirmed COVID-19 were included. All six and 22 cases that had nucleic-acid testing in vaginal mucus and breast milk samples, respectively, were negative for SARS-CoV-2. Only 4 cases of spontaneous miscarriage or abortion were reported. In the consecutive case series, 219/295 women had delivered at the time of reporting, and the majority of these had caesarean section. Only 8 neonates had birth weight <2500 g and nearly one-third of cases were transferred to the neonatal intensive care unit. There was one case each of neonatal asphyxia and neonatal death. In 155 neonates that had nucleic-acid testing in throat swab, all, except three cases, were negative for SARS-CoV-2. There were 7 maternal deaths, 4 intrauterine fetal deaths (one with twin pregnancy) and two neonatal deaths (twin pregnancy) reported in a non-consecutive case series of nine cases with severe COVID-19. From the case reports, two maternal deaths, one neonatal death and two cases of neonatal SARS-CoV-2 infection were reported.</p>
47	<p><u>Impact of COVID-19 Infection on Pregnancy Outcomes and the Risk of Maternal-To-Neonatal Intrapartum Transmission of COVID-19 During Natural Birth.</u> Khan S, Peng L, Siddique R, et al. Infect Control Hosp Epidemiol. 2020 Jun;41(6):748-750. doi: 10.1017/ice.2020.84.</p>	<p>Case report study of 3 pregnant women with laboratory confirmed COVID-19. All 3 had vaginal deliveries, only 1 patient delivered a preterm baby. The preterm baby tested negative for SARS-CoV-2, which suggests that the preterm delivery was not caused by vertical transmission of SARS-CoV-2. No neonatal death or stillbirth was observed.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
48	<p><u>Effects of SARS-CoV-2 Infection on Pregnant Women and Their Infants: A Retrospective Study in Wuhan, China.</u> Yang H, Hu B, Zhan S, et al. Archives of Pathology & Laboratory Medicine In-Press. https://doi.org/10.5858/arpa.2020-0232-SA</p>	<p>Twenty-seven laboratory or clinically confirmed SARS-CoV-2 infection pregnant women (4 early pregnancies included) and 24 neonates born to the 23 late pregnant mothers were analysed. No major complication were reported among the studied cohort, though one serious case and one perinatal infection were observed.</p>
49	<p><u>SARS-CoV-2 Infection in Pregnancy – a Review of the Current Literature and Possible Impact on Maternal and Neonatal Outcome.</u> Stumpfe F, Titzmann, Schneider MO, et al. Geburtsh Frauenheilk 2020; 80: 380–390.</p>	<p>The clinical course of COVID-19 disease may be complicated by pregnancy which could be associated with a higher mortality rate. Also transmission from mother to child in utero is unlikely. Breastfeeding is possible once infection has been excluded or the disease declared cured.</p>
50	<p><u>Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review</u> Yang Z., Wang M., Zhu Z., Liu Y. [Article in Press] J. Matern.-Fetal Neonatal Med. 2020</p>	<p>Summarizes the available evidence on maternal, fetal, and neonatal outcomes of pregnant women infected with Coronavirus Disease 2019 published from 1 January 2020 to 26 March 2020. In total, 18 studies comprising 114 pregnant women were included in the review. 91% of patients had cesarean delivery due to various indications. In terms of fetal and neonatal outcomes, there were reports of stillbirth (1.2%), neonatal death (1.2%), preterm birth (21.3%), low birth weight (<2500 g, 5.3%), fetal distress (10.7%), and neonatal asphyxia (1.2%). Although, there are reports of neonatal infection, but no direct evidence of intrauterine vertical transmission has been found.</p>
51	<p><u>Characteristics and outcomes of pregnant women hospitalised with confirmed SARS-CoV-2 infection in the UK: a national cohort study using the UK Obstetric Surveillance System (UKOSS)</u> Marian Knight, Kathryn Bunch, Nicola Vousden, Edward Morris, Nigel Simpson, Christopher Gale, Patrick O'Brien, Maria Quigley, Peter Brocklehurst, Jennifer J Kurinczuk doi: https://doi.org/10.1101/2020.05.08.20089268</p>	<p>Prospective national population-based cohort study with 427 pregnant women admitted to hospital with confirmed Sars-CoV-2 infection between 01/03/2020 and 14/04/2020. 694 comparison women who gave birth between 01/11/2017 and 31/10/2018. Most pregnant women hospitalised with SARS-CoV-2 were in the late second or third trimester, supporting guidance for continued social distancing measures in later pregnancy. Most had good outcomes and transmission of SARS-CoV-2 to infants was uncommon.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
52	<p>Risks of Novel Coronavirus Disease (COVID-19) in Pregnancy; a Narrative Review Panahi L, Amiri M, Pouy S. Arch Acad Emerg Med. 2020 Mar 23;8(1):e34. eCollection 2020.</p>	<p>Review of 13 articles, considering possibility of vertical transmission, studying 37 mothers and 38 newborns. Six mothers had premature delivery. No reports of vertical transmission reported, with all babies healthy, with Apgar of 8– 10. Clinical symptoms of pregnancy women the same as non-pregnant cases. Due to uncertainties around data, it is necessary to monitor suspected pregnant women before and after delivery.</p>
53	<p>A systematic scoping review of COVID-19 during pregnancy and childbirth Elshafeey F, Magdi R, Hindi N, et al. Int J Gynaecol Obstet. 2020 Jul;150(1):47-52. doi: 10.1002/ijgo.13182. Epub 2020 May 17.</p>	<p>In 33 studies looking at 385 women with COVID-19 infection, 17 women were admitted to intensive care. Results were:</p> <ul style="list-style-type: none"> • one maternal mortality • 69.4% of births were by caesarean • For 256 neonates recorded, there were 2 stillbirths and one neonatal death <p>Authors concluded that, “COVID-19 infection during pregnancy probably has a clinical presentation and severity resembling that in non-pregnant adults. It is probably not associated with poor maternal or perinatal outcomes.”</p>
54	<p>Maternal and Perinatal Outcomes with COVID-19: a systematic review of 108 pregnancies Zaigham M, Andersson O. Acta Obstet Gynecol Scand. 2020 Jul;99(7):823-829. doi: 10.1111/aogs.13867. Epub 2020 Apr 20.</p>	<p>Systematic review, looking at presentations and outcomes of 108 pregnancies with COVID-19. Severe maternal morbidity was reported, and careful monitoring of pregnancies is needed. Most reports described women presenting in the third trimester with fever (68%) and coughing (34%). Lymphocytopenia (59%) with elevated C-reactive protein (70%) was observed and 91% of the women were delivered by cesarean section. Three maternal intensive care unit admissions were noted but no maternal deaths. One neonatal death and one intrauterine death were also reported. Vertical transmission could not be ruled out.</p>
55	<p>Why are pregnant women susceptible to COVID-19? An immunological viewpoint Liu H, Wang LL, Zhao SJ, et al. J Reprod Immunol. 2020 Mar 19;139:103122. doi: 10.1016/j.jri.2020.103122. [Epub ahead of print]</p>	<p>Discusses 18 mothers diagnosed with COVID-19. Five minute Apgar scores of new-borns were between 8 and 10. 10 births were before 37 weeks, suggesting possible risk of preterm delivery. All neonates were negative for the virus, although one neonate died.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
56	<p><u>Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals</u> Breslin N., Baptiste C., Gyamfi-Bannerman C., Miller R., Martinez R., Bernstein K., Ring L., Landau R., Purisch S., Friedman A.M., Fuchs K., Sutton D., Andrikopoulou M., Rupley D., Sheen J.-J., Aubey J., Zork N., Moroz L., Mourad M., Wapner R., Simpson L.L., D'Alton M.E., Gofman D. [Article in Press] American Journal of Obstetrics and Gynecology MFM 2020 Article Number 100118</p>	<p>A retrospective review of clinical documentation for 43 pregnant women who tested positive for COVID-19 using SARS-CoV-2 PCR nasopharyngeal swab. Records related to neonates born to these COVID-19 positive mothers were also reviewed. Of 43, 10 patients (71.4%) developed symptoms of coronavirus disease 2019 over the course of their delivery admission or early after postpartum discharge. Of the other 29 patients (67.4%) who presented with symptomatic coronavirus disease 2019, 3 women ultimately required antenatal admission for viral symptoms, and another patient re-presented with worsening respiratory status requiring oxygen supplementation 6 days postpartum after a successful labor induction. There were no confirmed cases of coronavirus disease 2019 detected in neonates upon initial testing on the first day of life.</p>
57	<p><u>Coronavirus in pregnancy and delivery: rapid review</u> Mullins E, Evans D, Viner RM, et al. Ultrasound Obstet Gynecol. 2020 Mar 17. doi: 10.1002/uog.22014. [Epub ahead of print]</p>	<p>Review of available literature. From reports of 32 women COVID-19 pregnant women, delivering 30 babies, seven (22%) were asymptomatic and two (6%) were admitted to the intensive care unit (ICU), one of whom remained on extracorporeal membrane oxygenation. No maternal deaths have been reported to date. Delivery was by Cesarean section in 27 cases and by vaginal delivery in two, and 15 (47%) delivered preterm. There was one stillbirth and one neonatal death. In 25 babies, no cases of vertical transmission were reported; 15 were reported as being tested with reverse transcription polymerase chain reaction after delivery.</p>
58	<p><u>An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes</u> Schwartz DA. Arch Pathol Lab Med. 2020 Mar 17. doi: 10.5858/arpa.2020-0901-SA.</p>	<p>Review of 38 cases of COVID-19 in pregnancies. No deaths and intrauterine transmission were reported and all neonatal specimens were also negative.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
59	<u>Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study</u> Li N, Han L, Peng M, et al. Clinical Infectious Diseases doi: 10.1093/cid/ciaa352	Severe maternal and neonatal complications were not observed in pregnant women with COVID-19 pneumonia who had vaginal delivery or caesarean section. Mild respiratory symptoms of pregnant women with COVID-19 pneumonia highlight the need of effective screening on admission.
60	<u>Novel Coronavirus Infection in Newborn Babies Under 28 Days in China</u> Zhang ZJ, Yu XJ, Fu T, et al. Eur Respir J. 2020 Apr 8. pii: 2000697. doi: 10.1183/13993003.00697-2020. [Epub ahead of print]	Study of 4 cases of COVID-19 infection in newborns. Symptoms were mild and outcomes less severe as compared to adults. There was a lack of evidence for intrauterine vertical transmission.
61	<u>COVID-19 Obstetrics Task Force, Lombardy, Italy: executive management summary and short report of outcome.</u> Ferrazzi EM, Frigerio L, Cetin I, et al. Int J Gynaecol Obstet. 2020 Apr 8. doi: 10.1002/ijgo.13162. [Epub ahead of print]	Summary of the experience of a hospital in Italy. Strict management was put in place, with a triage based on symptoms established, with PPE worn by staff and mothers, including during breastfeeding. 42 pregnant women were diagnosed with COVID-19, accounting for 0.6% of the expected 7,000 deliveries in the region over the time period. 43% of deliveries were by caesarean, with 2 cases of spontaneous preterm delivery.
62	<u>Management of pregnant women infected with COVID-19.</u> Luo Y, Yin K. Lancet Infect Dis. 2020 Mar 24. pii: S1473-3099(20)30191-2. doi: 10.1016/S1473-3099(20)30191-2. [Epub ahead of print]	Authors report the clinical features and obstetric and neonatal outcomes of pregnancy with COVID-19 pneumonia in Wuhan, China. Seven pregnant women with COVID-19 pneumonia were assessed and the onset symptoms were similar to those reported in non-pregnant adults with COVID-19. All patients received oxygen therapy and antiviral treatment in isolation. All patients had caesarean section after consultation with a multidisciplinary team and the outcomes of the pregnant women and neonates were good. Three neonates were tested SARS-CoV-2. One was found to be infected with COVID-19 36 hours after birth.
63	<u>Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: Information for healthcare professionals.</u> Poon LC, Yang H, Kapur A, et al. Int J Gynaecol Obstet. 2020 Jun;149(3):273-286. doi: 10.1002/ijgo.13156.	Guidelines from FIGO for management of pregnancy and puerperium with COVID-19, and providing guidance on medical treatment of pregnant women with COVID-19.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
64	<u>ISUOG Consensus Statement on rationalization of early-pregnancy care and provision of ultrasonography in context of SARS-CoV-2</u> Bourne T, Kyriacou C, Coomarasamy A, et al. Ultrasound Obstet Gynecol. 2020 Jun;55(6):871-878. doi: 10.1002/uog.22046.	ISUOG consensus report for management of early pregnancy complications by early-pregnancy care providers during the COVID-19 pandemic.
65	<u>Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy.</u> Liu Y, Chen H, Tang K, et al. J Infect. 2020 Mar 4. pii: S0163-4453(20)30109-2. doi: 10.1016/j.jinf.2020.02.028. [Epub ahead of print]	Description of epidemiology and clinical characteristics of COVID-19 infection during pregnancy.
66	<u>Preparing an obstetric unit in the heart of the epidemic strike of COVID-19: quick reorganization tips</u> Capanna F, Haydar A, McCarey C, et al. J Matern Fetal Neonatal Med. 2020 Mar 29:1-11. doi: 10.1080/14767058.2020.1749258. [Epub ahead of print]	Review suggesting key points of strategies to implement to prepare obstetric units in the emergency situation
67	<u>Guidelines for pregnant women with suspected SARS-CoV-2 infection</u> Favre G, Pomar L, Qi X, et al. Lancet Infect Dis. 2020 Mar 3. pii: S1473-3099(20)30157-2. doi: 10.1016/S1473-3099(20)30157-2. [Epub ahead of print]	Short review summarising care for pregnant women and newborns with and curing the COVID-19 pandemic.
68	<u>ISUOG Interim Guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals</u> Poon LC, Yang H, Lee JCS, et al. Ultrasound Obstet Gynecol. 2020 Mar 11. doi: 10.1002/uog.22013. [Epub ahead of print]	Guidance from the ISUOG on COVID-19 infection during pregnancy, covering diagnosis and management of patients.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
69	<p>A global recommendation for restrictive provision of fertility treatments during the COVID-19 pandemic Rodriguez-Wallberg KA, Wikander I. Acta Obstet Gynecol Scand. 2020 Apr 8. doi: 10.1111/aogs.13851. [Epub ahead of print]</p>	Short editorial outlining recommendations from global organisations, acknowledging the lack of evidence and the differences in advice.
70	<p>Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy Dashraath P, Jing Lin Jeslyn W, Mei Xian Karen L, et al. Am J Obstet Gynecol. 2020 Jun;222(6):521-531. doi: 10.1016/j.ajog.2020.03.021.</p>	Large review of COVID-19 in pregnancy, discussing diagnostic methods, treatment options as well as methods to keep care providers safe while continuing to provide care.
71	<p>Safe Delivery for COVID-19 Infected Pregnancies Qi H, Luo X, Zheng Y, et al. BJOG. 2020 Mar 26. doi: 10.1111/1471-0528.16231. [Epub ahead of print]</p>	Recommendations guidelines for safe delivery during COVID-19 pandemic in infected mothers.
72	<p>COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals Breslin N, Baptiste C, Gyamfi-Bannerman C, et al. Am J Obstet Gynecol MFM. 2020 Apr 9 : 100118. doi: 10.1016/j.ajogmf.2020.100118 [Epub ahead of print]</p>	In a series of 43 COVID-19-positive pregnant women identified over a two-week period, infection was often asymptomatic, still supporting a role for universal testing of pregnant women being admitted to the Labor Unit. 86% of the women has mild disease, similar to non-pregnant adults.
73	<p>Coronavirus Disease 2019 (COVID-19) and pregnancy: what obstetricians need to know Rasmussen SA, Smulian JC, Lednicky JA, et al Am J Obstet Gynecol. 2020 May;222(5):415-426. doi: 10.1016/j.ajog.2020.02.017.</p>	Principles of management of coronavirus disease 2019 in pregnancy include early isolation, aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, consideration of empiric antibiotics (secondary to bacterial infection risk), laboratory testing for the virus and coinfection, fetal and uterine contraction monitoring, early mechanical ventilation for progressive respiratory failure, individualized delivery planning, and a team-based approach with multispecialty consultations.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Pregnancy outcomes and management

No.	Publication	Notes
74	<u>Placental Pathology in Covid-19 Positive Mothers: Preliminary Findings.</u> Baergen RN, Heller D Pediatr Dev Pathol. 2020 May-Jun;23(3):177-180. doi: 10.1177/1093526620925569.	This study describes the pathology and clinical information on 20 placentas whose mother tested positive for the novel Coronavirus (2019-nCoV) cases. Ten of the 20 cases showed some evidence of fetal vascular malperfusion or fetal vascular thrombosis. The significance of these findings is unclear and needs further study.
75	<u>Covid-19 and pregnancy.</u> BMJ 2020;369:m1672	The aim of the guideline is to support health professionals to provide safe care for pregnant women, whether they have suspected or confirmed covid-19, or are asymptomatic.
76	<u>Breastfeeding and Coronavirus Disease-2019. Ad interim indications of the Italian Society of Neonatology endorsed by the Union of European Neonatal & Perinatal Societies</u> Davanzo R, Moro G, Sandri F, et al. Matern Child Nutr. 2020 Apr 3:e13010. doi: 10.1111/mcn.13010. [Epub ahead of print]	Review of breastfeeding guidelines, from the Italian Society for Neonatology, for pregnancies during COVID-19, including for infected and non-infected mothers.
77	<u>Evidence and possible mechanisms of rare maternal-fetal transmission of SARS-CoV-2.</u> Egloff C, Vauloup-Fellous C, Picone O, et al. J Clin Virol. 2020 Jul;128:104447. doi: 10.1016/j.jcv.2020.104447. Epub 2020 May 18.	In 179 new-borns tested for SARS-CoV-2 at birth from mothers with COVID-19, transmission was suspected in 8 cases, 5 with positive nasopharyngeal SARS-CoV-2 RT-PCR and 3 with SARS-CoV-2 IgM. According to these data, the transmission risk is probably very low.
78	<u>Lack of Viral Transmission to Preterm Newborn From a COVID-19 Positive Breastfeeding Mother at 11 Days Postpartum.</u> Perrone S, Giordano M, Meoli A, et al. J Med Virol . 2020 May 21. doi: 10.1002/jmv.26037. Online ahead of print.	During stay in hospital, infected mother and healthcare caregivers followed recommended hygiene measures. In this setting, no horizontal transmission occurred. RT-PCR assay for SARS-CoV-2 performed on breast milk during mother febrile peak was negative.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
79	Analysis of SARS-CoV-2 vertical transmission during pregnancy. Fenzia C, et al. Nat Commun. 2020 Oct 12;11(1):5128. doi: 10.1038/s41467-020-18933-4.	The impact of SARS-CoV-2 infection during gestation remains unclear. SARS-CoV-2 genome was detected in one umbilical cord blood and in two at-term placentas, in one vaginal mucosa and in one milk specimen. Anti-SARS-CoV-2 IgM and IgG antibodies were found in one umbilical cord blood and in one milk specimen. In 3 documented cases of vertical transmission, SARS-CoV-2 infection was accompanied by a strong inflammatory response. These data support the hypothesis that in utero SARS-CoV-2 vertical transmission, while low, is possible.
80	COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. Pettiroso E, et al. Aust N Z J Obstet Gynaecol. 2020 Oct;60(5):640-659	Sixty articles were included in this review, with 1287 confirmed SARS-CoV-2 positive pregnant cases reported. Where universal testing was undertaken, asymptomatic infection occurred in 43.5-92% of cases. In the cohort studies, severe and critical COVID-19 illness rates were similar to the general population. Eight maternal deaths, 6 neonatal deaths, 7 stillbirths and 5 miscarriages were reported. Nineteen neonates were SARS-CoV-2 positive. Vertical transmission is possible; however, it is unclear whether SARS-CoV-2 positive neonates were infected in utero, intrapartum or postpartum.
81	Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women. Chambers C, et al. JAMA. 2020 Oct 6;324(13):1347-1348.	In 18 women with confirmed SARS-CoV-2 infection, all but one of whom had symptomatic disease, one breast milk sample had detectable SARS-CoV-2 RNA on day of symptom onset, but samples taken 1 day prior and 12 and 41 days later were negative. Breast milk is not thought to be a source of infection.
82	No evidence for vertical transmission of SARS-CoV-2 in two neonates with mothers infected in the second trimester. Yang J-Y, et al. Infect Dis (Lond). Nov-Dec 2020;52(12):913-916.	In two pregnant women with symptomatic COVID-19, one had positive IgG and IgM to SARS-CoV-2 before delivery, while the other was only positive for IgG before delivery. Both newborns were IgM negative but became IgG positive after birth. Neither neonate developed symptoms and outcomes were good.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
83	<p>Possible vertical transmission and antibodies against SARS-CoV-2 among infants born to mothers with COVID-19: A living systematic review.</p> <p>Bwire GM, et al. J Med Virol. 2020 Oct 22. doi: 10.1002/jmv.26622.</p>	<p>A total of 205 infants born to COVID-19 positive mothers were studied. 6.3% of the infants tested positive for SARS-CoV-2 at birth. IgG/IgM were detected in 90% infants who tested negative for COVID-19 virus. The current evidence revealed a low chance of vertical transmission of COVID-19 and antibodies against SARS-CoV-2 were detected among vertically exposed but negative infants.</p>
84	<p>Single-cell expression profiles of ACE2 and TMPRSS2 reveals potential vertical transmission and fetus infection of SARS-CoV-2.</p> <p>Lu M, et al. Aging (Albany NY). 2020 Oct 26;12(20):19880-19897</p>	<p>Using transcriptomic analysis of the placenta and other tissues, ACE2 was found to be expressed on a small proportion of trophoblast cells, suggesting a low possibility of vertical transmission during pregnancy. The fetal adrenal gland, heart, kidney and stomach were found to be susceptible to SARS-CoV-2 infection, due to the high expression of TMPRSS2 in these organs. ACE2 expressing alveolar cells were absent in neonates - caution is therefore needed to avoid triggering ACE2 expression in fetal and placental tissue.</p>
85	<p>The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis.</p> <p>Diriba K, et al. Eur J Med Res. 2020 Sep 4;25(1):39.</p>	<p>Thirty-nine studies involving 1316 pregnant women were included. The most common clinical features were fever, cough, and myalgia with prevalence. Maternal outcomes rates were: preterm births < 37 weeks, 14.3%; preeclampsia, 5.9%; miscarriage, 14.5%; preterm premature rupture of membranes, 9.2%; fetal growth restriction, 2.8%. 56.9% of deliveries were by caesarean. Only, 1.2% of neonates had apgar score < 7 at 5 min. None of the studies reported transmission of CoV from the mother to the fetus in utero, which may be due to a very low expression of angiotensin-converting enzyme-2 in early maternal-fetal interface cells.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
86	A Message from the Human Placenta: Structural and Immunomodulatory Defense against SARS-CoV-2. Kreis N-N, et al. Cells. 2020 Jul 25;9(8):1777. doi: 10.3390/cells9081777.	Based on these data, we conclude that vertical transmission may occur but rare, ascribed to the potent physical barrier, the fine-regulated placental immune defense and modulation strategies. Particularly, immunomodulatory mechanisms employed by the placenta may mitigate violent immune response, maybe soften cytokine storm tightly associated with severely ill COVID-19 patients, possibly minimizing cell and tissue damages, and potentially reducing SARS-CoV-2 transmission.
87	Vertical transmission of SARS CoV-2: a systematic review. Deniz M, Tezer H. J Matern Fetal Neonatal Med. 2020 Jul 21;1-8. doi: 10.1080/14767058.2020.1793322. Online ahead of print.	In 50 studies, 17 newborns tested positive for SARS CoV-2 by RT-PCR. In three neonates, SARS-CoV-2 antibodies were elevated. Eight placental tissues testing positive for the virus were reported. These data show the potential for vertical transmission of SARS-CoV-2.
88	SARS-CoV-2 possible contamination of genital area: implications for sexual and vertical transmission routes. Delfino M, et al. J Eur Acad Dermatol Venereol. 2020 Aug;34(8):e364-e365. doi: 10.1111/jdv.16591. Epub 2020 Jun 4.	However, mother-to-child SARS-CoV-2 transmission through the placenta probably does not occur, or likely occurs very rarely. All the studies conducted on COVID-19 pregnant women involved patients undergoing cesarean section, but the indications for such delivery modality were not clearly stated.
89	Probable Vertical Transmission of SARS-CoV-2 Infection. Demirjian A, et al. Pediatr Infect Dis J. 2020 Sep;39(9):e257-e260. doi: 10.1097/INF.0000000000002821.	Following cesarean section, the neonate was kept in strict isolation. Molecular tests for SARS-CoV-2 on respiratory samples, blood, and meconium were initially negative, but positive on a nasopharyngeal aspirate on the third day of life. On day 5, the neonate developed fever and coryza, which spontaneously resolved. Viral genomic analysis from the mother and neonate showed identical sequences except for 1 nucleotide.
90	Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Kotlyar AM, et al. Am J Obstet Gynecol. 2020 Jul 31;S0002-9378(20)30823-1. doi: 10.1016/j.ajog.2020.07.049. Online ahead of print.	Vertical transmission of severe acute respiratory syndrome coronavirus 2 is possible and seems to occur in a minority of cases of maternal coronavirus disease 2019 infection in the third trimester.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
91	<p><u>Transplacental transmission of SARS-CoV-2 infection.</u> Vivanti A, et al. Nat Commun. 2020 Jul 14;11(1):3572. doi: 10.1038/s41467-020-17436-6.</p>	<p>Transplacental transmission of SARS-CoV-2 was demonstrated in a neonate born to a mother infected in the last trimester and presenting with neurological compromise. The transmission is confirmed by comprehensive virological and pathological investigations. In detail, SARS-CoV-2 causes: (1) maternal viremia, (2) placental infection demonstrated by immunohistochemistry and very high viral load; placental inflammation, as shown by histological examination and immunohistochemistry, and (3) neonatal viremia following placental infection. The neonate is studied clinically, through imaging, and followed up. The neonate presented with neurological manifestations, similar to those described in adult patients</p>
92	<p><u>Does the maternal-fetal transmission of SARS-CoV-2 occur during pregnancy?</u> Elósegui JJH, et al. Rev Clin Esp. 2020 Jun 5;S0014-2565(20)30156-9. doi: 10.1016/j.rce.2020.06.001.</p>	<p>Four pregnant patients with mild acute COVID-19 symptoms in the second trimester of pregnancy were studied. RT-PCR was used to investigate the presence of SARS-CoV-2 nucleic acids in vaginal discharge and amniotic fluid. No evidence of the virus was found, suggest the virus is unlikely to passed on to the neonate via the amniotic fluid.</p>
93	<p><u>Evidence for and against vertical transmission for severe acute respiratory syndrome coronavirus 2.</u> Lamouroux A, et al. Am J Obstet Gynecol. 2020 Jul;223(1):91.e1-91.e4. doi: 10.1016/j.ajog.2020.04.039.</p>	<p>Issues regarding vertical transmission of SARS-CoV-2 are emerging. 12 were reviewed that reported on 68 deliveries and 71 neonates with maternal infection in the third trimester of pregnancy. To determine whether infection occurred congenitally or perinatally, perinatal exposure, mode of delivery, and time interval from delivery to the diagnosis of neonatal infection were considered. Neonates with severe acute respiratory syndrome coronavirus 2 infection are usually asymptomatic. In 4 cases, a diagnostic test for severe acute respiratory syndrome coronavirus 2 infection was performed within 48 hours of life. Furthermore, detection rates of RT-PCR and the interpretation of IgM and IgG antibodies levels in cord and neonatal blood were discussed in relation with the immaturity of the fetal and neonatal immune system.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
94	Incidence of SARS-CoV-2 vertical transmission: a meta-analysis. Goh XL, et al. Arch Dis Child Fetal Neonatal Ed . 2020 Jun 25;fetalneonatal-2020-319791.	Seventeen studies were included in this meta-analysis. Four hundred and two COVID-19-positive mothers delivered 405 newborns, of which 330 newborns underwent early RT-PCR tests. Nine of 330 newborns tested positive for SARS-CoV-2. The average pooled incidence of vertical transmission was 16 per 1000 newborns. Therefore, current evidence shows that the risk of vertical transmission of SARS-CoV-2 is low.
95	Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: A systematic review and critical analysis. Walker KF, et al. BJOG. 2020 Jun 12;10.1111/1471-0528.16362. doi: 10.1111/1471-0528.16362.	49 studies which included 666 neonates and 655 women was included in this review. 28/666 (4%) neonates had confirmed COVID-19 infection postnatally. Of the 291 women who delivered vaginally, 8/292 (2.7%) neonates were positive. Of the 364 women who had a Caesarean birth, 20/374 (5.3%) neonates were positive. Of the 28 neonates with confirmed COVID-19 infection, 7 were breast fed, 3 formula fed, 1 was given expressed breast milk and in 17 neonates the method of infant feeding was not reported. Neonatal COVID-19 infection is uncommon, uncommonly symptomatic, and the rate of infection is no greater when the baby is born vaginally, breastfed or allowed contact with the mother.
96	Vertical transmission and materno-fetal outcomes in 13 patients with coronavirus disease 2019. Masmajan S, et al. Clin Microbiol Infect. 2020 Jul 8 doi: 10.1016/j.cmi.2020.06.035 [Epub ahead of print]	In a retrospective case series, 13 women with SARS-CoV-2 infection during pregnancy were identified (12 with positive nasopharyngeal PCR and one who was symptomatic with positive serology but three negative PCRs). None of the placenta, cord blood or neonate nasopharyngeal swabs were positive for SARS-CoV-2. These results and the high proportion of negative results among newborn infants from infected mothers could indicate that maternal–placental–foetal infection seems to be rare and that vertical transmission is difficult to prove. 2 of 13 (84%) women had a caesarean section.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
97	<p>Vertical transmission of SARS-CoV-2 infection and preterm birth. Pulinx B, et al. Eur J Clin Microbiol Infect Dis. 2020 Jul 13 : 1–5. doi: 10.1007/s10096-020-03964-y [Epub ahead of print]</p>	<p>Case report of the first case of SARS-CoV-2 detection in both amniotic fluid and placental tissue from preterm fetuses born to a SARS-CoV-2-positive mother. A known SARS-CoV-2-positive woman gave preterm birth to two fetuses at Week 24 with SARS-CoV-2 positive testing in placental tissue and amniotic fluid. The placental histological examinations showed chronic intervillitis and extensive intervillous fibrin depositions with ischemic necrosis of the surrounding villi. The fetal death of fetus one was diagnosed and fetus two showed fetal heart rate decelerations. Due to unstoppable labour, the patient gave preterm birth to two fetuses with prepartal intrauterine death of both.</p>
98	<p>Vertical transmission risk of SARS-CoV-2 infection in the third trimester: a systematic scoping review. Thomas P, et al. J Matern Fetal Neonatal Med. 2020 Jul 1;1-8. doi: 10.1080/14767058.2020.1786055.</p>	<p>18 studies consisting of 157 mothers and 160 neonates were included in this review. Currently, there is no conclusive evidence to suggest that vertical transmission of SARS-CoV-2 occurs. Amongst 81 (69%) neonates who were tested for SARS-CoV-2, 5 (6%) had a positive result. However, amongst these 5 neonates, the earliest test was performed at 16 h after birth, and only 1 neonate was positive when they were later re-tested. However, this neonate initially tested negative at birth, suggesting that the SARS-CoV-2 infection was likely hospital-acquired rather than vertically transmitted. 13 (8%) neonates had complications or symptoms. Finding suggest that vertical transmission did not occur.</p>
99	<p>Adverse outcomes in SAR-CoV-2 (COVID-19) and SARS virus related pregnancies with probable vertical transmission. Bahadur G, et al. JBRA Assist Reprod. 2020 Jul-Sep; 24(3): 351–357.</p>	<p>Most publications studied small numbers of babies. Out of 10 babies positive for the virus, 3 were positive for IgG/IgM antibodies. As IgM do not cross placenta, appears these babies acquired infection in utero. In 11 studies looking at placentas, on 3 from second and third trimesters were infected, with evidence of infiltration of inflammatory cells, increased intervillous fibrin deposition, no vasculopathy and localisation of virus to syncytiotrophoblast cells. Viral transmission from the maternal to the fetal side could be accomplished via canonical (ACE2) or alternative (CD147) receptors present in the placenta to which SARS-CoV2 can bind. Risk of vertical transmission appears low but remains a potential.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
100	<p>Vertical transmission of COVID-19: SARS-CoV-2 RNA on the fetal side of the placenta in pregnancies with COVID-19 positive mothers and neonates at birth. Patanè L, Morotti D, Giunta MR, et al. American Journal of Obstetrics & Gynecology MFM. Available online 18 May 2020, 100145</p>	Of the 22 neonates born, 2 tested positive for SARS-CoV-2. Both recovered and were discharged. The virus was also detected in the placentas of the mothers of the infected neonates. These findings support the possibility for vertical transmission.
101	<p>The SARS-CoV-2 receptor ACE2 expression of maternal-fetal interface and fetal organs by single-cell transcriptome study Li M., Chen L., Zhang J., Xiong C., Li X. PLoS ONE 2020 15:4 Article Number e0230295</p>	The authors concluded, "This study demonstrates the expression of SARS-CoV-2 receptors in human maternal-fetal interface and the main fetal organs. Both the vertical transmission and the placenta dysfunction/abortion caused by SARS-CoV-2 need to be further carefully investigated in clinical practice."
102	<p>Single-Cell RNA Expression Profiling of ACE2 and AXL in the Human Maternal-Fetal Interface Zheng Q.-L., Duan T., Jin L.-P. Reproductive and Developmental Medicine 2020 4:1 (7-10)</p>	This study provides a possible infection route and mechanism for the SARS-CoV-2-infected mother-to-fetus transmission disease, which could be informative for future therapeutic strategy development
103	<p>Intrauterine vertical transmission of SARS-CoV-2: what we know so far. Wang C, Zhou YH, Yang HX, et al. Ultrasound Obstet Gynecol. 2020 Apr 7. doi: 10.1002/uog.22045. [Epub ahead of print]</p>	Review of knowledge of risk of intrauterine transmission. While several studies have investigated the possibility, data is mixed and cannot be conclusively defined without further high quality research.
104	<p>Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, et al. Fetal Pediatr Pathol. 2020 Jun;39(3):246-250. doi: 10.1080/15513815.2020.1747120. Epub 2020 Apr 2.</p>	Review of 31 pregnancies and births. No cases of vertical transmission reported, with no infection detected in neonates or placentas. Two mothers died; paper concluded mothers may be at an increased risk for more severe complications.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
105	<u>Perinatal aspects on the covid-19 pandemic: a practical resource for perinatal-neonatal specialists</u> Mimouni F, Lakshminrusimha S, Pearlman SA et al. J. Perinatol. doi: 10.1038/s41372-020-0665-6. Epub 2020 Apr 10.	Summarises available data, and concludes that vertical transmission is unlikely. Whether pregnancy is a risk factor for severe disease is unknown, as are details about the severity in neonates.
106	<u>Evidence of mother-newborn infection with COVID-19.</u> Sun M, Xu G, Yang Y, et al. Br J Anaesth. 2020 Apr 28. doi: 10.1016/j.bja.2020.04.066 [Epub	Report of 3 mothers diagnosed with COVID-19, with neonates delivered by caesarean. Each neonate was only handled by staff wearing full PPE. Two babies tested positive for SARS-CoV-2; the third was diagnosed with COVID-19. Although the method of infection is unclear, vertical transmission cannot be ruled out.
107	<u>Lack of vertical transmission of severe acute respiratory syndrome coronavirus 2, China.</u> Li Y, Zhao R, Zheng S, et al. Emerg Infect Dis. 2020 Jun;26(6):1335-1336. doi: 10.3201/eid2606.200287. Epub 2020 Jun 17.	Case report of neonate delivered by caesarean to mother with COVID-19. Sputum sample was positive, however, urine, faeces, amniotic fluid, cord blood and placenta were negative for SARS-CoV-2. All samples from the neonate were negative, suggesting vertical transmission unlikely.
108	<u>Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers With Coronavirus Disease 2019 (COVID-19) Pneumonia</u> Hu X, Gao J, Luo X, et al. Obstet Gynecol. 2020 Apr 24. doi: 10.1097/AOG.0000000000003926. [Epub ahead of print]	Of seven births from mothers with COVID-19 that were all isolated immediately after birth, one tested positive for SARS-CoV-2 infection. RT-PCR of throat swabs, blood, faeces and urine were negative for the rest of the neonates.
109	<u>Severe COVID-19 during Pregnancy and Possible Vertical Transmission</u> Alzamora MC, Paredes T, Caceres D, et al. Am J Perinatol. 2020 Jun;37(8):861-865. doi: 10.1055/s-0040-1710050. Epub 2020 Apr 18.	Case study of a pregnant COVID-19 patient requiring mechanical ventilation. Baby was delivered by caesarean delivery. The neonate tested positive for SARS-COV-2 on first day of life, suggesting the potential for vertical transmission.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
110	<p>Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records Chen H, Guo J, Wang C, et al. Lancet. 2020 Mar 7;395(10226):809-815. doi: 10.1016/S0140-6736(20)30360-3.</p>	Review of nine cases of pregnancies with COVID-19, reviewing clinical characteristics, which were similar as non-pregnant cases, with no evidence for intrauterine infection.
111	<p>Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn Dong L, Tian J, He S, et al. JAMA. 2020 Mar 26. doi: 10.1001/jama.2020.4621. [Epub ahead of print]</p>	Case report of a mother infected with COVID-19, and a neonate born who had increased antibody levels and elevated cytokine, although tests for COVID-19 using PCR were negative. Vertical transmission cannot be excluded.
112	<p>Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2: A Systematic Review. Yang Z, Liu Y. Am J Perinatol. 2020. doi: 10.1055/s-0040-1712161.</p>	There is currently no direct evidence to support intrauterine vertical transmission of SARS-CoV-2. Additional RT-PCR tests on amniotic fluid, placenta, and cord blood are needed to ascertain the possibility of intrauterine vertical transmission.
113	<p>Detection of SARS-COV-2 in Placental and Fetal Membrane Samples Penfield CA, Brubaker SG, Limaye MA et al. Am J Obstet Gynecol MFM. 2020 May 8:100133. doi: 10.1016/j.ajogmf.2020.100133. [Epub ahead of print]</p>	This is the first study to demonstrate the presence of SARS-CoV-2 RNA in placental or membrane samples. While there were no clinical signs of vertical transmission, our findings raise the possibility of intrapartum viral exposure.
114	<p>Fetal Diagnosis and Therapy during the COVID-19 Pandemic: Guidance on Behalf of the International Fetal Medicine and Surgery Society. Deprest J, Choolani M, Chervenak F et al. Fetal Diagn Ther. 2020 May 6:1-10. doi: 10.1159/000508254. [Epub ahead of print]</p>	There is, to date, minimal, unconfirmed evidence of spontaneous vertical transmission, though it may theoretically be increased with some procedures. Knowing a mother's preoperative SARS-CoV-2 status would enable us to avoid or defer certain procedures while she is contagious and to protect health care workers appropriately. Some fetal conditions may alternatively be managed neonatally.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

Vertical transmission and management

No.	Publication	Notes
115	<p>SARS-CoV-2: Is it the newest spark in the TORCH? Muldoon K.M., Fowler K.B., Pesch M.H., Schleiss M.R. Journal of Clinical Virology 2020 127 Article Number 104372</p>	<p>Authors stated that there is not enough information on outcomes of COVID-19 on pregnancy and neonates, hence, "Research regarding the potential routes of acquisition of SARS-CoV-2 infection in the prenatal and perinatal setting is of a high public health priority. Vaccines targeting women of reproductive age, and in particular pregnant patients, should be evaluated in clinical trials and should include the endpoints of neonatal infection and disease."</p>
116	<p>Analysis of Maternal Coronavirus Infections and Neonates Born to Mothers with 2019-nCoV; a Systematic Review. Muhidin S, Moghadam ZB, Vizeh M. Arch Acad Emerg Med. 2020; 8(1): e49.</p>	<p>Systematic review of 11 papers, with 89 pregnant patients. Pregnant patients in late pregnancy had clinical manifestations similar to non-pregnant adults. The risk of fetal distress, preterm delivery and prelabour rupture of membranes (PROM) rises with the onset of COVID-19 in the third trimester of pregnancy. There is no evidence of intrauterine and transplacental transmission of COVID-19 to the fetus in the third trimester of pregnancies.</p>
117	<p>Clinical Characteristics of COVID-19 Infection in Newborns and Pediatrics: A Systematic Review. Panahi L, Amiri M, Pouy S. Arch Acad Emerg Med. 2020; 8(1): e50.</p>	<p>A total of 2228 children, new-borns and infants were studied. Clinical manifestation in children may be mild (72%), moderate (22%) or severe (6%). The most common symptoms were dry cough (91%) and fever (96%). In the included articles, 2 children died, one of which was a 14-year-old boy, and the other was a male new-born with gestational age of 35 weeks and 5 days, birth weight of 2200, Apgar score of 8, 8 (1 min and 5 min) and his first symptom was increased heart rate.</p>
118	<p>COVID-19 in Children, Pregnancy and Neonates: A Review of Epidemiologic and Clinical Features. Zimmermann P, Nigel C. The Pediatric Infectious Disease Journal: June 2020 - Volume 39 - Issue 6 - p 469-477 doi: 10.1097/INF.0000000000002700</p>	<p>11 case series including a total of 333 infants and children are reviewed. Neonatal complications included respiratory distress or pneumonia (18%), disseminated intravascular coagulation (3%), asphyxia (2%) and 2 perinatal deaths. Four neonates (3 with pneumonia) were reported to be SARS-CoV-2 positive despite strict infection control during delivery and separation of mother and neonates, meaning vertical transmission could not be excluded.</p>



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

New-born child and management

No.	Publication	Notes
119	Birth and Infant Outcomes Following Laboratory-Confirmed SARS-CoV-2 Infection in Pregnancy - SET-NET, 16 Jurisdictions, March 29-October 14, 2020. Woodworth KR, et al. MMWR Morb Mortal Wkly Rep. 2020 Nov 6;69(44):1635-1640. doi: 10.15585/mmwr.mm6944e2.	Supplementary information on pregnancy and infant outcomes among 5,252 women with laboratory-confirmed SARS-CoV-2 infection reported during March 29-October 14, 2020. Among 610 infants (21.3%) with reported SARS-CoV-2 test results, perinatal infection was infrequent (2.6%) and occurred primarily among infants whose mother had SARS-CoV-2 infection identified within 1 week of delivery.
120	Characteristics of Newborns Born to SARS-CoV-2-Positive Mothers: A Retrospective Cohort Study. Farghaly MAA, et al. Am J Perinatol. 2020 Nov;37(13):1310-1316. doi: 10.1055/s-0040-1715862. Epub 2020 Sep 3.	A retrospective cohort study which found that neonates born to mothers with confirmed or suspected SARS-CoV-2 are most of the time asymptomatic. However, neonatal critical illness due to SARS-CoV-2 is still a possibility.
121	Clinical Analysis of Neonates Born to Mothers with or without COVID-19: A Retrospective Analysis of 48 Cases from Two Neonatal Intensive Care Units in Hubei Province. Liu W, et al. Am J Perinatol. 2020 Nov;37(13):1317-1323. doi: 10.1055/s-0040-1716505. Epub 2020 Sep 6.	48 neonates were admitted to Tongji Hospital and Huangshi Maternal and Child Healthcare Hospital. The neonates were divided into three groups: neonates born to mothers with confirmed COVID-19, neonates born to mothers with clinically diagnosed COVID-19, and neonates born to mothers without COVID-19. None of the neonates showed any signs of COVID-19 symptoms.
122	Clinical manifestations and outcomes of COVID-19 in the paediatric population: a systematic review. Jahangir M, et al. Hong Kong Med J. 2020 Sep 30. doi: 10.12809/hkmj208646. Online ahead of print.	A systemic literature review identified 17 relevant papers which showed that the prevalence of COVID-19 in the paediatric population accounts for a small percentage of patients, whose clinical signs and symptoms are often milder than those of adults.
123	Concomitant SARS-CoV-2 infection and severe neurologic involvement in a late-preterm neonate. Di Nicola P, et al. Neurology. 2020 Nov 3;95(18):834-835.	An 18-day-old girl, born at 35+1 week of postmenstrual age was discharged five days after birth from a center where pregnant women with COVID-19 were treated. The baby experienced severe neurologic impairment in the presence of SARS-CoV-2 infection and mild symptoms attributable to COVID-19.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

New-born child and management

No.	Publication	Notes
123	Death of a neonate with suspected coronavirus disease 2019 born to a mother with coronavirus disease 2019 in Iran: a case report. Rashidan T, et al. J Med Case Rep. 2020 Oct 6;14(1):186.	A case study reports the death of a neonate born to a mother with coronavirus disease 2019, 11 hours after birth. There is a paucity of data on the vertical transmission and the adverse maternal-fetal consequences of this disease, so vertical transmission from mother to child remains to be confirmed
124	Neonatal management and outcomes during the COVID-19 pandemic: an observational cohort study. Salvatore C, et al. Lancet Child Adolesc Health . 2020 Oct;4(10):721-727.	An observational cohort study at New York Presbyterian Hospitals in NYC identified neonates born to mothers with SARS-CoV 2 at delivery. The data suggest that perinatal transmission of COVID-19 is unlikely to occur if correct hygiene precautions are undertaken. None of the neonates had symptoms of COVID-19.
125	Newborns of COVID-19 mothers: short-term outcomes of colocating and breastfeeding from the pandemic's epicenter. Patil UP, et al. J Perinatol. 2020 Oct;40(10):1455-1458.	A retrospective cross-sectional study at NYC H+H/Elmhurst found that caring for newborns at a center with high incidence of maternal SARS-CoV-2, newborns did not show signs of infection after birth. No reports of short-term adverse neonatal outcomes with skin-to-skin care, rooming-in, or breastfeeding in infants of SARS-CoV-2 positive mothers in our population.
126	Outcomes in COVID-19 Positive Neonates and Possibility of Viral Vertical Transmission: A Narrative Review. Sheth S, et al. Am J Perinatol. 2020 Oct;37(12):1208-1216.	Review of 39 studies comprising 326 COVID-19 positive peripartum mothers with respective neonatal outcomes. Twenty-three neonates have been reported to be COVID-19 positive. Male neonates were affected significantly more (79%) than female neonates. Approximately 3% neonates acquired infection through suspected vertical transmission. Strict infection prevention measures during the perinatal time can significantly reduce the chance of horizontal transmission of the virus. Overall, neonates were asymptomatic or mildly symptomatic regardless of gestational age at birth and required only supportive measures. There was 0% mortality in COVID-19 positive neonates.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

New-born child and management

No.	Publication	Notes
127	Potential effects of SARS-CoV-2 infection during pregnancy on fetuses and newborns are worthy of attention. Dang D, et al. J Obstet Gynaecol Res. 2020 Oct;46(10):1951-1957.	This literature review reveals that SARS-CoV-2 infection not only affects pregnant women but also affects the development of fetuses and newborns, resulting in a variety of pregnancy complications and endangering the normal development of newborns until they reach adulthood. The potential adverse effects after maternal SARS-CoV-2 infection on fetuses and newborns, include; preterm delivery, respiratory dyspnea, intrauterine growth restriction and abnormal development of the respiratory and nervous systems.
128	Severe Neonatal Coronavirus Disease 2019 Presenting as Acute Respiratory Distress Syndrome. Trieu C, et al. Pediatr Infect Dis J. 2020 Nov;39(11):e367-e369.	This report highlights a lesser known clinical presentation of COVID-19 in newborns - a severe case of neonatal COVID-19 with acute respiratory distress syndrome. While severe clinical disease remains a rarity in newborns, physicians involved in the care of children should be aware of this likelihood and utilise an early and multidisciplinary approach for improved clinical outcomes.
129	Synthesis and systematic review of reported neonatal SARS-CoV-2 infections. Raschetti R, et al. Nat Commun. 2020 Oct 15;11(1):5164.	A meta-analysis of 176 published cases of neonatal SARS-CoV-2 infection reported 70% and 30% of infections are due to environmental and vertical transmission. A lack of mother-neonate separation from birth is associated with late SARS-CoV-2 infection.
130	The clinical course of SARS-CoV-2 positive neonates. De Bernardo G, et al. J Perinatol. 2020 Oct;40(10):1462-1469.	A literature review was conducted on PubMed database from December 2019 to April 27, 2020. The findings reported 25 neonates affected by SARS-CoV-2. Main symptoms were fever, cough, or shortness of breath but often these neonates did not show other symptoms during length stay in hospital. No deaths occurred.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

New-born child and management

No.	Publication	Notes
131	<p>Clinical Features and Outcome of SARS-CoV-2 Infection in Neonates: A Systematic Review. Dhir SK, et al. J Trop Pediatr. 2020 Aug 28;fmaa059. doi: 10.1093/tropej/fmaa059. Online ahead of print.</p>	Unlike children, most COVID-positive neonates were symptomatic and required intensive care. Postpartum acquisition was the commonest mode of infection in neonates, although a few cases of congenital infection have also been reported.
132	<p>Management of neonates after postpartum discharge and all children in the ambulatory setting during the coronavirus disease 2019 (COVID-19) pandemic. Harriel KL, et al. Curr Opin Pediatr. 2020 Aug;32(4):610-618. doi: 10.1097/MOP.0000000000000931.</p>	Extra precautions should be taken during the transition period between postpartum discharge and follow-up in the ambulatory setting to ensure the safety of all patients and practice team members. This should include restructuring office flow by visit type and location, limiting in-person visits during well infant exams, instituting proper procedures for personal protective equipment and for cleaning of the office, expanding telehealth capabilities for care and education, and prioritizing universal vaccinations and routine well child screenings.
133	<p>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. Gabriel MAM, et al. Pediatr Infect Dis J. 2020 Sep 11. doi: 10.1097/INF.0000000000002902. Online ahead of print</p>	COVID-19 transmission was not found during delivery or throughout the first month of life in the newborns included in our study. Exclusive breast-feeding rates at discharge and at 1 month of age were lower than expected.
134	<p>Neonatal Late Onset Infection with Severe Acute Respiratory Syndrome Coronavirus 2. Buonsenso D, et al. Am J Perinatol. 2020 Jun;37(8):869-872. doi: 10.1055/s-0040-1710541.</p>	Study to evaluate postdischarge SARS-CoV-2 status of newborns to mothers with COVID-19 in pregnancy that, at birth, were negative to SARS-CoV-2. Seven pregnant women with documented SARS-CoV-2 infection were evaluated. One had a spontaneous abortion at 8 weeks, four women recovered and are still in follow-up, and two women delivered. Two newborns were enrolled in the study. At birth and 3 days of life, newborns were negative to SARS-CoV-2. At 2-week follow-up, one newborn tested positive although asymptomatic. Findings highlight the importance of follow-up of newborns to mothers with COVID-19 in pregnancy, since they remain at risk of contracting the infection in the early period of life and long-term consequences are still unknown.



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

New-born child and management

No.	Publication	Notes
135	<u>Fatal Outcome of COVID-19 Disease in a 5-month Infant With Comorbidities.</u> Climent FJ, Calvo C, Garcia-Guereta L, et al. Revista Española de Cardiología (English Edition). Available online 27 April 2020. https://doi.org/10.1016/j.rec.2020.04.011	Case report of 5-month old infant. Had been diagnosed with heart failure and mucopolysaccharidosis type I-Hurler syndrome at age 1 month. Clinical course of our patient was very short, reaching the hyperinflammation phase in just 3 to 4 days from the onset of symptoms. Patient experienced cardiac arrest that proved fatal.
136	<u>Delivery in pregnant women infected with SARS-CoV-2: A fast review</u> Parazzini F, Bortolus R, Mauri PA, et al. Int J Gynaecol Obstet. 2020 Apr 9. doi: 10.1002/ijgo.13166. [Epub ahead of print]	Review of delivery outcomes and vertical transmission of COVID-19. Concluded that there is a low risk of vertical transmission and generally favorable neonatal outcomes.
137	<u>Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study.</u> Yu N, Li W, Kang Q et al Lancet Infect Dis. 2020 May;20(5):559-564. doi: 10.1016/S1473-3099(20)30176-6	The maternal, fetal, and neonatal outcomes of patients who were infected in late pregnancy appeared good, and these outcomes were achieved with intensive, active management that might be the best practice in the absence of more robust data. The clinical characteristics of these patients with COVID-19 during pregnancy were similar to those of non-pregnant adults with COVID-19 that have been reported in the literature.
138	<u>Novel Coronavirus disease (COVID-19) in newborns and infants: What we know so far</u> De Rose D.U., Piersigilli F., Ronchetti M.P., Santisi A., Bersani I., Dotta A., Danhaive O., Auriti C. Italian Journal of Pediatrics 2020 46:1 Article Number 56	A review published on the data published till April 07th, 2020 with an overview of the on SARS-CoV-2 epidemiology, transmission, the associated clinical presentation and outcomes in newborns and infants up to 6 months of life.
139	<u>Managing COVID-19-Positive Maternal-Infant Dyads: An Italian Experience</u> Salvatori G., De Rose D.U., Concato C., Alario D., Olivini N., Dotta A., Campana A. [Article in Press] Breastfeeding medicine : the official journal of the Academy of Breastfeeding Medicine 2020	Two reports of maternal-infant cases describing the clinical Features of newborns with Postnatal Confirmed SARS-CoV-2 infection and their Mothers. Neither the mothers nor the infants any intensive care. The authors stated that, “medical staff and nurses should not only focus on care of COVID-19 mothers and infants, but also protect, promote, and support breastfeeding. Breastfeeding creates a unique relationship between mother and child, thus reducing the length of hospital stay and the negative effects linked to quarantine and stress because of this pandemic.”



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Last updated
27/11/2020

Pregnancy, maternal-fetal and new-born related outcomes

New-born child and management

No.	Publication	Notes
140	<u>Neonatal Resuscitation Where the Mother Has a Suspected or Confirmed Novel Coronavirus (SARS-CoV-2) Infection: Suggestion for a Pragmatic Action Plan</u> Trevisanuto D, Moschino L, Doglioni N, et al. Neonatology. 2020 Apr 24;1-8. doi: 10.1159/000507935. [Epub ahead of print]	Perspective, giving overview for delivery and neonatal resuscitation of neonates born to mothers with COVID-19.
141	<u>Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (First edition)</u> Wang L, Shi Y, Xiao T, et al. Ann Transl Med. 2020 Feb;8(3):47. doi: 10.21037/atm.2020.02.20.	Measures from a Chinese expert working group for a national management plan for helping prevent and control COVID-19 infection.
142	<u>Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection</u> Chen D, Yang H, Cao Y, et al. Int J Gynaecol Obstet. 2020 Mar 20. doi: 10.1002/ijgo.13146. [Epub ahead of print]	Recommendations from a multidisciplinary consensus meeting, gives ten recommendation for the management of COVID-19 in pregnancy, including recommending that staff be trained for infection control.
143	<u>Coronavirus disease (COVID-19) and neonate: What neonatologist need to know</u> Lu Q, Shi Y. J Med Virol. 2020 Mar 1. doi: 10.1002/jmv.25740. [Epub ahead of print]	A review describing current understanding of COVID-19 in newborns and children.
144	<u>Perinatal-Neonatal Management of COVID-19 Infection - Guidelines of the Federation of Obstetric and Gynecological Societies of India (FOGSI), National Neonatology Forum of India (NNF), and Indian Academy of Pediatrics (IAP)</u> Chawla D, Chirla D, Dalwai S, et al. Indian Pediatr. 2020 Jun 15;57(6):536-548. doi: 10.1007/s13312-020-1852-4.	Guidelines from FOGSI, reviewing existing guidelines and literature. Twenty recommendations are given for pregnancies with confirmed infection, neonatal care, prevention and control, diagnosis and general queries.
145	<u>Neonatal Resuscitation and Postresuscitation Care of Infants Born to Mothers with Suspected or Confirmed SARS-CoV-2 Infection</u> Chandrasekharan P, Vento M, Trevisanuto D, et al. Am J Perinatol. 2020 Apr 8. doi: 10.1055/s-0040-1709688. [Epub ahead of print]	Outline of precautions and steps of managing newborns born to COVID-19 infected mothers, discussing different strategies and promoting shared-decision making for management decisions.



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Last updated
27/11/2020

SARS-CoV-2 and early pregnancy risk for fetus

Summary

- Early infection with SARS-CoV-2 is not thought to increase the risk for early pregnancy loss¹⁻³
- Gene expression of the ACE2 receptor in early fetal development suggests the possibility that early fetuses are susceptible to SARS-CoV-2 infection⁵
- Despite a biological potential for adverse outcomes,⁴ in cases of early pregnancy infection with SARS-CoV-2, this has not been demonstrated to be harmful to the developing fetus. Furthermore, amniocentesis of amniotic fluid has been reported as negative via PCR¹⁻⁹



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Last updated
27/11/2020

SARS-CoV-2 and early pregnancy risk for fetus

No.	Publication	Notes
1	<p>Coronavirus disease 2019 and first-trimester spontaneous abortion: a case-control study of 225 pregnant patients. Cosma S, et al. Am J Obstet Gynecol. 2020 Oct 8;S0002-9378(20)31177-7.</p>	<p>SARS-CoV-2 infection during the first trimester of pregnancy did not seem to predispose to early pregnancy loss. There was no difference in incidence of COVID-19 between the cases (11%) and the controls (9.6%). COVID-19 was not an independent predictor of early pregnancy loss. COVID-19 appears to have a favorable maternal course at the beginning of pregnancy, consistent with what has been observed during the second and third trimesters.</p>
2	<p>COVID-19 pandemic effect on early pregnancy: are miscarriage rates altered, in asymptomatic women? Rotshenker-Olshinka K, et al. Arch Gynecol Obstet. 2020 Nov 9;1-7.</p>	<p>113 women came for a first-trimester viability scan in the study period, and 172 in the control period (5-11 weeks gestational age). Pregnancy rate was not different between the two groups (76.1 vs. 80.2% in the pandemic and pre-pandemic groups). No significant difference was seen in the total number of arrested pregnancies or in each type of miscarriage. The COVID-19 pandemic environment does not seem to affect early first-trimester miscarriage rates in asymptomatic patients.</p>
3	<p>SARS-CoV-2 in first trimester pregnancy: a cohort study. Freiesleben N la C, et al. Hum Reprod. 2020 Nov 4;deaa311.</p>	<p>Maternal SARS-CoV-2 infection had no effect on the nuchal translucency thickness and there was no significant increased risk of pregnancy loss for women with SARS-CoV-2 infection in first trimester pregnancy. Evidence concerning COVID-19 in pregnancy is limited. These data show that SARS-CoV-2 infection does not pose a significant threat in first trimester pregnancies.</p>
4	<p>Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its effect on gametogenesis and early pregnancy. Singh B, et al. Am J Reprod Immunol. 2020 Sep 23;e13351</p>	<p>Sixty-two studies were included in the review. There is potential for infection with SARS-CoV-2 in testis, ovaries, and placenta, as they express ACE2 receptor activity. In males, SARS-CoV-2 infection could lead to functional abnormalities leading to spermatogenic failure and male infertility. In females, an alteration of the ACE2 cascade via SARS-CoV-2 infection could lead to impairment in important follicular and luteal processes. There is also evidence of significant placental pathology in SARS-CoV-2 infection, but it is unclear what effects there may be for early pregnancy.</p>



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Last updated
27/11/2020

SARS-CoV-2 and early pregnancy risk for fetus

No.	Publication	Notes
5	<p>Expression of SARS-CoV-2 receptor ACE2 and the protease TMPRSS2 suggests susceptibility of the human embryo in the first trimester. Weatherbee, et al. Open Biol. 2020 Aug;10(8):200162. doi: 10.1098/rsob.200162. Epub 2020 Aug 5.</p>	Human pre-gastrulation embryos were examined to determine the expression patterns of the genes ACE2, encoding the SARS-CoV-2 receptor, and TMPRSS2, encoding a protease that cleaves both the viral spike protein and the ACE2 receptor to facilitate infection. We show expression and co-expression of these genes in the trophoblast of the blastocyst and syncytiotrophoblast and hypoblast of the implantation stages, which develop into tissues that interact with the maternal blood supply for nutrient exchange.
6	<p>COVID-19 and first trimester spontaneous abortion: a case-control study of 225 pregnant patients. Cosma C, et al. medRxiv 2020.06.19.20135749; doi: https://doi.org/10.1101/2020.06.19.20135749</p>	Twenty-three (10.2%) of 225 women tested positive for COVID-19 infection. There was no difference in the cumulative incidence of COVID-19 between the cases (11/100, 11%) and the controls (12/125, 9.6%) (p=0.73). Logistic regression analysis confirmed that COVID-19 was not an independent predictor of abortion (1.28 confidence interval 0.53-3.08). Interpretation COVID-19 infection during the first trimester of pregnancy does not appear to predispose to abortion;
7	<p>SARS-CoV-2 in First Trimester Pregnancy – Does It Affect the Fetus? Freiesleben N C, et al. medRxiv 2020.06.08.20125195; doi: https://doi.org/10.1101/2020.06.08.20125195</p>	Maternal SARS-CoV-2 infection did not seem harmful in first trimester pregnancies. Infection had no effect on the nuchal translucency thickness and women with SARS-CoV-2 antibodies were not overrepresented among women with pregnancy loss
8	<p>The "scar" of a pandemic: Cumulative incidence of COVID-19 during the first trimester of pregnancy. Cosma S, et al. J Med Virol. 2020 Jul 7;10.1002/jmv.26267. doi: 10.1002/jmv.26267. Online ahead of print.</p>	Patients tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin M/immunoglobulin G antibody levels and SARS-CoV-2 detection in sera and nasopharyngeal swab samples. COVID-19 cumulative incidence during the first trimester was of 10.1% with high prevalence of asymptomatic patients (42.8%). Similar to the course of the disease in non pregnant adults, 80% to 90% of infections were not severe.
9	<p>Study of amniotic fluid in pregnant women infected with SARS-CoV-2 in first and second trimester. Is there evidence of vertical transmission? Lorente AMR, et al. J Matern Fetal Neonatal Med. 2020 Aug 30;1-3. doi: 10.1080/14767058.2020.1811669. Online ahead of print.</p>	Two cases of pregnant women with COVID-19 infection during the first and second trimester of gestation in which a PCR study of SARS-CoV-2 in amniotic fluid extracted by amniocentesis is performed to try to determine if there is vertical transmission. In both cases, the PCR result was negative.



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Last updated
27/11/2020