

The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document — including a complete list of sources consulted — please see our [National Health Library and Knowledge Service Summary of Evidence Protocol](#).

QUESTION 198

What is the risk of severe disease during pregnancy?

Question 206 was prepared by the National Health Library and Knowledge Service in collaboration with the Research Subgroup of the National Immunisation Advisory Committee (NIAC).



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NIAC



What is the risk of severe disease in pregnant patients with COVID-19?

Main Points

- 1. Pregnancy is regarded as an underlying medical condition which increases a person's risk of developing severe illness. Specific risk factors include maternal age, obesity, non-white ethnicity, pre-existing medical conditions and pregnancy specific disorders such as gestational diabetes and pre-eclampsia.**
- 2. Pregnancy does not increase susceptibility to SARS-COV-2 but can worsen the clinical course of the disease compared to non-pregnant patients of the same age.**
- 3. Pregnant people with COVID-19 have higher rates of ICU admission but are not at increased risk of death from COVID-19.**
- 4. SARS-COV-2 infection at the time of birth can lead to higher rates of foetal death, pre-term birth, preeclampsia and emergency Caesarean section. There were no additional negative neonatal outcomes seen other than those associated with pre-term birth. Risk of transmission of the disease to neonates is low.**

Please refer to the [National Health Library Levels of Evidence Table](#) used to grade the levels of evidence included below.

☒ Inclusion criteria: Levels 1-5.

Please note that individual studies may not have been critically appraised and that designation at a certain level is not a final determination of the quality of a given study.

Summary of Evidence

Pregnancy is considered an underlying medical condition that increases a person's risk of developing severe illness from COVID-19^{1,3,4}. Risk factors for severe COVID-19 in pregnancy include increasing maternal age, high body mass index (BMI), non-white ethnicity, pre-existing comorbidities, and pregnancy specific disorders such as gestational diabetes and pre-eclampsia^{1,8}.

A number of systematic reviews consider the clinical manifestations and perinatal outcomes of pregnant people with COVID-19^{8,10,12,13,14,15}. Jafari et al found that pregnant patients show the same manifestations of COVID-19 as non-pregnant adult patients.¹²

Allotey et al⁸ found that pregnant and recently pregnant patients were at an increased risk of admission to an intensive care unit, receiving invasive ventilation and extra corporeal membrane oxygenation treatment compared with non-pregnant women of reproductive age. Han et al¹⁰ reported that the rate of ICU admission and intubation in pregnant women suffering from COVID-19 was high; they also reported that the number of maternal deaths accounted for 0.05% - 0.41% of all deaths. A high rate of Caesarean section and preterm delivery was also reported.

Current evidence suggests that pregnancy does not increase susceptibility to SARS-CoV-2 infection but appears to worsen the clinical course of COVID-19 compared with non-pregnant patients of the same age^{2,5,7}.

According to the Royal College of Obstetrics and Gynaecologists in Britain⁶, more than 2/3 of pregnant people with COVID-19 are asymptomatic. Compared to non-pregnant people with COVID-19, pregnant people with COVID-19 have higher rates of ICU admission but are not at increased risk of death from COVID-19.

Hessami et al¹¹ conducted a systematic review of currently available evidence regarding maternal, fetal and neonatal mortality associated with COVID-19 infection. The authors concluded that there seemed to be a relatively small number of maternal mortalities associated with COVID-19 infection and that pregnant people and their foetuses or neonates do not seem to have an increased risk of mortality compared with the general population.

A large population-based cohort study in England¹⁶ published in May 2021 suggests that SARS-CoV-2 infection at the time of birth is associated with higher rates of foetal death, preterm birth, preeclampsia and emergency Caesarean delivery.

Dube et al⁹ investigated mother to child transmission and perinatal outcomes and concluded that the chances of mother to child transmission of the SARS-CoV-2 virus is low. The authors assert that it is unlikely that stillbirth or neonatal death rate are increased in babies born to SARS CoV-2 positive mothers. Symptoms when present in infected neonates were most often mild and outcomes were found to be favourable.

Irish and/or International Guidance

Level 1

[World Health Organization \(2020\) Coronavirus disease \(COVID-19\): Pregnancy and childbirth¹](#)

Pregnant women or recently pregnant women who are older, overweight and have pre-existing medical conditions such as hypertension and diabetes seem to have an increased risk of developing severe COVID-19. When pregnant women develop severe disease, they also seem to more often require care in intensive care units than non-pregnant women of reproductive age.

Due to changes in their bodies and immune systems, it is known that pregnant women can be badly affected by some respiratory infections. Therefore, it is important that pregnant women take precautions to protect themselves against COVID-19, and report possible symptoms including fever, cough or difficulty in breathing to their healthcare provider.

Level 1

[Centers for Disease Control and Prevention \(United States\) \(May 2021\) Pregnant and Recently Pregnant People²](#)

See Section: INCREASED RISK OF SEVERE ILLNESS

Pregnant and recently pregnant people (for at least 42 days following end of pregnancy) are more likely to get severely ill from COVID-19 compared with non-pregnant people. Changes that occur in the body during pregnancy that increase risk for severe illness from respiratory viral infections such as COVID-19 can

¹ World Health Organization (2 September 2020) Coronavirus disease (COVID-19): Pregnancy and childbirth <https://www.who.int/news-room/q-a-detail/coronavirus-disease-COVID-19-pregnancy-and-childbirth> [Accessed 28/05/2021]

² Centers for Disease Control and Prevention (May 2021) Pregnant and Recently Pregnant People. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnant-people.html#ref3> [Accessed 27/05/2021]

continue after pregnancy. For example, increased risk for developing blood clots during pregnancy can continue after pregnancy and increase the risk for severe illness as seen in cases of H1N1 influenza in recently pregnant people.

 Level 1

[Centers for Disease Control and Prevention \(United States\) \(May 2021\) Scientific Evidence for Conditions that Increase Risk of Severe Illness³](#)

This document presents a table of evidence that includes a list of underlying medical conditions that increase a person's risk of severe illness from COVID-19. The inclusion of pregnancy as an underlying condition is designated as "*supported by meta-analysis/systematic review,*" defined as having a significant association in at least one meta-analysis or systematic review.

 Level 1

[European Centers for Disease Prevention and Control \(2021\) Risk factors and risk groups⁴](#)

Severity of COVID-19 is associated with increased age, male sex and pre-existing medical conditions. Underlying health conditions reported among adult patients with severe COVID-19 disease include: diabetes; obesity; hypertension; history of heart failure; ischaemic heart disease; solid organ tumours; chronic obstructive pulmonary disease (COPD); chronic respiratory disease; chronic kidney disease; immunocompromised status; cancer; neurologic conditions; smoking; and pregnancy. Severe disease is defined as ICU or hospital admission, mechanical ventilation, or death.

 Level 1

³ Centers for Disease Control and Prevention (May 2021) Scientific Evidence for Conditions that increase risk of severe illness https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhcp%2Fclinical-care%2Funderlying-evidence-table.html [Accessed 28/05/2021]

⁴ ECDC (2021) Risk factors and risk groups <https://www.ecdc.europa.eu/en/COVID-19/latest-evidence/risk-factors-risk-groups> [Accessed 28/05/2021]

[American College of Obstetricians and Gynecologists \(2021\) Vaccinating Pregnant and Lactating Patients Against COVID-19⁵](#)

See Section: COVID-19 INFECTION RISK IN PREGNANCY

Available data suggest that symptomatic pregnant patients with COVID-19 are at increased risk of more severe illness compared with non-pregnant peers. Although the absolute risk for severe COVID-19 is low, an increased risk of ICU admission, need for mechanical ventilation or ventilatory support and death is reported in pregnant women with symptomatic COVID-19 infection compared with symptomatic non-pregnant women. Pregnant patients with comorbidities such as obesity or diabetes may be at higher risk of severe illness consistent with these comorbidities in the general population. ACOG note that CDC has included pregnancy as a factor that leads to increased risk of severe COVID-19 illness. Similar to the general population, Black and Hispanic individuals who are pregnant have disproportionately higher rates of COVID-19 infection and death. Risk of ICU admission was higher for pregnant Asian and Native Hawaiian or Pacific Islander individuals. These disparities are due to a range of social and structural factors including disparities in socioeconomic status, access to health services, rates of chronic conditions, occupational exposure, systemic racism, and continued health inequities.

 Level 1

[Royal College of Obstetrics and Gynaecology \(Great Britain\) \(2021\) Coronavirus \(COVID-19\) Infection in Pregnancy⁶](#)

5 The American College of Obstetricians and Gynecologists (April 2021) Vaccinating Pregnant and Lactating Patients Against COVID-19. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-COVID-19> [Accessed 28/05/2021]

6 Royal College of Midwives/Royal College of Obstetrics and Gynaecology (19/02/2021) Coronavirus (COVID-19) Infection in Pregnancy
Version 13: updated 19 February 2021. Guidance for healthcare professionals on coronavirus (COVID-19) infection in pregnancy, published by the RCOG, Royal College of Midwives, Royal College of Paediatrics and Child Health, Public Health England and Public Health Scotland.
<https://www.rcog.org.uk/en/guidelines-research-services/guidelines/coronavirus-pregnancy/> [Accessed 28/05/2021]

See 1.5.2: SEVERE ILLNESS WITH COVID-19 IN PREGNANT WOMEN

- More than 2/3 of pregnant women with COVID-19 are asymptomatic.
- Compared to non-pregnant women with COVID-19, pregnant women with COVID-19:
 - have higher rates of intensive care unit (ICU) admission. This may reflect a lower threshold for admission to ICU, rather than more severe disease.
 - are not at increased risk of death from COVID-19, according to the largest systematic review.
 - are however found in more recent data from the United States and Mexico to have a slightly higher risk of death in these specific national healthcare settings.
- Compared to pregnant women without COVID-19, pregnant women with symptomatic COVID-19 requiring hospitalization have overall worse maternal outcomes, including an increased risk of death, although the risk remains very low (in Britain, the maternal mortality rate from COVID-19 is 2.2 per 100,000 maternities).

Evidence Synopsis Resources

 Level 2

[UpToDate \(2021\) COVID-19: Pregnancy issues and antenatal care⁷](#)

See section: COURSE IN PREGNANCY/MATERNAL COURSE

⁷ UpToDate (14/05/2021) COVID-19: Pregnancy issues and antenatal care
<https://www.uptodate.com/contents/COVID-19-pregnancy-issues-and-antenatal-care> [Accessed 28/05/2021]

Evidence suggests that pregnancy does not increase susceptibility to SARS-CoV-2 infection but appears to worsen the clinical course of COVID-19 compared with non-pregnant females of the same age. However, at least one study has reported a higher rate of SARS-CoV-2 infection in pregnant people compared with similarly aged adults and one has reported a lower rate of in-hospital mortality in pregnant patients hospitalized with COVID-19 and viral pneumonia compared with non-pregnant female patients of reproductive age. Limitations of available data include difficulties in distinguishing behavioral from biological determinants of infection susceptibility and differences in infection assessment.

Although most (>90 percent) infected pregnant persons recover without undergoing hospitalization, rapid clinical deterioration can occur, and symptomatic pregnant patients appear to be at increased risk of severe disease and death compared with symptomatic non-pregnant females of reproductive age. Risk factors for severe disease and death in pregnancy include older mean age (especially ≥ 35 years), obesity, and preexisting medical comorbidities—particularly hypertension and diabetes; or, more than one comorbidity.

Maternal death rates of 0.14% to 0.80% have been attributed to COVID-19. This rate appears to be higher than that in uninfected pregnant people but may be a result of under ascertainment of patients with mild or asymptomatic infection and the small number of deaths. In a systematic review, the odds of death in studies of pregnant people with COVID-19 were higher than in uninfected pregnant people (OR 2.85, 95% CI 1.08–7.52) but not higher than in non-pregnant reproductive-age females with COVID-19 (OR 0.96, 95% CI 0.79–1.118).

Irish and/or International Literature

Level 1

[Allotey, J et al \(2020\) Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis⁸](#)

OBJECTIVE: To determine the clinical manifestations, risk factors and maternal and perinatal outcomes in pregnant and recently pregnant women with suspected or confirmed coronavirus disease 2019 (COVID-19).

DESIGN: A living systematic review and meta-analysis.

STUDY SELECTION: Cohort studies reporting the rates, clinical manifestations, risk factors and maternal and perinatal outcomes in pregnant and recently pregnant women with suspected or confirmed COVID-19.

DATA EXTRACTION: At least two researchers independently extracted the data and assessed study quality. Random effects meta-analysis was performed, with estimates pooled as odds ratios and proportions with 95% confidence intervals. All analyses will be updated regularly.

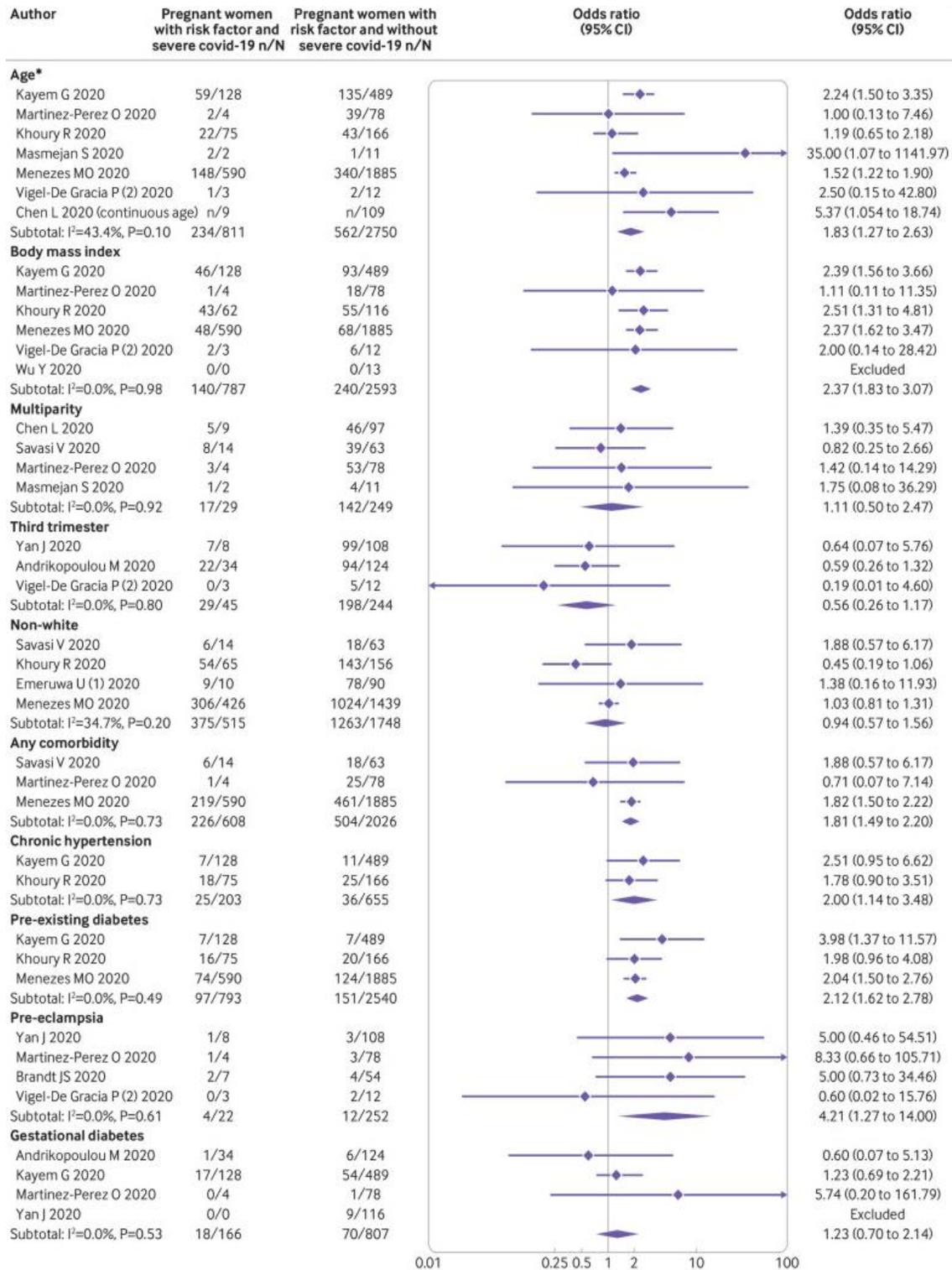
RESULTS: 77 studies were included. Overall, 10% (95% CI, 7% to 14%; 28 studies, 11,432 women) of pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed as having suspected or confirmed COVID-19. The most common clinical manifestations of COVID-19 in pregnancy were fever (40%) and cough (39%). Compared with non-pregnant women of reproductive age, pregnant and recently pregnant women with COVID-19 were less likely to report symptoms of fever (OR 0.43, 95% CI 0.22 to 0.85; 5 studies, 80,521 women) and myalgia (OR 0.48, 95% CI 0.45 to 0.51; 3 studies, 80,409 women)

⁸ Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, Debenham L, Llavall AC, Dixit A, Zhou D, Balaji R, Lee SI, Qiu X, Yuan M, Coomar D, van Wely M, van Leeuwen E, Kostova E, Kunst H, Khalil A, Tiberi S, Brizuela V, Broutet N, Kara E, Kim CR, Thorson A, Oladapo OT, Mofenson L, Zamora J, Thangaratinam S; for PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020 Sep 1;370:m3320. doi: 10.1136/bmj.m3320. PMID: 32873575; PMCID: PMC7459193.

and were more likely to need admission to an Intensive Care Unit (OR 1.62, 95% CI 1.33 to 1.96) and invasive ventilation (OR 1.88, 95% CI 1.36 to 2.60; 4 studies, 91,606 women). 73 pregnant women (0.1%; 26 studies, 11 580 women) with confirmed COVID-19 died from any cause. Increased maternal age (OR 1.78, 95% CI 1.25 to 2.55; 4 studies, 1058 women), high body mass index (OR 2.38, 95% CI 1.67 to 3.39; 3 studies, 877 women), chronic hypertension (OR 2.0, 95% CI 1.14 to 3.48; 2 studies, 858 women), and pre-existing diabetes (OR 2.51, 95% CI 1.31 to 4.80; 2 studies, 858 women) were associated with severe COVID-19 in pregnancy. Pre-existing maternal comorbidity was a risk factor for admission to an Intensive Care Unit (OR 4.21, 95% CI 1.06 to 16.72; 2 studies, 320 women) and invasive ventilation (OR 4.48, 95% CI 1.40 to 14.37; 2 studies, 313 women). Spontaneous preterm birth rate was 6% (95% CI 3% to 9%; 10 studies, 870 women) in women with COVID-19. The odds of any preterm birth (OR 3.01, 95% CI 1.16 to 7.85; 2 studies, 339 women) was high in pregnant women with COVID-19 compared to those without the disease. 25% of all neonates born to mothers with COVID-19 were admitted to the neonatal unit and were at increased risk of admission (OR 3.13, 95% CI 2.05 to 4.78; 1 study, 1,121 neonates) than those born to mothers without COVID-19.

CONCLUSION: Pregnant and recently pregnant women are less likely to manifest COVID-19 related symptoms of fever and myalgia than non-pregnant women of reproductive age and are potentially more likely to need ICU treatment 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 higher in pregnant women with COVID-19 than in pregnant women without the disease.

Figure: Risk factors associated with severe COVID-19 in pregnant and recently pregnant women



[Dube, R et al \(2020\) COVID-19 in pregnancy: the foetal perspective—a systematic review⁹](#)

OBJECTIVE: To determine the effects of confirmed cases of COVID-19 in pregnant women from the foetal perspective by estimation of mother to child transmission, perinatal outcome and possible teratogenicity.

METHODS: A systematic review of the literature.

DATA SOURCES: Eligible studies between 1 November 2019 and 10 August 2020 were retrieved from PubMed, Embase, LitCOVID, Google Scholar, EBSCO MEDLINE, CENTRAL, CINAHL, MedRxiv, BioRxiv and Scopus. English language case reports, case series and cohort studies of SARS-CoV-2 confirmed pregnant women with data on perinatal outcome, congenital anomalies and mother to child transmission were analyzed.

RESULTS: 38 case reports and 34 cohort studies and case series describing 1,408 neonates were included for evidence acquisition of mother to child transmission. 29 case reports and 31 cohort studies and case series describing 1,318 fetuses were included for the evaluation of perinatal outcome and congenital anomalies. A pooled proportion of 3.67% of neonates had positive SARS-CoV-2 viral RNA nasopharyngeal swab results and 7.1% had positive cord blood samples. 11.7% of the placenta, 6.8% of amniotic fluid, 9.6% of faecal and rectal swabs and 0% of urine samples were positive. The rate of preterm labour was 26.4% (OR 1.45, 95% CI 1.03 to 2.03; p=0.03) the rate of and Caesarean delivery (CS) was 59.9% (OR 1.54, 95% CI 1.17 to 2.03; p=0.002). The most common neonatal symptom was breathing difficulty (1.79%). Stillbirth rate was 9.9 per 1,000 total births in babies born to COVID-19 mothers.

CONCLUSION: The chances of mother to child transmission of the SARS-CoV-2 virus is low. The perinatal outcome for the foetus is favourable. There are increased chances of CS, but not of preterm

⁹ Dube R, Kar SS COVID-19 in pregnancy: the foetal perspective—a systematic review *BMJ Paediatrics Open* 2020;4:e000859. doi: 10.1136/bmjpo-2020-000859

<https://bmjpaedsopen.bmj.com/content/4/1/e000859> [Accessed 28/05/2021]

delivery. The stillbirth and neonatal death rates are low. There are no reported congenital anomalies in babies born to SARS CoV-2 positive mothers.

Level 1

[Han, Y et al \(2020\) Clinical manifestation, outcomes in pregnant women with COVID-19 and the possibility of vertical transmission: a systematic review of the current data¹⁰](#)

OBJECTIVES: To assess perinatal outcomes of COVID-19 infections during pregnancy and the possibility of vertical transmission.

METHODS: An analysis was performed using Stata 15.0, and a Q-test was used to evaluate the heterogeneity of the included studies.

RESULTS: The most common symptoms were found to be fever (64.78%), cough (59.81%), and shortness of breath or dyspnea (23.86%). 88.73% of patients demonstrated typical COVID-19 signs on chest CT or X-ray. Intubation was carried out in 35.87% of patients, and 4.95% of mothers were admitted to the Intensive Care Unit, where the rate of maternal death was <0.01% and that of premature delivery was 25.32%. The rate of birth weight being <2,500g was 30.65%, and that of Neonatal Intensive Care Unit admission was 24.41%. Positive nasopharynx swabs or sputum from newborns was <0.01%.

CONCLUSIONS: Pregnant patients with COVID-19 most commonly presented with fever, cough, shortness of breath and dyspnea, most of which possessed imaging manifestations. The risk of intubation and admission to the Intensive Care Unit were high. The risk of premature delivery was higher, leading to a high risk of Neonatal Intensive Care Unit admission and low neonatal birthweight. Vertical transmission of SARS-CoV-2 from mother to child was found to be unlikely.

¹⁰ Han Y, Ma H, Suo M, Han F, Wang F, Ji J, Ji J, Yang H. Clinical manifestation, outcomes in pregnant women with COVID-19 and the possibility of vertical transmission: a systematic review of the current data. *J Perinat Med.* 2020 Nov 26;48(9):912-924. doi: 10.1515/jpm-2020-0431. PMID: 33068387.

[Hessami, K \(2020\) COVID-19 and maternal, fetal and neonatal mortality: a systematic review¹¹](#)

OBJECTIVE: To review currently available evidence regarding maternal, fetal and neonatal mortality associated with coronavirus disease 2019 (COVID-19) infection, up to July 2020.

METHODS: The authors systematically searched PubMed, Scopus, Google Scholar and Web of Science to identify any reported cases of maternal, fetal or neonatal mortality associated with COVID-19 infection.

RESULTS: Of 2,815 studies screened, 10 studies reporting 37 maternal and 12 perinatal mortality cases [7 of fetal demise and 5 of neonatal death] were eligible for inclusion in the review. All maternal deaths were seen in women with previous comorbidities, of which the most common were obesity, diabetes, asthma and advanced maternal age. Acute Respiratory Distress Syndrome (ARDS) and severe pneumonia were the leading causes of maternal mortalities except for one case of thromboembolism during postpartum period. Fetal and neonatal mortalities resulted from the severity of maternal infection or the extent of prematurity, respectively. There was no evidence of vertical transmission or positive COVID-19 test results among expired neonates.

CONCLUSION: Current available evidence suggests that maternal mortality mostly happened among women with previous comorbidities; and that neonatal mortality seems to be a result of prematurity rather than infection. However, further reports are needed so that the magnitude of maternal and perinatal mortality may be determined more precisely.

¹¹ Hessami K, Homayoon N, Hashemi A, Vafaei H, Kasraeian M, Asadi N. COVID-19 and maternal, fetal and neonatal mortality: a systematic review. *J Matern Fetal Neonatal Med.* 2020 Aug 16:1-6. doi: 10.1080/14767058.2020.1806817. Epub ahead of print. PMID: 32799712.

[Jafari, M \(2021\) Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: A systematic review and meta-analysis¹²](#)

In a large-scale study, 128,176 non-pregnant (228 studies) and 10,000 pregnant (121 studies) confirmed COVID-19 cases were included in the meta-analysis. The mean age and gestational age of admission (GA) in pregnant women was 33 years (95% CI, 28-37) and 36 weeks (95% CI, 34-37), respectively. Pregnant women show the same manifestations of COVID-19 as non-pregnant adult patients. Fever (pregnant: 75.5%; non-pregnant: 74%) and cough (pregnant: 48.5%; non-pregnant: 53.5%) are the most common symptoms in both groups, followed by myalgia (26.5%) and chill (25%) in pregnant and dysgeusia (27%) and fatigue (26.5%) in non-pregnant patients. Pregnant women are less probable to show cough (OR 0.7; 95% CI 0.67-0.75), fatigue (OR 0.58; 95% CI 0.54-0.61), sore throat (OR 0.66; 95% CI 0.61-0.7), headache (OR 0.55; 95% CI 0.55-0.58) and diarrhea (OR 0.46; 95% CI 0.4-0.51) than non-pregnant adult patients. The most common imaging found in pregnant women is ground-glass opacity (57%) and in non-pregnant patients consolidation (76%). Pregnant women have higher proportion of leukocytosis (27% *vs.* 14%), thrombocytopenia (18% *vs.* 12.5%) and have lower proportion of raised C-reactive protein (52% *vs.* 81%) compared with non-pregnant patients. Leucopenia and lymphopenia are almost the same in both groups. The most common comorbidity in pregnant patients is diabetes (18%), and in non-pregnant patients is hypertension (21%). Case fatality rate (CFR) of non-pregnant hospitalized patients is 6.4% (4.4-8.5), and all-cause mortality for pregnant patients is 11.3% (9.6-13.3). Regarding the complications

12 Jafari M, Pormohammad A, Sheikh Neshin SA, Ghorbani S, Bose D, Alimohammadi S, Basirjafari S, Mohammadi M, Rasmussen-Ivey C, Razizadeh MH, Nouri-Vaskeh M, Zarei M. Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: A systematic review and meta-analysis. *Rev Med Virol.* 2021 Jan 2:e2208. doi: 10.1002/rmv.2208. Epub ahead of print. PMID: 33387448; PMCID: PMC7883245.

of pregnancy, postpartum hemorrhage (54.5% [7-94]), Caesarean delivery (48% [42-54]), preterm labor (25% [4-74]) and preterm birth (21% [12-34]) are in turn the most prevalent complications. Comparing the pregnancy outcomes show that Caesarean delivery (OR 3; 95% CI 2-5), low birth weight (LBW) (OR 9; 95% CI 2.4-30) and preterm birth (OR 2.5; 95% CI 1.5-3.5) are more probable in pregnant woman with COVID-19 than pregnant women without COVID-19. The most prevalent neonatal complications are Neonatal Intensive Care Unit admission (43% [2-96]), fetal distress (30% [12-58]) and LBW (25% [16-37]). The rate of vertical transmission is 5.3% (1.3-16), and the rate of positive SARS-CoV-2 tests for neonates born to mothers with COVID-19 is 8% (4-16). Overall, pregnant patients present with similar clinical characteristics of COVID-19 when compared with the general population, but they may be more asymptomatic. Higher odds of Caesarean delivery, LBW and preterm birth among pregnant patients with COVID-19 suggest a possible association between COVID-19 infection and pregnancy complications. Low risk of vertical transmission is present, and SARS-CoV-2 can be detected in all conception products, particularly placenta and breast milk. These findings should be interpreted cautiously due to the heterogeneity between studies.

 Level 1

[Papapanou, M \(2021\) Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews¹³](#)

BACKGROUND: A considerable number of systematic reviews with substantial heterogeneity regarding their methods and included populations on the impact of COVID-19 on infected pregnant women and their neonates has emerged.

¹³ Papapanou M, Papaioannou M, Petta A, Routsis E, Farnaki M, Vlahos N, Siristatidis C. Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews. *Int J Environ Res Public Health*. 2021 Jan 12;18(2):596. doi: 10.3390/ijerph18020596. PMID: 33445657; PMCID: PMC7828126.

OBJECTIVE: To describe the obstetric-perinatal and neonatal outcomes of infected pregnant women and their newborns during the COVID-19 pandemic.

METHODS: Three bibliographical databases were searched (last search: September 10, 2020). Quality assessment was performed using the AMSTAR-2 tool. Primary outcomes included mode of delivery, preterm delivery/labor, premature rupture of membranes (PROM/pPROM) and abortions/miscarriages. Outcomes were mainly presented as ranges. A separate analysis, including only moderate and high-quality systematic reviews, was also conducted.

RESULTS: 39 systematic reviews were analyzed. Reported rates, regarding both preterm and term gestations, varied between 52.3% and 95.8% for Cesarean sections; 4.2%-44.7% for vaginal deliveries; 14.3%-63.8% specifically for preterm deliveries, and 22.7%-32.2% for preterm labor; 5.3%-12.7% for PROM and 6.4%-16.1% for pPROM. Maternal anxiety for potential fetal infection contributed to abortion decisions, while SARS-CoV-2-related miscarriages could not be excluded. Maternal ICU admission and mechanical ventilation rates were 3%-28.5% and 1.4%-12%, respectively. Maternal mortality rate was <2%, while stillbirth, neonatal ICU admission and mortality rates were <2.5%, 3.1%-76.9% and <3%, respectively. Neonatal PCR positivity rates ranged from 1.6% to 10%. After accounting for the quality of included studies, ranges of primary outcomes remained almost unchanged; and among secondary outcomes, maternal ICU admission (3%-10%) and mechanical ventilation rates (1.4%-5.5%) were found to be relatively lower

CONCLUSIONS: Increased rates of Caesarean sections and preterm birth rates were found, with iatrogenic reasons potentially involved. In cases of symptomatic women with confirmed infection, high maternal and neonatal ICU admission rates should raise some concerns. The probability of vertical transmission cannot be excluded. Further original studies on women from all trimesters are warranted.

[Servante, J et al \(2021\) Haemostatic and thrombo-embolic complications in pregnant women with COVID-19: a systematic review and critical analysis¹⁴](#)

BACKGROUND: As pregnancy is a physiological prothrombotic state, pregnant women may be at increased risk of developing coagulopathic and/or thromboembolic complications associated with COVID-19.

METHODS: Two biomedical databases were searched between September 2019 and June 2020 for case reports and series of pregnant women with a diagnosis of COVID-19 based either on a positive swab or high clinical suspicion where no swab had been performed. Additional registry cases known to the authors were included. Steps were taken to minimise duplicate patients. Information on coagulopathy based on abnormal coagulation test results or clinical evidence of disseminated intravascular coagulation (DIC) and on arterial or venous thrombosis were extracted using a standard form. If available, detailed laboratory results and information on maternal outcomes were analyzed.

RESULTS: 1,063 women met the inclusion criteria, of which 3 (0.28, 95% CI 0.0 to 0.6) had arterial and/or venous thrombosis, 7 (0.66, 95% CI 0.17 to 1.1) had DIC, and a further 3 (0.28, 95% CI 0.0 to 0.6) had coagulopathy without meeting the definition of DIC. 537 women (56%) had been reported as having given birth and 426 (40%) as having an ongoing pregnancy. There were 17 (1.6, 95% CI 0.85 to 2.3) maternal deaths in which DIC was reported as a factor in two.

CONCLUSIONS: Data suggest that coagulopathy and thromboembolism are both increased in pregnancies affected by COVID-19. Detection of the former may be useful in the identification of women at risk of deterioration.

¹⁴ Servante J, Swallow G, Thornton JG, Myers B, Munireddy S, Malinowski AK, Othman M, Li W, O'Donoghue K, Walker KF. Haemostatic and thrombo-embolic complications in pregnant women with COVID-19: a systematic review and critical analysis. *BMC Pregnancy Childbirth*. 2021 Feb 5;21(1):108. doi: 10.1186/s12884-021-03568-0. PMID: 33546624; PMCID: PMC7863033.

[Yee, J et al \(2020\) Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis¹⁵](#)

A systematic review and meta-analysis which aimed to evaluate the impact of COVID-19 on pregnant women. The authors searched for qualified studies in PubMed, Embase and Web of Science. The clinical characteristics of pregnant women with COVID-19 and their infants were reported as means and proportions with a 95% confidence interval. 11 studies involving 9,032 pregnant women with COVID-19 and 338 infants were included in the meta-analysis. Pregnant women with COVID-19 have relatively mild symptoms. However, abnormal proportions of laboratory parameters were similar or even increased, compared to the general population. Around 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%, whereas neonatal death was found in 0.4%.

 Level 4

[Gurol-Urganci, I et al \(2021\) Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study¹⁶](#)

OBJECTIVE: To determine the association between SARS-CoV-2 infection at the time of birth and maternal and perinatal outcomes.

METHODS: A population-based cohort study in England. The inclusion criteria were women with a recorded singleton birth

15 Yee J, Kim W, Han JM, Yoon HY, Lee N, Lee KE, Gwak HS. Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. *Sci Rep.* 2020 Oct 22;10(1):18126. doi: 10.1038/s41598-020-75096-4. PMID: 33093582; PMCID: PMC7581768.

16 Gurol-Urganci I, Jardine JE, Carroll F, Draycott T, Dunn G, Fremeaux A, Harris T, Hawdon J, Morris E, Muller P, Waite L, Webster K, VAN DER Meulen J, Khalil A. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study. *Am J Obstet Gynecol.* 2021 May 20:S0002-9378(21)00565-2. doi: 10.1016/j.ajog.2021.05.016. Epub ahead of print. PMID: 34023315; PMCID: PMC8135190.

between 29 May 2020 and 31 January 2021 in a national database of hospital admissions. Maternal and perinatal outcomes were compared between pregnant women with a laboratory-confirmed SARS-CoV-2 infection recorded in the birth episode and those without. Study outcomes were fetal death at or beyond 24 weeks' gestation (stillbirth); preterm birth (<37 weeks' gestation); small for gestational age infant (SGA; birthweight <10th centile); preeclampsia/eclampsia; induction of labor; mode of birth; specialist neonatal care; composite neonatal adverse outcome indicator; maternal and neonatal length of hospital stay following birth (3 days or more); and 28-day neonatal or 42-day maternal hospital readmission. Adjusted odds ratios (aOR) and their 95% confidence interval (CI) for the association between SARS-CoV-2 infection status and outcomes were calculated using logistic regression, adjusting for maternal age, ethnicity, parity, pre-existing diabetes, pre-existing hypertension and socioeconomic deprivation measured using Index of Multiple Deprivation 2019. Models were fitted with robust standard errors to account for hospital-level clustering. Analysis of neonatal outcomes was repeated for those born at term (≥ 37 weeks' gestation) since preterm birth has been reported to be more common in pregnant women with SARS-CoV-2 infection.

RESULTS: The analysis included 342,080 women, of whom 3,527 had laboratory-confirmed SARS-CoV-2 infection. Laboratory-confirmed SARS-CoV-2 infection was more common in women who were younger, of non-White ethnicity, primiparous, residing in the most deprived areas, or in women who had comorbidities. Fetal death (aOR, 2.21, 95% CI 1.58–3.11; $P < 0.001$) and preterm birth (aOR 2.17, 95% CI 1.96–2.42; $P < 0.001$) occurred more frequently in women with SARS-CoV-2 infection than those without. Risk of preeclampsia/eclampsia (aOR 1.55, 95% CI 1.29–1.85; $P < 0.001$), birth by emergency Cesarean delivery (aOR 1.63, 95% CI 1.51–1.76; $P < 0.001$) and prolonged admission following birth (aOR 1.57, 95% CI 1.44–1.72; $P < 0.001$) were significantly higher for women with SARS-CoV-2 infection than those without. There were no significant differences in the rate of other maternal

outcomes. Risk of neonatal adverse outcome (aOR 1.45, 95% CI 1.27-1.66; $P < 0.001$), need for specialist neonatal care (aOR 1.24, 95% CI 1.02-1.51; $P = 0.03$), and prolonged neonatal admission following birth (aOR 1.61, 95% CI 1.49-1.75; $P < 0.001$) were all significantly higher for infants with mothers with laboratory-confirmed SARS-CoV-2 infection. When the analysis was restricted to pregnancies delivered at term (≥ 37 weeks), there were no significant differences in neonatal adverse outcome ($P = 0.78$), need for specialist neonatal care after birth ($P = 0.22$) or neonatal readmission within four weeks of birth ($P = 0.05$). Neonates born at term to mothers with laboratory-confirmed SARS-CoV-2 infection were more likely to have prolonged admission following birth (21.1% compared to 14.6%, aOR 1.61, 95% CI 1.49-1.75; $P < 0.001$).

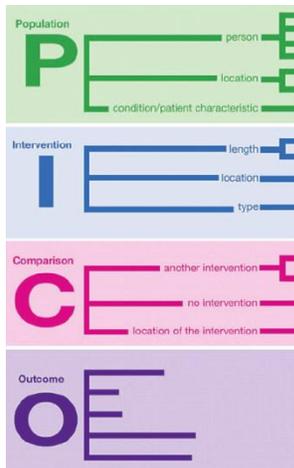
CONCLUSIONS: SARS-CoV-2 infection at the time of birth is associated with higher rates of fetal death, preterm birth, preeclampsia and emergency Caesarean delivery. There were no additional adverse neonatal outcomes, other than those related to preterm delivery. Pregnant women should be counselled regarding risks of SARS-COV-2 infection and should be considered a priority for vaccination.

Produced by the members of the National Health Library and Knowledge Service Evidence Team[†]. Current as at [31 May 2021]. This evidence summary collates the best available evidence at the time of writing and does not replace clinical judgement or guidance. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

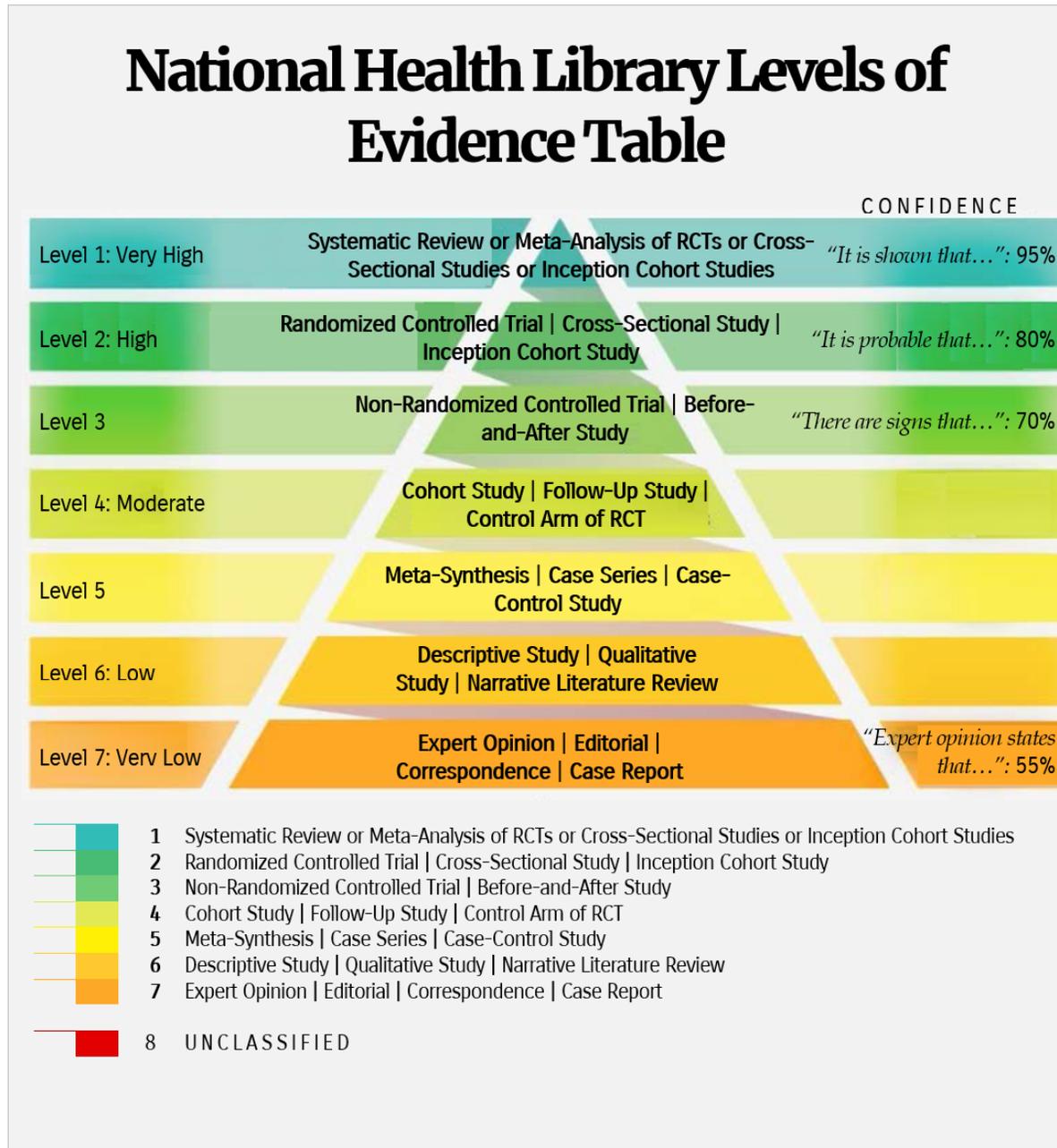


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The following PICO(T) was used as a basis for the evidence summary:



The following schema was used to grade the levels of evidence included:



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