Emerging Evidence on COVID-19

Evidence Brief of Pregnancy and Severity of COVID-19

Introduction

Are pregnant women at higher risk of severe COVID-19 disease than non-pregnant women of reproductive age?

Pregnant women are potentially a vulnerable population, and may be expected to experience different symptoms and disease outcomes compared to the general population due to physiological changes during pregnancy. The objective of this evidence brief was to summarize studies conducted on COVID-19 related outcomes among pregnant women to assess whether there is evidence indicating their COVID-19 disease outcomes are more severe than the general population. This brief focused on COVID-19 disease outcomes and did not summarize birth outcomes or neonate outcomes, and includes studies published up to July 13, 2020.

Key Points

- Studies looking at severity of COVID-19 disease among pregnant women compared to non-infected pregnant women or non-pregnant COVID-19 cases present variable results that are not comparable from one study to the next due to their study design.

- Prospective studies of pregnant women in the population find a low proportion of women were infected with COVID-19 during the initial stage of the epidemic (note this was not compared to infection in the general population). Many COVID-19 positive pregnant women were asymptomatic at the time of enrollment, which ranged from first trimester visits to delivery. Many of these studies report close to zero hospitalizations or severe outcomes (Table 1).

- Prospective and retrospective case series report on a spectrum of COVID-19 disease severity outcomes in pregnant women, with significant heterogeneity across estimates between studies and within the systematic review meta-analyses (Table 2 & 3). Most of these studies did not indicate that the proportions reported were higher or different from the general population. A summary of the range in proportions reported across studies for each outcome is listed below:
    - Severe COVID-19 disease: 5.3% - 26.1%
    - Critical COVID-19 disease: 1.4% - 5%
    - Mortality: 0 – 2.0% / ICU mortality: 15.4%
    - Hospitalized for COVID-19: 0% - 28%
    - Oxygen therapy among hospitalized COVID-19 cases: 7% - 32%
    - ICU overall COVID-19 cases: 2% -10%
    - Mechanical Ventilation overall COVID-19 cases: 2 - 3.4% / ICU: 11 - 61.5%

- o ECMO overall COVID-19 cases: 0.03% - 2.3%
- o Induction of delivery due to COVID-19 disease: 9% - 19.0%

- One study based on USA surveillance data reported that the adjusted risk ratio for hospitalizations among pregnant women during the beginning of the epidemic was 5.4 times that of non-pregnant women of reproductive age (Ellington et al., 2020). This study also reported higher adjusted relative risk of ICU admission 1.5 times and mechanical ventilation 1.7 times, but no difference in the adjusted relative risk of mortality. This data could not distinguish hospitalizations for COVID-19 from other reasons for hospital admission (e.g., pregnancy-related treatment, or labor and delivery, which are common during pregnancy), thus it is unknown what proportion of the risk of hospitalization between pregnant and non-pregnant women can be attributed to pregnancy versus a possible increased risk due to COVID-19 during pregnancy.

- Another large hospital dataset from New York, USA compared the hospitalization rates of weeks one and four of the epidemic between pregnant women [RR 14.81 (95%CI 2.07-107.38) N=3064] and total hospitalizations [RR 46.99 (95% CI, 36.72-60.15) N=21980] (Tekbali et al., 2020). The study concludes that the increase in risk of the general population being hospitalized was more than for pregnant women in the first month of the epidemic. However, without a measure of excess hospitalizations due to COVID-19, these results are difficult to interpret.

- A study from China, documented that pregnant women were more likely to be admitted to the hospital sooner and with more mild symptoms compared to non-pregnant COVID-19 cases, which may bias outcomes such as hospitalization when comparing pregnant women to non-pregnant populations (Wang, Wang, & Xiong, 2020).

- There was no association with COVID-19 status and spontaneous abortion in the first trimester (S. Cosma et al., 2020b).

- There was some indication that women in the third trimester are more likely to have clinical symptoms and be diagnosed with pneumonia related to SARS-CoV-2 infection compared to those in the first trimester (Crovetto et al., 2020).

- Risk factors for severe COVID-19 disease among pregnant women included age>35, comorbidities and/or obesity (Table 2 & 3) (Cohen, Vignaux, & Jacquemard, 2020; Khalil et al.; Vivanti et al., 2020).

Overview of the Evidence

A range of retrospective and prospective case series and cohorts, case-control studies, cross-sectional data from surveillance and systematic reviews of relevant outcomes were identified, and provide evidence for this review. Retrospective observational studies, case reports and case series are considered to have a high risk of bias. The case-control study in this review did not have a large enough sample size to detect a difference between groups. The prospective studies and cohort designs have moderate to low risk of bias. Included

systematic reviews were evaluated using the AMSTAR quality assessment tool, and only reviews of moderate and high quality were summarized as those of low quality were missing key methodological steps. Those systematic reviews that were also evaluated by McMaster Plus are noted along with their quality score.

A large amount of heterogeneity across studies was identified for most outcomes that relate to severity of COVID-19 in pregnant women. This is likely due to variation in where and how the observations were collected, as well as the wide variability in sample size.

CONTENTS

OBSERVATIONAL STUDIES

Observational study data that has exposed and unexposed, diseased and healthy individuals in the sampling frame are needed to address the question of whether pregnant women are at higher risk of severe COVID-19 disease. Recent research from the USA and surveillance data from the CDC (July 16, 2020) suggest that pregnant women are at higher risk of hospitalization (3381/10156), ICU admission (160/3302) and mechanical ventilation (63/2856), but their risk for death is the same. These conclusions are supported by an MMWR paper based on the same surveillance data, in which the authors analyzed COVID-19 outcomes for all women of reproductive age (Ellington et al., 2020). Their analysis reports significantly higher adjusted risk ratios for hospitalization, ICU admittance and mechanical ventilation among women who are pregnant, controlling for age, ethnicity and presence of comorbidities. However, due to the nature of this dataset it is unknown if hospitalization, ICU or mechanical ventilation were due to COVID-19 disease, or due to conditions related to pregnancy.

Another large hospitalizations dataset from New York in the beginning of the epidemic compared the hospitalization rates of pregnant women vs. total hospitalizations (Tekbali et al., 2020). They report that the increased risk of hospitalization for pregnant women over the first four weeks of the epidemic in New York was lower [RR 14.81 (95%CI 2.07-107.38) N=3064] than for the rest of the population [RR 46.99 (95% CI, 36.72-60.15) N=21980] (Tekbali et al., 2020). This analysis did not control for any potential confounders and the results imply that the increased risk of hospitalization was lower during the first four weeks of the epidemic for pregnant women compared to the general population. However, the reasons for this difference were not explored. Another study from China documented that pregnant women were more likely to be admitted to the hospital sooner and with more mild symptoms compared to non-pregnant COVID-19 cases

(Wang et al., 2020). During pregnancy women may be admitted to the hospital for several reasons that would be unrelated to COVID-19 (e.g., to deliver, for pregnancy related complications and illness) which makes it difficult to interpret the high relative risk for hospitalization presented by (Ellington et al., 2020) or the lower increase in risk of hospitalization for pregnant women in the first four weeks of the epidemic in New York (Tekbali et al., 2020).

Several studies prospectively enrolled pregnant women attending the first trimester visit, a third trimester visit, or at delivery during the pandemic. Enrolled women were screened for SARS-CoV-2 infection and the impact of COVID-19 infection was evaluated compared to non-infected pregnant women (S. Cosma et al., 2020a; S. Cosma et al., 2020b; Fassett et al., 2020; Mohr-Sasson et al., 2020; Ruggiero, Somigliana, Tassis, & et al., 2020). There was no evidence that COVID-19 infection is associated with spontaneous abortions [RR 1.28 (95%CI 0.53-3.08)] in first trimester pregnancies (S. Cosma et al., 2020b). Two studies reported infected first trimester pregnancies were largely asymptomatic and none were hospitalized (S. Cosma et al., 2020a; Crovetto et al., 2020). Serological evidence of exposure to SARS-CoV-2 in first trimester and third trimester women report risk of exposure is the same, and that women in the third trimester were more likely to be hospitalized (0% vs. 9%) and treated for pneumonia (0% vs. 4.2%) (Crovetto et al., 2020). Post-partum complications resulting in re-admittance to the hospital was reported to be significantly higher in COVID-19 positive cases 12.9% (N=70) compared to non-COVID-19 controls 4.5% (N=605), p<0.001 (Prabhu et al., 2020). Other studies conclude that most infected pregnant women are not at higher risk of hospitalization compared to non-infected pregnant women (Fassett et al., 2020; Mohr-Sasson et al., 2020). In one study, there was no evidence of an association with COVID-19 status among pregnant women and other risk factors (e.g., age and comorbidities) (Ruggiero et al., 2020).

There were few deaths recorded among the observational studies (Table 1-3) of pregnant women. One study of USA surveillance data concluded that mortality was the same among pregnant and non-pregnant women with COVID-19 of reproductive age (Ellington et al., 2020).

Table 1: Observational studies (cohorts, case control studies), N=10 published June 8- July 10*, that compared pregnant COVID-19 cases to severity outcomes in the general population or severe outcomes in non-infected pregnant groups.

Reference	Country	Dates	Trimester	Study Design	Key outcomes
Primary Research					
(Ellington et al., 2020)	USA	Jan 22- Jun 7	Not specified	Cross-section of surveillance data Data represents 50 states Women age 15-44 with confirmed COVID-19	Hospitalization: pregnant 31.5%, control 5.8% aRR 5.4 (95%CI 5.1-5.6) (Data were not available to distinguish hospitalization for COVID-19–related circumstances (e.g., worsening respiratory status) from hospital

				N=91412 (8207 pregnant)	admission for pregnancy-related treatment or procedures (e.g., delivery).) ICU aRR 1.5 (95%CI 1.2-1,8) Mechanical Ventilation aRR 1.7 (95%CI 1.2-2.4) Mortality : pregnant 0.2% and control 0.2% aRR 0.9 (95%CI 0.5-1.5) *Adjusted for comorbidities, age, ethnicity
(S. Cosma et al., 2020a)	Italy	Apr 16 – Jun 4	1st trimester	Prospective cohort – consecutive pregnant women (n=138) attending their 12 week appointment at a single hospital	Prevalence 10.1% 14/138 (8 seropositive, 6 RT-PCR) None of the patients were hospitalized or treated for pneumonia associated with COVID-19
(Prabhu et al., 2020)	USA	Mar 22-Apr 27	> 20 weeks	Prospective cohort- women (n=675) admitted for delivery at 3 New York hospitals	COVID-19 cases 10.4% (70/675), 55 asymptomatic Readmission for postpartum complication COVID-19 12.9% vs. control 4.5%, p<0.001 ICU 1 No woman had mechanical ventilation No maternal deaths
(Fassett et al., 2020)	USA	Apr 6- May 11	3rd trimester	Prospective Cohort – women (N=3963) admitted to delivery at the KPSC hospitals in southern California	Prevalence COVID-19: 0.43%; 95% CI 0.23-0.63%, (17/3923) All COVID-19 cases were asymptomatic on admission
(Tekbali et al., 2020)	USA	Mar 2- Mar 29	NR	Analysis of the COVID-19 cases collected from a 14 hospital database.(N=21980 admissions of which 3064 were pregnant)	Over the four week period the relative risk of hospital admission for COVID-19 increased: Pregnant: RR 14.81 (95%CI 2.07-107.38) All hospital admissions : RR 46.99 (95% CI, 36.72-60.15) Study does not try to adjust for age or other confounders/risk factors. It is also discussed that reproductive age women are younger and less likely to be symptomatic or get tested, and most of the

					admissions for pregnant women were for labor and delivery
(Mohr-Sasson et al., 2020)	Israel	NR	3rd trimester	Case-control study comparing 11 pregnant COVID-19 cases with 25 age-matched non-pregnant controls. This study was underpowered	Hospitalization 7/11 pregnant vs. 20/25 controls p=0.29, lower admission rate, but not significant Noted clinical measures of severity that were different in the COVID-19 group: • Lymphocyte count to WBC was significantly reduced in the pregnant group compared to the controls [13.6% (4.5–19.3) vs. 26.5% (15.7–29.9); p=0.003, • pCO_2 was significantly lower [39 (31–43 vs.46 (45–57); p=0.004] • base excess was significantly elevated [(−2.9)[(−7.9) − (−1.7)] vs. 0.4(0.05–2); p=0.004]
(Crovetto et al., 2020) *Preprint*	Spain	Apr 14- May 5	1st Trimester (N=372) and 3rd trimester (N=502)	Cohort of pregnant women (N=874) at their first trimester appointment or delivery. Serology, and a questionnaire collected data on previous COVID-19 status	Seropositivity to SARS-CoV-2 were the same in 1st trimester (14.3%) and 3rd trimester patients (14.1%), the authors concluded there is no difference in susceptibility between 1st and 3rd trimester. Hospital admission for COVID-19 was 0% and 9.9% for 1st and 3rd trimester. Severity of COVID-19, 1st vs. 3rd trimester Asymptomatic 70.4% vs. 52.1% Mild: 29.6% vs. 43.7% Pneumonia 0% vs. 4.2% There were higher proportions of symptomatic infections in the 3rd trimester, which is in line with other studies where a high proportion are in the 3rd trimester.

(S. Cosma et al., 2020b)	Italy	Feb 22- May 21	1st trimester	Case control study comparing spontaneous abortion and COVID-19 status	Cumulative incidence of COVID-19 between the cases (11/100, 11%) and the controls (12/125, 9.6%) (p=0.73) was the same. Logistic regression analysis confirmed that COVID-19 was not an independent predictor of abortion (1.28, 95%CI 0.53-3.08).
(RUGGIERO et al., 2020)	Italy	Apr 7 – May 6	3rd trimester	Cohort of all women delivering (N=315) at an obstetrics hospital in Milan	COVID-19 8.9%, 95%CI: 6.2–12.5%, 28/315 There was no difference between the COVID-19 group and the control group in terms of risk factors or disease outcomes.
(Wang et al., 2020)	China	Dec 8 – Apr 1	NR	Retrospective study of 30 pregnant COVID-19 cases and 42 non-pregnant COVID-19 cases in Wuhan	Pregnant women were admitted to the hospital earlier (0.25 vs. 11.00 days; P<0.001), and with milder symptoms. The proportion of asymptomatic pregnant women were 26.7% vs. 0% among non-pregnant COVID-19 cases.

* The most recent systematic review on this topic searched the literature up to June 8, 2020 and is described in Table 2.

aRR= adjusted risk ratio, RR= risk ratio

SYSTEMATIC REVIEWS

There were 38 studies that identified as a systematic review, meta-analysis, scoping review, rapid review or umbrella review and had outcomes on severity of COVID-19 in pregnant women. Only nine of these were considered of moderate or high quality with most reviews failing to describe *a priori* development of a protocol and to a lesser extent other key components of conducting synthesis research.

Studies included in the systematic reviews vary depending on search date, inclusion and exclusion criteria. Most included studies are case reports and case series with some of the newer ones also identifying case control studies. Meta-analysis or raw data on the proportions of hospitalization, severe/critical COVID-19, ICU admission, oxygen therapy, mechanical ventilation and death are reported in the systematic reviews and most have a significant amount of heterogeneity across studies (Table 2). A comparable proportion in a non-pregnant population was not reported in most reviews as the data is based largely on case series. Sources of heterogeneity likely include the selection procedure for inclusion in a study, e.g., prospective enrollment, retrospective medical records, or just a summary of a couple of cases without details of selection. There is also likely

variation depending on the spectrum of COVID-19 severity, outpatient clinic vs. hospital case selection, admittance to labor and delivery or hospitalized for COVID-19.

Table 2: Summary of the findings of systematic reviews evaluated to be of moderate or high quality (9/38) using the AMSTAR quality assessment tool with outcomes relevant to severity of COVID-19 in pregnant women.

Reference	Study Design	Quality (AMSTAR)	# Studies/ Observations/ Details	Key Outcomes
Systematic Review				
(Khalil et al., 2020)	Systematic Review and meta-analysis. Search data June 8, 2020.	High	17 studies with > 15 observations (86 included in qualitative summary) global/ 25676 pregnancies/ most women were in the 3rd trimester or post partum	Asymptomatic: 253/1205, 14.5% (5.6–32.5%), I^2=97.0% Prevalence of Risk Factors across samples: • Obesity 509/1725, 38.2% (23.6–55.4%), I^2=97% • Any co-morbidity 252/776, 32.5% (29.3–35.8%), I^2=0% ICU: 159/1591, 7% (95%CI 4-11), I^2=82% Oxygen Support: 295/1623, 18.2% (9.8–31.1%), I^2=95.5% Mechanical Ventilation 92/1680, 3.4% (1.5–7.7%), I^2=90.2% ECMO 13/1896, 0.7% (0.4–1.2%), I^2=0.0% Mortality 43/2650, 0.9% (0.3–2.9%), I^2=84.4% Deliver due to COVID-19 related reason: 95/497, 19.0% (8.9–36.0%), I^2=89.4% - ICU in pregnant women with COVID-19 was ~7% across studies for pregnant women, which is higher than 4.2% (CDC COVID-19 Response Team, 2020) reported by USA surveillance data for the reproductive age group. - ICU admittance was associated with older age (>35) and comorbidities (p<0.05). Trimester of pregnancy, ethnicity and obesity did not explain the heterogeneity in ICU or maternal death.
(Trippella et al., 2020)	Systematic Review. Search	Moderate	37 (China and Other countries)/275	Oxygen therapy: 36/275 (13%) ICU: 10/275 (4%) Mechanical ventilation: 5/275 (2%)

	date April 18, 2020. Includes epidemiological studies, case reports	(9/10 McMaster Plus)	pregnancies, 239 deliveries	ECMO: 1/275 (0.03%) Mortality: 1/275 (0.03%) The majority of pregnant women had mild or moderate disease with a low incidence of severe complications and low mortality rates.
(Huntley et al., 2020)	Systematic Review. Reports of >10 observations. Search date April 29, 2020. Includes mainly case reports and case series.	High (9/10 McMaster Plus)	13 (China, US, Italy, Data Jan-Apr 4)/538 pregnancies % 438 deliveries	Mild COVID-19: 86.1% (81.5–89.7) Severe COVID-19: 15.3% (11.1–20.8) ICU admission: 3.0% (95% CI 1.6–5.9, 8/263) Critical disease: 1.4% (95% CI 0.5–4.1, 3/209) Deaths: 0% (95% CI 0.0–1.1, 0/348) Approximately 1 in 3 pregnant women with SARS-CoV-2 had a comorbidity across studies.
(Juan et al., 2020)	Systematic Review. Search date April 20, 2020. Includes 9 case series and 15 case reports.	Moderate (8/10 McMaster Plus)	24 (China, Australia, Canada, France, Korea, Iran, Italy, Sweden, Turkey, USA)/324 pregnancies/ maternal age 20-44 and gestational age 5-41 weeks	Severe pneumonia 0-14% across studies, most admitted to ICU One case series from Iran of severe COVID-19 pregnant women had 7 death/9 ICU admitted cases on mechanical ventilation. This review also summarizes comorbidities and reports the frequency to be similar to the general population.
(Gao, Ye, & Zhang, 2020) *Preprint*	Systematic Review. Search Date April 16,	Moderate	14 (China, USA)/ 236 pregnancies	Pregnant Women Severe case or death MA: 12%, 95%CI: 0.03~0.20, I^2 =0%, P=0.006 Co-morbidities MA: 33%, 95%CI: 0.21~0.44, I^2=70%, P=0.000

	2020. Only studies with >5 observations. Includes case reports, case series and observational studies			
(Smith et al., 2020)	Systematic Review. Search date March 28, 2020 Includes: case series and 1 controlled before and after study design.	Moderate (8/10 McMaster Plus)	9 (China)/ 92 pregnancies	Hospitalized:34.7%, 32/92 Oxygen therapy: 28.1%, 9/32 hospitalized ICU: 3.1%, 1/32 hospitalized Mortality: 0/32 Many pregnant women captured across these studies were asymptomatic and afebrile at presentation. Lymphopenia: 66.7% (similar to SARS 67% and MERS 50%) and was NOT associated with worse prognosis in pregnant women. ICU and mortality for pregnant women with SARS-CoV-2 appears lower than for SARS (15-18%/30%) and MERS (25-27%/ 60%)
(Yang, Wang, Zhu, & Liu, 2020)	Systematic Review. Search date March 26, 2020 Includes case reports, case series and 1 case control.	Moderate	18/114 pregnancies	Severe/Critical: 5.3%, 6/114 ECMO 0.9%: 1/114 The only case-control study suggested no differences in preeclampsia, gestational diabetes mellitus, and premature rupture of membrane between COVID-19 and non-COVID-19 groups. In general, the clinical characteristics of pregnant women are similar to those of non-pregnant adults
(Gajbhiye, Modi, & Mahale, 2020) *Preprint*	Systematic Review. Search Date May 3, 2020.	Moderate	50 (china, USA, Iran, Australia, Canada, Korea, Honduras, Jordan, Spain, Peru, Sweden,	ICU with mechanical ventilation: 11% Oxygen therapy: 24% ECMO: 2.3%, 10/441 Deaths: 2.0%, 9/441

	Includes case series, case reports.		Turkey, Italy, Portugal, Switzerland, India)/ 441 pregnancies, 387 deliveries/ 95% of the women were in the 3rd trimester	
(Sun et al., 2020) *Preprint*	Systematic Review. Search Date March 11, 2020.	High	17/ 21 SARS, 11 MERS, 41 COVID-19 pregnancies	Hospital stay >15 days: COVID-19 (50% [95%CI -0·19-1·19], p＞0·05) MERS: (80% [95%CI 0·45-1·15], p＜0·05) Fatality Rate COVID-19: 0% MERS: 40% ([95%CI -0·03-0·83], p＞0·05) SARS: 25% ([95%CI 0·01-0·49], p＜0·05)

CASE SERIES

Case series and case reports are the most common study design used to describe COVID-19 impacts on pregnancy. As this review question was about whether there is more severe COVID-19 disease among pregnant women we targeted new case series with more than 30 observations. There were 16 case reports published between June 8-July 10 that were excluded by this cut point.

Table 3: Case series (>30 women) published June 8- July 10 summarizing the probability of severe outcomes in pregnant COVID-19 cases.

Reference	Country	Dates	Trimester	Study Design	Key outcomes
Primary Research					

(Cohen et al., 2020)}	France	Not specified	1-3 (27 weeks median, range 4-34)	Survey of pregnant women with COVID-19 in France (self-identified) N=194. Only data on RT-PCR confirmed cases was analysed, N= 88. Recruitment bias	Hospitalization 18/88 (20%) Severe disease with oxygen therapy 6/88 (7%) Uterine contractions 15/88 (2 severe) Delivery: 14/88 (1 severe) Severe disease was seen in older women p=0.009., higher BMI p=0.002, and those with diabetes (50% vs. 5%) p=0.006
(Vivanti et al., 2020)	France	Mar 12- Apr 13	14 weeks and 2 days postpartum	Retrospective multicenter review of medical records (N=100)	Hospitalized 52/100 ICU 10/100 Oxygen therapy 32/100 Risk factors for hospitalization: - BMI high vs. lower p=0.003 - Not significant were maternal age, gestational age, parity, and comorbidities.
(Sentilhes et al., 2020)	France	Mar 1- Apr 3	NR	Retrospective case series of all pregnant women with COVID-10 (N=54) in Strasbourg	Oxygen therapy 24.1%, 13/54 Mechanical ventilation in 3/13 ECMO 1/13 Medically indicated premature birth (>37 weeks) due to severe COVID-19: 5/54
(Lokken, Walker, & Adams Waldorf, 2020)	USA	Jan21- Apr 17	2nd trimester (N=20), 3rd trimester (N=23)	Retrospective Case series of pregnant women with hospital entries for COVID-19 (N=46) in Washington State hospitals	Severe 15%, 6/46 (all overweight or with comorbidities) Hospitalization: 16%, 7/46 ICU 1/46
(Khoury et al., 2020)	USA	Mar 13 – Apr 12	Term	Prospective cohort of COVID-19 cases (N=241) that gave birth across 5 New York medical centers	Asymptomatic 42.1%, 102/241 Mild 26.5%,, 64/241 Severe 26.1%, 63/241 Critical 5%, 12/241 ICU 7.1%, 17/241 Mechanical ventilation 3.7%, 9/241 Deaths 0%

					Risk Factors: BMI was associated with severity p=0.001
(Blitz et al., 2020)	USA	Mar 1- May 6	NR	Case Series of COVID-19 confirmed cases in pregnant women (N=462) in 10 hospitals in New York state	Severe or critical 15.2% 70/462 ICU 18.6%, 13/70 Deaths 15.4%, 2/13 (and overall) Invasive mechanical ventilation 61.5%, 8/13 5 emergency deliveries were performed in the ICU cases prior to invasive mechanical ventilation due to COVID-19 symptoms.
(San-Juan et al., 2020)	Spain	Mar 5- Apr 6	2nd trimester (N=9), 3rd trimester (N=22)	Retrospective cohort, patients enrolled at diagnosis (N=52)	COVID-19 pneumonia was diagnosed in 61.5%, 32/54 Oxygen therapy 56%,18/32 ARDS 25%, 8/32 ICU 6.4%, 2/32 Mortality 0/32

* The most recent systematic review on this topic searched the literature up to June 8, 2020 and is described in Table 2.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: pregnancy or pregnant or maternal
This review contains research published up to July 14, 2020
Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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References

Blitz, M. J., Rochelson, B., Minkoff, H., Meirowitz, N., Prasannan, L., London, V., Nimaroff, M. (2020). Maternal mortality among women with COVID-19 admitted to the intensive care unit. *American Journal of Obstetrics and Gynecology,* doi:10.1016/j.ajog.2020.06.020

CDC COVID-19 Response Team. (2020). Severe outcomes among patients with coronavirus disease 2019 (COVID-19) - united states, february 12-march 16, 2020. *MMWR.Morbidity and Mortality Weekly Report, 69*(12), 343-346. doi:10.15585/mmwr.mm6912e2 [doi]

Cohen, J., Vignaux, O., & Jacquemard, F. (2020). Covid-19 in pregnant women: General data from a french national survey. *Eur J Obstet Gynecol Reprod Biol, 251*, 267-268. doi:10.1016/j.ejogrb.2020.06.002

Cosma, S., Borella, F., Carosso, A., Sciarrone, A., Cusato, J., Corcione, S., Benedetto, C. (2020a). The "scar" of a pandemic: Cumulative incidence of COVID-19 during the first trimester of pregnancy. *J Med Virol,* doi:10.1002/jmv.26267

Cosma, S., Carosso, A., Cusato, J., Borella, F., Carosso, M., Bovetti, M., Benedetto, C. (2020b). COVID-19 and first trimester spontaneous abortion: A case-control study of 225 pregnant patients. *Medrxiv,* , 2020.06.19.20135749. doi:10.1101/2020.06.19.20135749

Crovetto, F., Crispi, F., Llurba, E., Figueras, F., Gomez-Roig, M., & Gratacos, E. (2020). Seroprevalence and clinical spectrum of sars-cov-2 infection in the first versus third trimester of pregnancy. *Medrxiv,* , 2020.06.17.20134098. doi:10.1101/2020.06.17.20134098

Ellington, S., Strid, P., Tong, V. T., Woodworth, K., Galang, R. R., Zambrano, L. D., Gilboa, S. M. (2020). Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - united states, january 22-june 7, 2020. *MMWR Morb Mortal Wkly Rep, 69*, 769-775. doi:10.15585/mmwr.mm6925a1

Fassett, M. J., Lurvey, L. D., Yasumura, L., Nguyen, M., Colli, J. J., Volodarskiy, M., Getahun, D. (2020). Universal SARS-cov-2 screening in women admitted for delivery in a large managed care organization. *Am J Perinatol,* doi:10.1055/s-0040-1714060

Gajbhiye, R., Modi, D., & Mahale, S. (2020). Pregnancy outcomes, newborn complications and maternal-fetal transmission of SARS-CoV-2 in women with COVID-19: A systematic review of 441 cases. *Medrxiv,* , 2020.04.11.20062356. doi:10.1101/2020.04.11.20062356

Gao, Y., Ye, L., & Zhang, J. (2020). Clinical features and outcomes of pregnant women with COVID-19: A systematic review and meta-analysis. *Research Square Prepub,* Retrieved from https://www.researchsquare.com/article/rs-27148/v1

Huntley, B. J. F., Huntley, E. S., Di Mascio, D., Chen, T., Berghella, V., & Chauhan, S. P. (2020). 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. *Obstet Gynecol,* doi:10.1097/aog.0000000000004010

Juan, J., Gil, M. M., Rong, Z., Zhang, Y., Yang, H., & Poon, L. C. (2020). Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: Systematic review. *Ultrasound Obstet Gynecol, 56*, 15-27. doi:10.1002/uog.22088

Khalil, A., Kalafat, E., Benlioglu, C., O'Brien, P., Morris, E., Draycott, T., Magee, L. A.SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. *Eclinicalmedicine,* doi:10.1016/j.eclinm.2020.100446

Khoury, R., Bernstein, P. S., Debolt, C., Stone, J., Sutton, D. M., Simpson, L. L., Dolan, S. M. (2020). Characteristics and outcomes of 241 births to women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at five new york city medical centers. *Obstetrics and Gynecology,* doi:10.1097/AOG.0000000000004025

Lokken, E. M., Walker, C. L., & Adams Waldorf, K. M. (2020). Estimating frequency of severe disease in pregnant patients with COVID-19. *American Journal of Obstetrics and Gynecology,* doi:10.1016/j.ajog.2020.06.027

Mohr-Sasson, A., Chayo, J., Bart, Y., Meyer, R., Sivan, E., Mazaki-Tovi, S., & Yinon, Y. (2020). Laboratory characteristics of pregnant compared to non-pregnant women infected with SARS-CoV-2. *Arch Gynecol Obstet,* doi:10.1007/s00404-020-05655-7

Prabhu, M., Cagino, K., Matthews, K. C., Friedlander, R. L., Glynn, S. M., Kubiak, J. M., Riley, L. E. (2020). Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in new york city: A prospective cohort study. *Bjog,* doi:10.1111/1471-0528.16403

RUGGIERO, M., SOMIGLIANA, E., TASSIS, B., & et al. (2020). Covid-19 in the second half of pregnancy: Prevalence and clinical relevance. *Research Square Prepub,* Retrieved from https://www.researchsquare.com/article/rs-34492/v1

San-Juan, R., Barbero, P., Fernández-Ruiz, M., López-Medrano, F., Lizasoáin, M., Hernández-Jiménez, P., Aguado, J. M. (2020). Incidence and clinical profiles of COVID-19 pneumonia in pregnant women: A single-centre cohort study from spain. *Eclinicalmedicine,* doi:10.1016/j.eclinm.2020.100407

Sentilhes, L., De Marcillac, F., Jouffrieau, C., Kuhn, P., Thuet, V., Hansmann, Y., Deruelle, P. (2020). COVID-19 in pregnancy was associated with maternal morbidity and preterm birth. *American Journal of Obstetrics and Gynecology,* doi:10.1016/j.ajog.2020.06.022

Smith, V., Seo, D., Warty, R., Payne, O., Salih, M., Chin, K. L., Wallace, E. (2020). Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *PLoS One, 15*, e0234187. doi:10.1371/journal.pone.0234187

Sun, P., Gao, H., Huang, X., Zheng, H., Cai, H., Tan, W., Luo, D. (2020). Comparison of perinatal outcomes of pregnant women with SARS, MERS and COVID-19: A systematic review and meta-analysis. *SSRN- Lancet Prepublication,* Retrieved from https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3582809

Tekbali, A., Grünebaum, A., Saraya, A., McCullough, L., Bornstein, E., & Chervenak, F. A. (2020). PMC7158836; pregnant vs nonpregnant severe acute respiratory syndrome coronavirus 2 and coronavirus disease 2019 hospital admissions: The first 4 weeks in new york. *Am J Obstet Gynecol, 223*, 126-127. doi:10.1016/j.ajog.2020.04.012

Trippella, G., Ciarcià, M., Ferrari, M., Buzzatti, C., Maccora, I., Azzari, C., Chiappini, E. (2020). COVID-19 in pregnant women and neonates: A systematic review of the literature with quality assessment of the studies. *Pathogens, 9*, 1-29. doi:10.3390/pathogens9060485

Vivanti, A. J., Mattern, J., Vauloup-Fellous, C., Jani, J., Rigonnot, L., El Hachem, L., Cordier, A. G. (2020). Retrospective description of pregnant women infected with severe acute respiratory syndrome coronavirus 2, france. *Emerg Infect Dis, 26* doi:10.3201/eid2609.202144

Wang, Z., Wang, Z., & Xiong, G. (2020). Clinical characteristics and laboratory results of pregnant women with COVID-19 in wuhan, china. *Int J Gynaecol Obstet,* doi:10.1002/ijgo.13265

Yang, Z., Wang, M., Zhu, Z., & Liu, Y. (2020). Coronavirus disease 2019 (COVID-19) and pregnancy: A systematic review. *J Matern Fetal Neonatal Med,* , 1-4. doi:10.1080/14767058.2020.1759541