



LJMU Research Online

Sathian, B, Banerjee, I, Mekkodathil, AA, van Teijlingen, ER, Pizarro, AB, Asim, M, Mancha, MA, Kabir, R, Simkhada, PP, do Nascimento, IJB and Al Hamad, H

Epidemiologic characteristics, clinical management, and public health implications of Coronavirus Disease 2019 (COVID-19) in pregnancy: A Systematic Review and Meta-analysis.

<https://researchonline.ljmu.ac.uk/id/eprint/17294/>

Article

Citation (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

Sathian, B ORCID logo[ORCID: https://orcid.org/0000-0003-0851-4762](https://orcid.org/0000-0003-0851-4762),
Banerjee, I ORCID logo[ORCID: https://orcid.org/0000-0003-2880-4695](https://orcid.org/0000-0003-2880-4695),
Mekkodathil, AA ORCID logo[ORCID: https://orcid.org/0000-0001-8431-8937](https://orcid.org/0000-0001-8431-8937),
van Teillinden. ER ORCID logo[ORCID: https://orcid.org/0000-0001-5523-](https://orcid.org/0000-0001-5523-)

LJMU has developed **LJMU Research Online** for users to access the research output of the University more effectively. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LJMU Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain.

The version presented here may differ from the published version or from the version of the record. Please see the repository URL above for details on accessing the published version and note that access may require a subscription.

For more information please contact researchonline@ljmu.ac.uk

<http://researchonline.ljmu.ac.uk/>

Epidemiologic characteristics, clinical management, and public health implications of Coronavirus Disease 2019 (COVID-19) in pregnancy: A Systematic Review and Meta-analysis

Brijesh Sathian¹, Indrajit Banerjee², Ahammed A Mekkodathil³, Edwin R. van Teijlingen⁴, Ana Beatriz Pizarro⁵, Mohammad Asim⁶, Maraeh Angela Mancha⁷, Russell Kabir⁸, Padam Simkhada⁹, Israel Júnior Borges do Nascimento¹⁰, Hanadi Al Hamad¹¹

Abstract:

Background: The novel Coronavirus Disease 2019 (COVID-19) outbreak, caused by the pathogenic severe acute respiratory syndrome-2 (SARS-CoV-2) virus, is exponentially spreading across the globe.

Methods: The current systematic review was performed utilising the following electronic databases PubMed, MEDLINE and EMBASE. We searched for the keywords "COVID-19 AND "pregnancy" between January 1, 2020 until December 31, 2020.

Results: Out of 4005 records which were identified, 36 original studies were included in this systematic review. Pooled prevalence of vertical transmission was 10%, 95% CI: 4-17%. Pooled prevalence of neonatal mortality was 7%, 95% CI: 0-21%.

Conclusion: The contemporary evidence suggests that the incubation period of COVID-19 is 2-14 days, and this infection could be transmitted even from the infected asymptomatic individuals. It is found that the clinical presentation of pregnant women with COVID-19 infection is comparable with the infected non-pregnant females, and the frequent symptoms were fever, cough, myalgia, sore throat and malaise. Some cases have severe maternal morbidity and perinatal deaths secondary to COVID-19 infection. Under these circumstances, pregnant women should focus on maintaining personal hygiene, proper nutrition and extreme social distancing to reduce the risk of COVID-19. Therefore, systematic data reporting for evidence based clinical assessment, management and pregnancy outcomes is essential for preventing of COVID-19 infection among pregnant women.

Keywords: Pandemic, Pregnancy, Childbirth, Complications, Clinical Management, Prevention

Correspondence: Dr. Brijesh Sathian, Scientist, Geriatrics and long term care Department, Rumailah Hospital, Doha, Qatar.

Email: drsathian@gmail.com

Received 05 Mar 2021/**Revised** 29 Sept 2021/**Accepted** 03 Oct 2021

Citation: Sathian B, Banerjee I, Mekkodathil AA, van Teijlingen ER, Pizarro AB, Asim M, Mancha MA, Kabir R, Simkhada P, Borges do Nascimento IJ, Al Hamad H. Epidemiologic characteristics, clinical management and public health implications of Coronavirus Disease 2019 (COVID-19) in pregnancy: A Systematic Review and Meta-analysis. Nepal J Epidemiol. 2021;11(4); 1103-1125.

DOI: 10.3126/nje.v11i4.41911

This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

Copyright © 2021 CEA& INEA. Published online by NepJOL-INASP.

www.nepjol.info/index.php/NJE

Introduction

The current pandemic of novel coronavirus disease 2019 (COVID-19) has accounted for more than 3 million infections with over 210,000 infection-related deaths worldwide [1]. It is considered a severe public health emergency due to a higher rate of infectivity and deadly nature affecting all ages and both genders. Particularly vulnerable populations including pregnant women, the elderly, adults with co-morbidities and paediatrics, are at increased risk of complications. Inadequate healthcare resources and workforce can further compromise the care of vulnerable individuals. The substantial morbidity associated with the disease and potential socioeconomic impact necessitates the implementation of drastic preventive measures across all continents, such as nationwide lockdowns and closure of borders. Notably, the current evidence suggests that COVID-19 infection has significant impacts on pregnant women and fetuses similar to the risk of complications associated with the 2009 pandemic of H1N1 influenza virus among pregnant women and the severe effects of Zika virus infections on foetal outcomes [2-5]. Concerning the maternal immune system during pregnancy, there is a cell-mediated immunity shift from T-helper 1 (Th1) towards the proliferation of T-helper 2 (Th2) cells which safeguard the foetus, but at the same time keeps the mother more vulnerable to infections, which the Th1 immune system can better protect. The unique immune system changes during pregnancy necessitate an integrated multispecialty approach for managing COVID-19 positive pregnant females. The current literature reported that the outcomes of 55 COVID-19 positive pregnant females and 46 newborns did not suggest the possibility of mother-to-foetus transmission of SARS-CoV-2 infection [6]. Similarly, the International Society of Infectious Disease in Obstetrics and Gynecology (ISIDOG) guidelines also suggested no indication of vertical transmission of COVID-19 during the second or third trimester of pregnancy [7].

The rapid onset of the COVID-19 outbreak significantly impacts the medical and public health facilities. So vulnerable groups, including pregnant women, should focus on infection prevention and management through strategic preparedness and evidence-based response planning. In the previous Ebola outbreak, clinicians are often cautious about treating or providing vaccination to pregnant women considering the foetal outcomes [8]. It is crucial to ensure that women receive substantial life-saving treatment despite the threat of a contagious disease unless there is a serious clinical contraindication. Moreover, it is necessary to carefully assess the potential benefits and risks of the interventions prior to clinical-decision making to treat infected pregnant women. As

surveillance systems for COVID-19 positive patients are being established, it is crucial to analyse the maternal and foetal outcomes during pregnancy.

Interestingly, in the current COVID-19 outbreak, proportionally, more men are affected than women [9]. This gender disparity can be attributed to the variability in the reporting system, susceptibility of exposure, screening and diagnosis of infection. Notably, the frequently reported symptoms of COVID-19 are cough (82%), fever (83%) and shortness of breath (31%) among hospitalised patients and elderly males with associated co-morbidities are more likely to show severe respiratory distress [10]. As there is limited published data, the possible susceptibility of pregnancy towards COVID-19 infection or the potential risk of miscarriage or foetal anomalies remains unclear.

Methodology

Literature Searches

The current systematic literature review was performed utilising electronic databases PubMed, MEDLINE and EMBASE. We searched for the keywords "COVID-19 AND "pregnancy" between January 1, 2020, until December 31, 2020. Due to the rapid onset of the COVID-19 pandemic, literature is scarce on this topic, so all articles were considered for analysis. Medical subject headings (MeSH) terms used were "2019-nCoV" [Title/Abstract] OR "2020-nCov" [Title/Abstract] OR "2019-20 coronavirus*" [Title/Abstract] OR "2019-2020 coronavirus*" [Title/Abstract] OR "2019 coronavirus*" [Title/Abstract] OR "coronavirus* 2019" [Title/Abstract] OR "2020 coronavirus*" [Title/Abstract] OR "coronavirus* 2020" [Title/Abstract] OR "SARS-CoV-2" [Title/Abstract] OR "SARS coronavirus 2" [Title/Abstract] OR "COVID-19" [Title/Abstract] OR "COVID-2019" [Title/Abstract] OR "coronavirus disease 2019" [Title/Abstract] OR "coronavirus disease 2020"[Title/Abstract])) AND "Pregnancy". All the extracted relevant articles were considered for the review analysis. All research articles describing the epidemiology, clinical characteristics and management of COVID-19 in pregnancy were included during the mentioned period.

Inclusion/Exclusion Criteria

We included all published articles in the English language accessible on electronic databases and specific institutional sites. The retrieved articles were independently assessed and evaluated by five authors for inclusion. This process resulted in the selection of 36 articles related to clinical characteristics and management of COVID-19 in pregnancy for this review [11-46]. We have also utilised the bibliography of the retrieved articles (this process is also known as hand-searching), to look for other suitable associated articles for cross-referencing.

Data Extraction

Databases PubMed, MEDLINE and EMBASE were initially searched thoroughly for appropriate titles. The selected titles were then screened for the abstracts and full texts. Articles that met the eligibility requirements were considered for this systematic review. Five researchers independently conducted the literature evaluation (BS, HAIH, IB, MA, and AA). The extracted data include study authors, year, Sample size Study design, Confirmed SARS-CoV-2, Vertical transmission, Maternal mortality, Neonatal mortality, Age, Gestational Age (delivery), Maternal comorbidities, Clinical features- Fever on admission Fever after childbirth, Cough, Malaise, Dyspnea, Myalgia, Sore Throat, Diarrhoea, Laboratory characteristics, CT scan, Treatment, Delivery characteristics, Maternal outcome and Neonatal outcome.

Methodology Quality Assessment

The selected studies were assessed for methodological quality based on study design, case ascertainment, case definition, patient population, and the methodology description. We used the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical Cohort studies, with 11 domains assessing, similarity between groups, the similarity between exposures, validity and reliability of the exposure, confounding factors, freedom of the outcome, measurement of the outcomes, follow-up time and statistical analysis.

Data Analysis and Synthesis

Prevalence was calculated for categorical variables. The decision to select either fixed effect or random effects model depended on the results of statistical tests for heterogeneity. Data heterogeneity was assessed using the Cochrane Q homogeneity test (significance set at $p < 0.10$). If the studies were statistically homogeneous, a fixed-effect model was selected. A random-effects model was used when studies were statistically heterogeneous. The Higgins's I^2 test is the ratio of true heterogeneity to the total variation in observed effects. A rough guide to the interpretation of the I^2 test is 0-25%: might not be significant; 25-50%: may represent moderate heterogeneity; 50-75%: may represent substantial heterogeneity; and $> 75\%$: considerable heterogeneity. Publication bias was visually estimated by assessing funnel plots. Pooled estimates were calculated using R 3.5.1 software.

Results

Out of 4005 records that were identified, 476 duplicates were removed. One hundred eighty-nine records were screened, reviews, letters, news articles, patient-education handouts, retracted papers were excluded. Finally, 36 original studies were included in this systematic review.

We used the PRISMA diagram to illustrate the flow of information through the different phases of the systematic

review, it maps out the number of records identified, included and excluded (Figure 1).

Quality assessment

The risk of bias of included studies was assessed, for figure elaboration and analysis we implemented Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments as shown in Figures 2 and 3. Overall quality was low in the studies found; nevertheless, the domains of follow-up time, loss to follow up and strategies to address incomplete follow up were deficient in most of the studies because of no clear description or a statement in this regard.

Table 1 depicts the characteristics of studies included in this systematic review. Out of 36 original studies, 22 studies were conducted in China, nine in the USA (United States of America), two in the UK (United Kingdom), and one each in Italy, Portugal, and Iran. Two studies were case-control [11, 18], one was retrospective prospective study [25], two were prospective [32, 33], the remaining 31 studies were retrospective [12-17, 19-24, 26-31, 34-46]. The sample size and confirmed COVID-19 (%) are shown in Table 1.

Table 2 determines the maternal characteristics, consisting of maternal age and gestational age during delivery. The age of the patient was ranging from 19-41 and gestational age was 31-41 weeks. Table 3 depicts the mode of delivery comprised of caesarean section, preterm delivery, vaginal delivery and the total number of deliveries. The caesarean section was the preferred method of delivery in a study conducted by Na Li et al. [11]. The procedure was conducted in 87.5% of confirmed cases and 88.9% in suspected cases. In all 100% of cases, caesarean section was performed in the studies conducted by H.Chen et al., Yu et al., Chen et al., Fan et al., Khan et al., Hirshberg et al., and Cooke et al [12, 15, 16, 27, 31, 37, 40]. Vaginal delivery was the least preferred mode of delivery in all the selected studies. In a study conducted by Pierce-Williams et al., 88% were preterm delivery in severe COVID-19 patients.

Table 4 shows the clinical features of pregnant women due to COVID-19 viz. fever, cough, malaise, dyspnoea, myalgia, sore throat. The studies conducted by Khan et al. and Zheng et al. showed fever on admission in 66.7% and 73% cases [14,26]. Cough was present in 100% of patients in the study conducted by Khan et al [26]. In 60% of the cases in a study conducted by D. Liu et al. [19] myalgia and sore throat were not common clinical features.

Table 5 elicits the various laboratory findings, including lymphocytopenia, elevated CRP concentration, and confirmed SARS- Cov -2 cases. Table 6 shows the CT Scan findings of the patients.

Various pharmacological approaches of the patients are depicted in Table 7. Antibiotics were prescribed in most of the

patients. In a study conducted by Na Li et al. 100% of confirmed and suspected cases received antibiotics [11]. Similarly in studies conducted by H.Chen et al. 100%, Yu et al. 100%, D. Liu et al. 100%, C.Wu et al. 100%, Khan et al. 100%, Fan et al. 100%, Xu et al. 100%, and Hantoushzadeh et al. 100% patients received antibiotics therapy [12, 15, 19, 23, 26, 27, 35, 36]. Other modes of therapy were antiviral drugs, which were prescribed in 67% of cases in a study conducted by H. Chen al. and in 100% cases in the studies conducted by Yu et al., Hantoushzadeh et al., Hirshberg et al., Xu et al. and Khan et al. respectively[12, 15, 26, 36, 37, 35, 31]. High-flow O2 was given in 100% cases in studies conducted by H. Chen et al. and Yu et al. [12, 15]. Table 8 shows maternal comorbidities and maternal outcomes. A study conducted by Hantoushzadeh et al. reported 77% maternal mortality and a maternal ICU (Intensive Care Unit) admission of 77% Cooke et al. showed a maternal ICU admission in 100% of cases. In comparison, other studies included in this systematic review did not report high percentages of maternal ICU admission.

Table 9 shows the neonatal outcomes which varied a lot: 1% of neonatal death was reported by Yan et al., 36% by Hantoushzadeh et al., 13% by Lokken et al. and 2% by London et al., respectively [20, 36, 42, 44]. Other neonatal outcomes such as Intrauterine Fetal Death, Vertical Transmission, Intrauterine Fetal Distress, Mean Birth Weight, Low Birth Weight, APGAR score at 1 minute and five after birth is shown in Table 8.

Outcome measures

Figure 4 depicts the meta-analysis of the four studies of pregnant COVID-19 patients based on their vertical transmission. Pooled prevalence of vertical transmission was 10%, 95% CI: 4-17% (Figure 4).

Figure 5 depicts the meta-analysis of the four pregnant COVID-19 patient studies based on neonatal mortality. Pooled prevalence of neonatal mortality was 7%, 95% CI: 0-21% (Figure 5).

Heterogeneity among included studies

The results for the heterogeneity test for the meta-analysis of the vertical transmission and neonatal mortality among pregnant COVID 19 patients are displayed towards the bottom of the Forest plot in the line. For vertical transmission group, $Q [\chi^2]=1.43$, $P=0.70$, $I^2=0\%$, (Figure 4). However, I^2 was $<25\%$, a fixed-effect model was considered for vertical transmission. For the neonatal mortality group, $Q [\chi^2] =13.91$, $P=0.001$, $I^2=78\%$, $\tau^2=0.109$ (Figure 5). However, I^2 was $>25\%$, a random-effect model was considered for neonatal mortality.

Publication bias and funnel plots

For all of the above analyses, sensitivity analysis yielded consistent results. Based on a visual inspection of the funnel plot, there was evidence of publication bias for the included

studies (Figure 6 and 7). The funnel plots exhibited studies with sizeable standard error and were not symmetrical.

Figure 1: The PRISMA flow diagram for the systematic Review and Metaanalysis

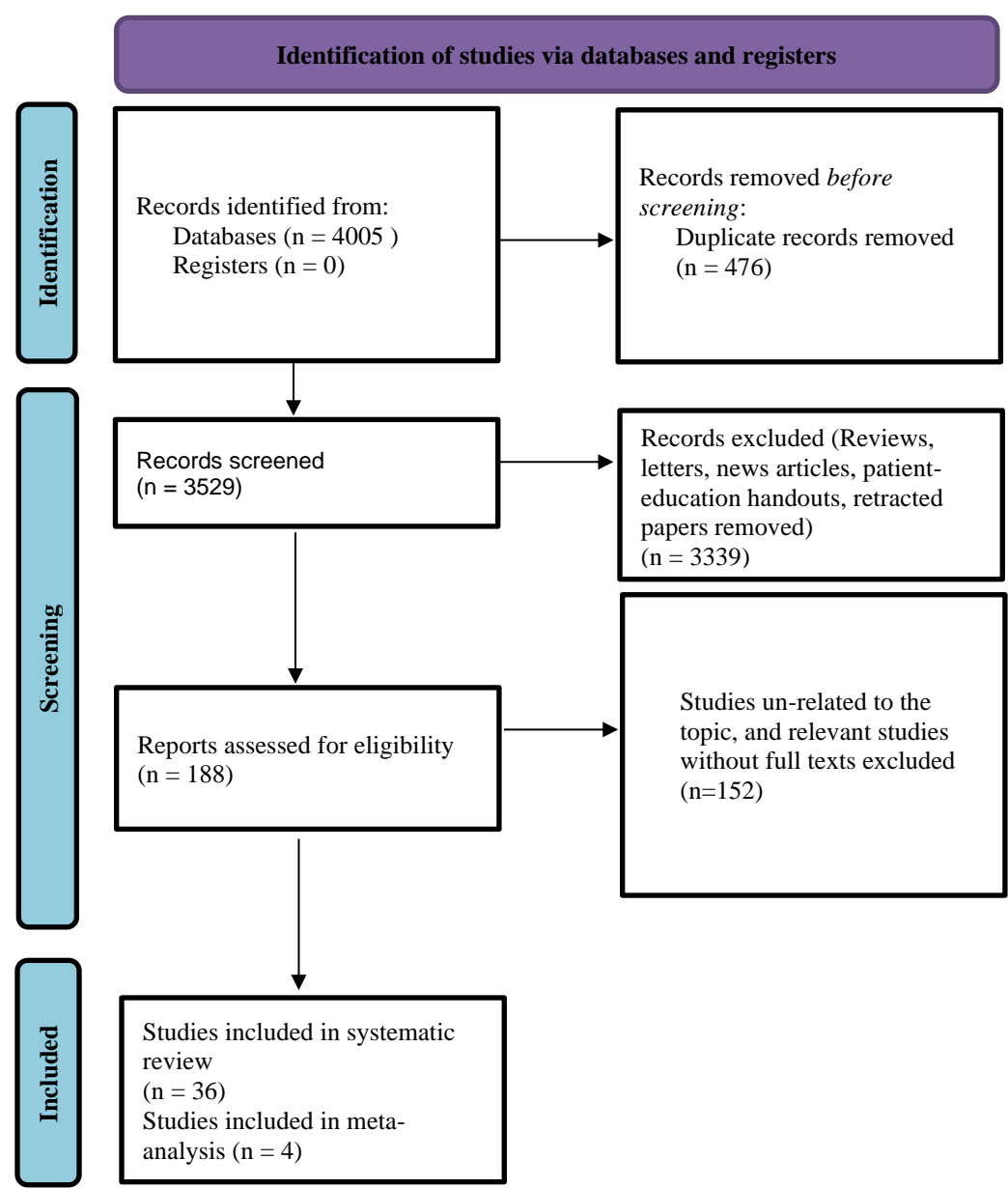


Figure 2: Risk of Bias

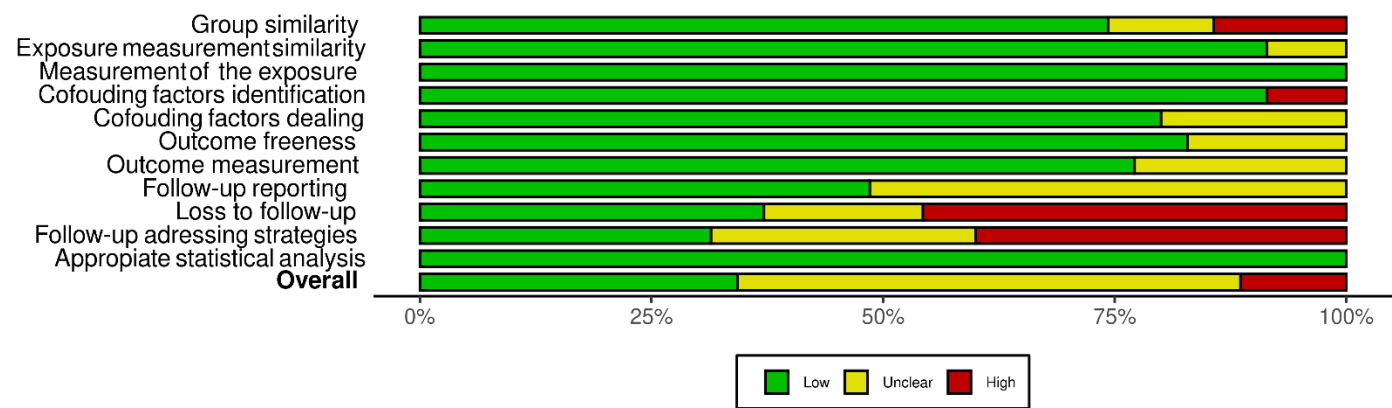
Study	Risk of bias											Overall
	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	
Breslin, et al. 2020a [21]	+	+	+	+	-	+	+	+	+	-	+	-
Breslin, et al. 2020b [22]	+	+	+	+	+	+	+	-	X	X	+	-
Campbell, et al.2020 [29]	X	+	+	+	-	+	+	+	+	-	+	-
Cao, et al. 2020 [34]	+	+	+	+	+	+	+	+	+	+	+	+
R. Chen, et al. 2020 [16]	+	-	+	+	+	+	+	-	X	X	+	-
Cooke, et al. 2020 [40]	+	+	+	+	+	+	-	-	X	X	+	-
Doria, et al. 2020 [41]	-	+	+	+	+	+	+	-	X	X	+	-
Fan et al. 2020 [27]	+	+	+	+	+	+	+	+	+	+	+	+
Ferrazi, et al. 2020 [46]	+	+	+	+	+	+	+	-	X	X	+	-
Govind, et al. 2020 [45]	+	+	+	+	-	+	+	-	X	X	+	-
H.Chen, et al. 2020 [12]	+	+	+	+	+	+	+	-	X	X	+	-
Hantoushzadeh, et al. 2020 [36]	-	+	+	+	+	+	+	+	+	+	+	+
Hirshberg, et al. 2020 [37]	+	+	+	+	+	+	+	+	+	+	+	+
Hu, et al. 2020 [39]	+	-	+	+	+	+	+	-	X	X	+	-
Khan, et al. 2020a [26]	+	-	+	+	+	+	+	-	X	X	+	-
Khan, et al. 2020b [31]	+	+	+	+	+	+	+	+	+	+	+	+
W. Liu, et al. 2020 [33]	-	+	+	+	+	+	+	+	+	+	+	+
H. Liu, et al. 2020 [17]	-	+	+	+	+	+	+	+	+	+	+	+
D. Liu, et al. 2020 [19]	+	+	+	+	+	+	+	+	+	+	+	+
Lokken, et al. 2020 [42]	+	+	+	X	+	+	+	-	-	-	+	-
London, et al. 2020 [44]	+	+	+	+	+	+	-	-	X	X	+	-
Na Li, et al. 2020 [11]	+	+	+	+	+	+	+	-	-	-	+	+
Pierce, et al. 2020 [25]	X	+	+	+	+	-	-	+	-	-	+	X
Qiancheng, et al. 2020 [38]	+	+	+	+	-	+	+	-	X	X	+	-
S Chen, et al. 2020 [13]	+	+	+	+	-	+	+	-	X	X	+	-
Savasi, et al. 2020 [43]	+	+	+	+	+	-	-	+	+	+	+	+
C. Wu, et al. 2020 [23]	X	+	+	+	+	-	-	+	X	-	+	X
X. Wu, al. 2020 [24]	+	+	+	+	-	+	+	-	X	X	+	-
Xu, et al. 2020 [35]	+	+	+	+	-	+	+	-	X	X	+	-
Y. Chen, et al. 2020 [28]	+	+	+	+	+	-	-	+	+	+	+	+
Yan, et al. 2020 [20]	+	+	+	+	+	+	+	+	+	+	+	+
Yang, et al. 2020 [18]	X	+	+	+	+	-	-	+	-	-	+	X
Yu, et al. 2020 [15]	+	+	+	X	+	+	+	-	-	-	+	-
Zheng, et al. 2020 [32]	X	+	+	+	+	-	-	+	X	-	+	X
Zhu, et al. 2020 [14]	+	+	+	X	+	+	+	-	-	-	+	-

D1: Group similarity
D2: Exposure measurement similarity
D3: Measurement of the exposure
D4: Confounding factors identification
D5: Confounding factors dealing
D6: Outcome freeness
D7: Outcome measurement
D8: Follow-up reporting
D9: Loss to follow-up
D10: Follow-up addressing strategies
D11: Appropriate statistical analysis

Judgement
High
Unclear
Low

Review authors' judgements about each risk of bias item for each included study.

Figure 3: Risk of bias summary



Review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 4: Forest plot of pregnant COVID 19 patients based on their vertical transmission

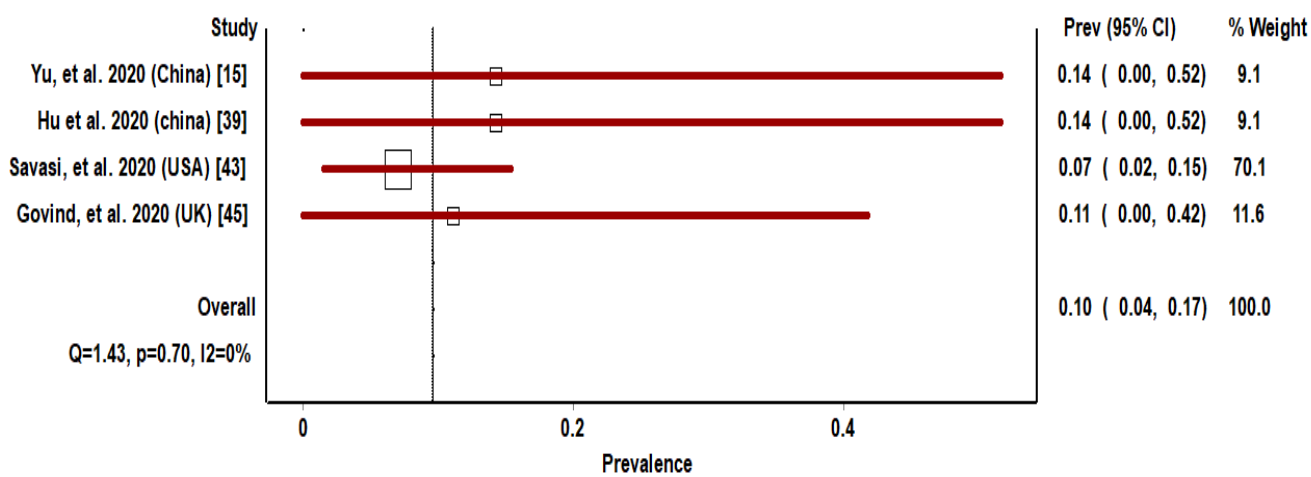


Figure 5: Forest plot pregnant COVID 19 patients based on their neonatal mortality

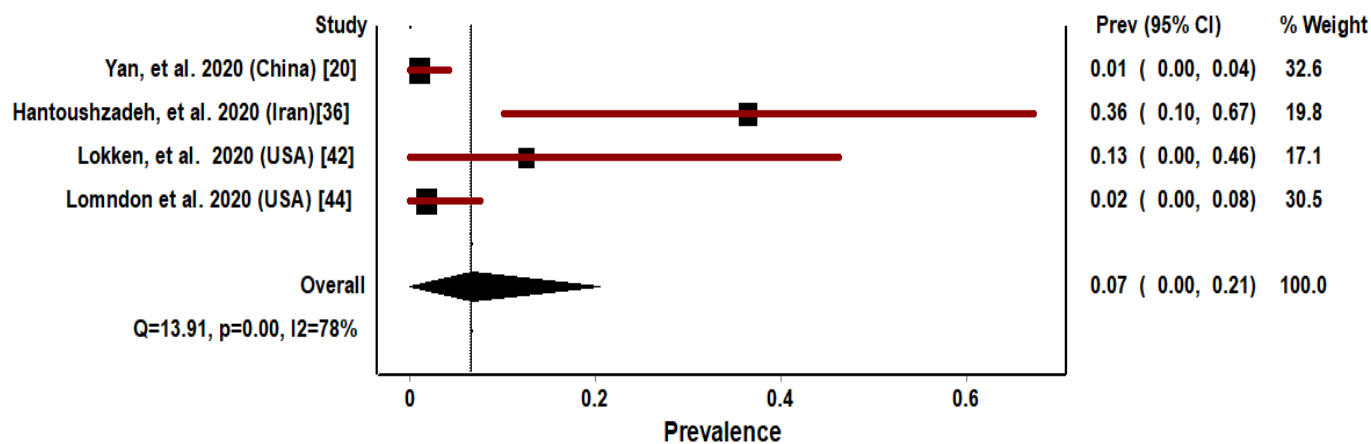


Figure 6: Funnel plot of pregnant COVID 19 patients based on their vertical transmission

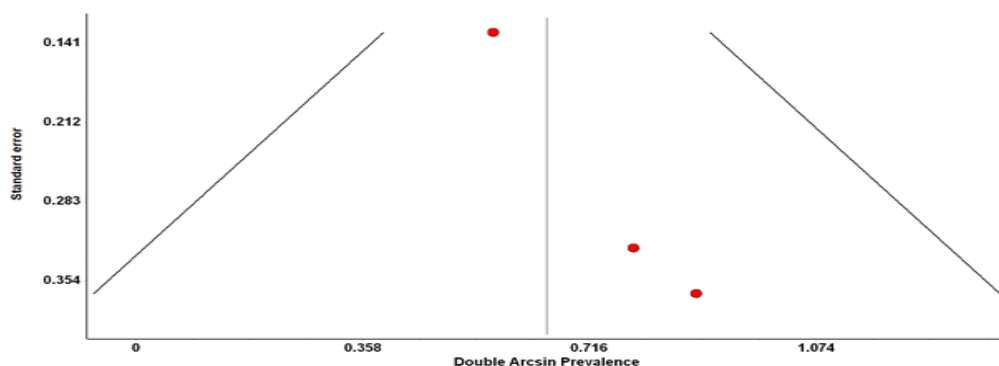


Figure 7: Funnel plot of COVID-19 pregnant patients based on their neonatal mortality

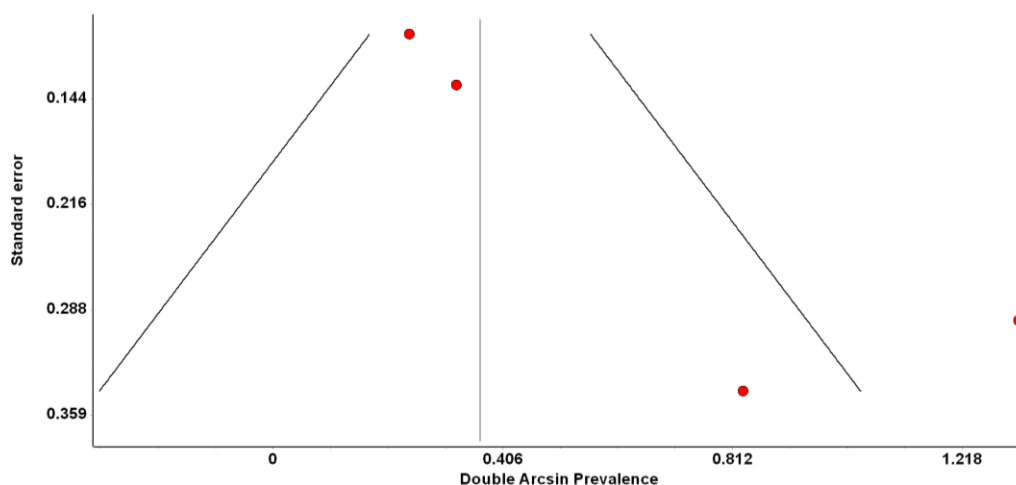


Table 1: Characteristics of studies included in the systematic review

Author, year (Country)	Sample size (N)	Study design	Confirmed SARS-CoV-2 (%)
Na Li, et al. 2020 (China) [11]	276	Retrospective case-control	16/276 (6.0)
H.Chen, et al. 2020 (China) [12]	9	Retrospective	9/9(100)
S. Chen. et al. 2020 (China) [13]	5	Retrospective	5/5(100)
Zhu et al. 2020 (China) [14]	9	Retrospective	9/9(100)
Yu, et al. 2020 (China) [15]	7	Retrospective	7/7(100)
R.Chen, et al. 2020 (China) [16]	17	Retrospective	17/17 (100)
H.Liu, et al. 2020 (China) [17]	41	Retrospective	41/41 (100)
Yang, et al. 2020 (China) [18]	55	Retrospective case-control	13/55(24)
D.Liu, et al. 2020 (China) [19]	15	Retrospective	15/15(100)
Yan, et al. 2020 (China) [20]	116	Retrospective	65/116(56.0)
Breslin, et al. 2020a (USA) [21]	43	Retrospective	43/43 (100)
Breslin, et al. 2020b (USA) [22]	7	Retrospective	7/7(100)
C.Wu, et al. 2020 (China) [23]	8	Retrospective	8/8 (100)
X.Wu, et al. 2020 (China) [24]	23	Retrospective	23/23 (100)
Pierce-Williams, et al. 2020 (USA) [25]	64	Multicenter Cohort Retrospective-Prospective	64/64 (100)

Khan, et al. 2020a (China) [26]	3	Retrospective	3/3 (100)
Fan, et al. 2020 (China) [27]	2	Retrospective	2/2(100)
Y. Chen, et al. 2020 (China) [28]	4	Retrospective	4/4(100)
Campbell, et al.2020 (USA) [29]	30	Retrospective	30/30 (100)
Baergen, et al. 2020 (USA) [30]	20	Retrospective	20/20 (100)
Khan, et al. 2020b (China) [31]	17	Retrospective	17/17 (100)
Zheng, et al. 2020 (China) [32]	33	Prospective	33/33 (100)
W.Liu, et al. 2020 (China) [33]	19	Prospective	19/19 (100)
Cao, et al. 2020 (China) [34]	10	Retrospective	10/10 (100)
Xu, et al. 2020 (China) [35]	5	Retrospective	5/5 (100)
Hantoushzadeh, et al. 2020 (Iran)[36]	9	Retrospective	9/9(100)
Hirshberg, et al. 2020 (USA) [37]	5	Retrospective	5/5 (100)
Qiancheng, et al. 2020 (China) [38]	28	Retrospective	28/28 (100)
Hu, et al. 2020 (China) [39]	7	Retrospective	7/7 (100)
Cooke, et al. 2020 (UK) [40]	2	Retrospective	2/2 (100)
Doria, et al. 2020 (Portugal) [41]	12	Retrospective	12/12 (100)
Lokken, et al. 2020 (USA) [42]	46	Retrospective	46/46 (100)
Savasi, et al. 2020 (USA) [43]	77	Retrospective	77/77 (100)
London, et al. 2020 (USA) [44]	68	Retrospective	68/68 (100)
Govind, et al. 2020 (UK) [45]	9	Retrospective	9/9 (100)
Ferrazi, et al. 2020 (Italy) [46]	42	Retrospective	42/42 (100)

Table 2: Maternal characteristics

Authors	Age	Gestational Age (delivery)
Na Li et al. 2020 [11]		
Confirmed Case (16)	30.9 ±3.2	38±0.2
Suspected Case (18)	29.8 ± 2.3	38±2. 9
Control 2020 (121)	30.1 ± 3.3	39±0.7
Control 2019 (121)	29.3 ± 2.6	38±6.9
H.Chen, et al. 2020 [12]	29.8 years	36-39 wks + 4 days
S.Chen. et al. 2020 [13]	29 years	38-41 weeks
Zhu et al. 2020 [14]	31 years	31-39 weeks
Yu, et al. 2020 [15]	32 years	39 weeks + 1 day
R.Chen, et al. 2020 [16]	29.1 years	>37 weeks
H.Liu, et al. 2020 [17]	31 years	-
Yang, et al. 2020 [18]		
Confirmed (13)	30.2 ± 2.3	38.2 ± 2.3
Control (42)	29.8 ± 3.4	38.8 ± 1.8
D.Liu, et al. 2020 [19]	32 ± 5	32 ± 8
Yan, et al. 2020 [20]	30.8 ± 3.8	38.0 (36.0,39.1)
Breslin, et al. 2020a [21]	29.7 ± 6.0	37 weeks
Breslin, et al. 2020b [22]	33.8 years	33 weeks+3 days
C.Wu, et al. 2020 [23]	29.8	33.3
X.Wu, et al. 2020 [24]	29	-
Pierce-Williams, et al. 2020 [25]		
Severe (44)	32.0±6.0	37.7±1.6
Critical (20)	35.9±4.3	31.9±3.8
Khan,et al. 2020a [26]	29.3	38 weeks

Fan, et al. 2020 [27]	31.5	36-38
Y.Chen, et al. 2020 [28]	29	37-39 weeks
Campbell, et al. 2020 [29]	30-35	37 weeks
Baergen, et al. 2020 [30]	19-41	32-40 weeks
Khan, et al. 2020b [31]	37.82	38.1
W.Liu, et al. 2020 [33]	31	38.6±1.5
Cao, et al. 2020 [34]	29-35	33-40
Xu, et al. 2020 [35]	29	36.4±3
Hantoushzadeh, et al. 2020 [36]	32	24-38
Hirshberg, et al. 2020 [37]	33	25-31
Qiancheng, et al. 2020 [38]	30 (26.75–32)	38 (36.5–39)
Hu, et al. 2020 [39]	33	37-41
Cooke, et al. 2020 [40]	34	28
Doria, et al. 2020 [41]	32	30-41
Lokken, et al. 2020 [42]	29 (26-34)	27 weeks
Savasi, et al. 2020 [43]	32	37
London, et al. 2020 [44]	30 years	65/68 in 3rd tri
Govind, et al. 2020 [45]	31 (18-39)	39 weeks
Ferrazi, et al. 2020 [46]	21-44	30 weeks

Table 3: Delivery characteristics

Authors	Total Number of Deliveries	Pt. not delivered during time of reporting	Cesarean delivery	Pre-term	Vaginal
Na Li et al. 2020[11]					
Confirmed Case (16)	152/276 (55.0)	124/276 (45.0)	14/16(87.5)	3 /16 (18.8)	2/16(12.5)
Suspected Case (18)			16/18 (88.9)	3/18 (16.7)	-
Control 2020 (121)			57/121 (47.1)	7/121 (5.8)	-
Control 2019 (121)			44 /121(36.4)	6/121 (5.0)	-
H.Chen, et al. 2020 [12]	9/9(100)	-	9/9(100)	4/9(44)	-
S.Chen. et al. 2020 [13]	5/5(100)	-	2/5(40)	-	3/5(60)
Zhu et al. 2020 [14]	9/9(100)	-	7/9(78)	5/9(56)	2/9(22)
Yu, et al. 2020 [15]	7/7(100)	-	7/7(100)	-	-
R.Chen, et al. 2020 [16]	17/17 (100)	-	17/17 (100)	3/17 (18)	-
H.Liu, et al. 2020 [17]	16/41 (39)	25/41 (61)	-	-	-
Yang, et al. 2020 [18]					
Confirmed (13)	55/55 (100)	-	9/13(69.2)	-	4/13(30.8)
Control (42)			30/42(71.4)	-	12/13(28.6)
D.Liu, et al. 2020 [19]	11/15 (73)	4/15(27)	10/11(91)	-	1/11(9)
Yan, et al. 2020 [20]	99/116 (85.3)	17/116 (14.6)	85/99 (85.9)	21/99 (21.2)	14/99(14.1)
Breslin, et al. 2020a [21]	18/43 (41.9)	25/43(58.1)	8/18(44.4)	-	10/18(55.5)
Breslin, et al. 2020b [22]	-	-	-	-	-
C.Wu, et al. 2020 [23]	8/8 (100)	-	6/8 (75)	1/8 (12.5)	2/8(25)
X.Wu, et al. 2020 [24]	20/23 (86.9)	-	18/20(90)	-	2/20 (10)
Pierce-Williams, et al. 2020 [25]					

Severe (44)	15/44 (34)	29/44 (66)	8/15 (53%)	4 /15 (27%)	7/15 (47%)
Critical (20)	17/20 (85)	3/20 (15)	16/17 (94%)	15/17 (88%)	1/17 (6%)
Khan, et al. 2020a [26]	3/3(100)	-	-	1/3 (33.3)	3/3 (100)
Fan et al. 2020 [27]	2/2 (100)	-	2/2 (100)	-	-
Y.Chen, et al. 2020 [28]	4/4 (100)	-	3/4 (75)	-	1/4(25)
Campbell, et al.2020 [29]	10/30 (33)	20/30 (66)	10/30 (33)	-	-
Baergen, et al. 2020 [30]	17/20 (85)	-	5/20 (25)	-	15/20 (75)
Khan, et al. 2020b [31]	17/17 (100)	-	17/17 (100)	5/17 (29.4)	-
Zheng, et al. 2020 [32]	33/33 (100)	-	27/33 (81)	4/33 (12)	-
W.Liu, et al. 2020 [33]	19/19 (100)	-	18/19 (95)	-	1/19 (5)
Cao, et al. 2020 [34]	10/10 (100)	-	8/10 (80)	3/10 (30)	2/10 (20)
Xu, et al. 2020 [35]	10/10(100)	-	4/5 (80)	2/5 (40)	1/5 (20)
Hantoushzadeh, et al. 2020 [36]	11/11 (100)	2/11 (18)	8/11 (73)	4/11 (36)	1/11 (9.1)
Hirshberg, et al. 2020 [37]	3/5 (60)	2/5 (40)	3/3 (100)	3/3 (100)	-
Qiancheng, et al. 2020 [38]	23/28 (82)	5/28 (18)	17/23 (74)	01/23 (4)	5/23 (22)
Hu, et al. 2020 [39]	7/7 (100)	-	6/7 (86)	-	1/7 (14)
Cooke, et al. 2020 [40]	2/2 (100)	-	2/2 (100)	2/2 (100)	-
Doria, et al. 2020 [41]	10/12 (83)	2/12 (17)	6/10 (60)	-	4/10 (40)
Lokken, et al. 2020 [42]	8/46 (17)	-	3/8 (37.5)	1/8 (12.5)	5/8 (62.5)
Savasi, et al. 2020 [43]	57/77 (74)	20/77 (26)	34/57 (61)	12/57 (21)	23/57 (39)
London, et al. 2020 [44]	55/67 (82)	12/67 (18)	22/55 (40)	12/55 (22)	33/55 (60)
Govind, et al. 2020 [45]	9/9 (100)	-	8/9 (89)	2/9 (22)	1/9 (11)
Ferrazi, et al. 2020 [46]	42/42 (100)	-	18/42 (43)	11/42 (26.2)	24/42 (57)

Table 4: Presenting signs and symptoms

Authors	Fever on admission	Fever after childbirth	Cough	Malaise	Dyspnea	Myalgia	Sore Throat	Diarrhea
Na Li et al. 2020 [11]								
Confirmed Case (16)	4/16 (25.0)	1/16 (5.6)	-	-	-	-	-	-
Suspected Case (18)	1 /18(5.6)	6/18 (33.3)	1/18 (5.6)	-	1/18 (5.6)	-	1 /18(5.6)	-
Control 2020 (121)	-	-	-	-	-	-	-	-
Control 2019 (121)	-	-	-	-	-	-	-	-
S.Chen. et al. 2020 [13]	-	5/5(100)	1/5(20)	-	-	-	-	-
Zhu et al. 2020 [14]	4/9(44)	2/9(22)	4/9(44)	-	-	-	1/9(11)	1/9(11)
Yu, et al. 2020 [15]	6/7(86)	-	1/7(14)	-	1/7(14)	-	-	-
R.Chen, et al. 2020 [16]	4/17 (24)	-	4/17 (24)	1/17 (6)	1/17 (6)	-	1/17 (6)	-
H.Liu, et al. 2020 [17]	16/41 (39)	14/41 (34)	15/41 (37)	5/41 (12)	5/41 (12)	-	-	-
Yang, et al. 2020 [18]								
Confirmed (13)	2/13(15.4)	8/13(61.5)	-	-	-	-	-	-
Control (42)	11/42(26.2)	20/42(47.6)	-	-	-	-	-	-
D.Liu, et al. 2020 [19]	13/15(87)	1/11(9)	9/15(60)	4/15(27)	1/15(7)	3/15(20)	1/15(7)	1/15(7)
Yan, et al. 2020 [20]	59/116(50.9)	-	33/116 (28.4)	15/116 (12.9)	3/116 (2.6)	6 /116 (5.2)	10/116 (8.6)	1 /116 (0.9)
Breslin, et al. 2020a [21]	14/29 (48.3)	-	19/29 (65.5)	11/29 (38)	7/29(24.1)	-	-	-
Breslin, et al. 2020b [22]	2/7 (28.5)	-	3/7 (43.0)	-	-	3/7(43.0)	-	-
C.Wu, et al. 2020 [23]	1/8(12.5)	3/8(37.5)	-	-	-	-	-	-

X.Wu, et al. 2020 [24]	4/23(17.4)	-	6/23(26.1)	-	-	-	-	-
Pierce-Williams, et al. 2020 [25]								
Severe (44)	-	-	-	-	-	-	-	-
Critical (20)	-	-	-	-	-	-	-	-
Khan, et al. 2020a [26]	2/3 (66.6)	-	3/3 (100)	-	1/3 (33.3)	-	-	-
Fan, et al. 2020 [27]	1/2 (50)	-	-	-	1/2 (50)	-	-	1/2 (50)
Y.Chen, et al. 2020 [28]	3/4(75)	-	2/4(50)	2/4(50)	2/4(50)	-	-	-
Campbell, et al.2020 [29]	-	-	-	-	-	-	-	-
Baergen, et al. 2020 [30]	10/20 (50)	-	-	-	-	-	-	-
Khan, et al. 2020b [31]	3/17 (18)	-	6/17 (35)	-	2/17 (12)	-	-	3/17 (18)
Zheng, et al. 2020 [32]	24/33 (73)	15/33 (45)	30/33 (91)	-	-	-	-	-
W.Liu, et al. 2020 [33]	11/19 (58)	-	5/19 (26)	-	-	-	-	-
Cao, et al. 2020 [34]	2/10 (20)	5/10 (50)	1/10 (10)	1/10 (10)	-	-	-	-
Xu, et al. 2020 [35]	1/5 (20)	3/5 (60)	2/5 (40)	-	2/5 (40)	-	-	-
Hantoushzadeh, et al. 2020 [36]	7/7 (100)	-	7/7 (100)	-	4/9 (44)	4/9 (44)	-	-
Hirshberg, et al. 2020 [37]	5/5 (100)	-	4/5 (80)	-	4/5 (80)	-	-	-
Qiancheng, et al. 2020 [38]	5/28 (18)	-	7 (25)	1 (3.6)	2 (7.1)	-	-	-
Hu, et al. 2020 [39]	4/7 (57.14)	-	2/7 (29)	-	-	-	-	1/7 (14)
Cooke, et al. 2020 [40]	1/2 (50)	-	1/2 (50)	-	1/2 (50)	-	-	1/2 (50)
Doria, et al. 2020 [41]	-	-	-	-	-	-	-	-
Lokken, et al. 2020 [42]	23/46 (50)	-	32/46 (70)	13/46 (28)	20/46 (44)	14/46(30)	12/46 (28)	3/46 (7)
Savasi, et al. 2020 [43]	41/77 (53)	-	50/77 (65)	-	19/77 (25)	-	-	-
London, et al. 2020 [44]	26/68 (38)	-	43/68 (63)	-	-	-	-	-
Govind, et al. 2020 [45]	4/9 (44)	-	8/9 (89)	6/9 (67)	4/9 (44)	5/9 (56)	-	-
Ferrazi, et al. 2020 [46]	20/42 (48)	6/42 (14)	18/42 (43)	-	8/42 (19)	-	-	2/42(5)

Table 5: Laboratory characteristics

Authors	Lymphocytopenia	Elavated CRP Concentration (mg/dl)	Confirmed SARS- CoV-2
Na Li et al. 2020 [11]			
Confirmed Case (16)	2/16 (12.5)	5/16 (31.3)	16/276 (6.0)
Suspected Case (18)	5/18(27.8)	11/18 (61.1)	
Control 2020 (121)	15/121 (12.4)	68/121 (56.2)	
Control 2019 (121)	14/121 (11.6)	57/121 (47.1)	
H.Chen, et al. 2020 [12]	5/9(56)	6/8(75)	9/9(100)
S.Chen. et al. 2020 [13]	4/5(80)	4/4(100)	5/5(100)
Zhu et al. 2020 [14]	-	-	9/9(100)
Yu, et al. 2020 [15]	5/7(71)	7/7(100)	7/7(100)
R.Chen, et al. 2020 [16]	25/41 (61)	27/41 (66)	16/41 (39)
H.Liu, et al. 2020 [17]	25/41 (61)	27/41 (66)	16/41 (39)
Yang, et al. 2020 [18]			
Confirmed (13)	-	-	13/13(100)
Control (42)	-	-	-
D.Liu, et al. 2020 [19]	12/15(80)	10/15(67)	15/15(100)
Yan, et al. 2020 [20]	51/116 (44.0)	51/116 (44.0)	65/116(56.0)
Breslin, et al. 2020a [21]	-	-	43/43 (100)

Breslin, et al. 2020b [22]	-	-	7/7(100)
C.Wu, et al. 2020 [23]	5/8(62.5)	8/8 (100)	6/6 (100)
X.Wu, et al. 2020 [24]	-	-	19/23 (82.6)
Pierce-Wiliams, et al. 2020 [25]			
Severe (44)	-	43.3±45.9	64/64 (100)
Critical (20)	-	141.9±88.6	
Khan, et al. 2020a [26]	-	2/3 (66.6)	3/3 (100)
Fan, et al. 2020 [27]	2/2(100)	-	2/2(100)
Y.Chen, et al. 2020 [28]	4/4(100)	4/4(100)	4/4(100)
Campbell, et al. 2020 [29]	-	-	30/30 (100)
Baergen, et al. 2020 [30]	-	-	20/20 (100)
Khan, et al. 2020b [31]	4/17 (24)	-	17/17 (100)
Zheng, et al. 2020 [32]	-	-	33/33 (100)
W.Liu, et al. 2020 [33]	-	-	19/19 (100)
Cao, et al. 2020 [34]	1/10 (10)	-	10/10 (100)
Xu, et al. 2020 [35]	-	-	5/5 (100)
Hantoushzadeh, et al. 2020 [36]	-	7/9 (78)	7/9(78)
Hirshberg, et al. 2020 [37]	-	1/5 (20)	5/5 (100)
Qiancheng, et al. 2020 [38]	8 (28.6)	17 (68)	28/28 (100)
Hu, et al. 2020 [39]	-	-	7/7 (100)
Cooke, et al. 2020 [40]	-	-	2/2 (100)
Doria, et al. 2020 [41]	-	-	12/12 (100)
Lokken, et al. 2020 [42]	-	-	46/46 (100)
Savasi, et al. 2020 [43]	19/77 (25)	39/77 (51)	77/77 (100)
London, et al. 2020 [44]	24/68 (35.3)	-	68/68 (100)
Govind, et al. 2020 [45]	2/9 (22)	-	9/9 (100)
Ferrazi, et al. 2020 [46]	6/42 (14)	17/42 (40)	42/42 (100)

Table 6: CT Scan findings

Authors	Unilateral pneumonia	Bilateral pneumonia	Typical viral infection
Na Li et al., 2020 [11]			
Confirmed Case (16)	8/16 (50.0)	7/16 (43.8)	-
Suspected Case (18)	10/18 (55.6)	7/18 (38.9)	-
Control 2020 (121)	-	-	-
Control 2019 (121)	-	-	-
H.Chen, et al. 2020 [12]	-	-	8/9(89)
S.Chen. et Al., 2020 [13]	2/5(40)	3/5(60)	-
Zhu et al. 2020 [14]	-	-	9/9(100)
Yu, et al. 2020 [15]	6/7(86)	1/7(14)	-
R.Chen, et al. 2020 [16]	12/41 (29)	26/41 (63)	-
H.Liu, et al. 2020 [17]	12/41 (29)	26/41 (63)	-
D.Liu, et al. 2020 [19]	-	-	15/15(100)
Yan, et al. 2020 [20]	-	-	104/116 (96.3)
C.Wu, et al. 2020 [23]	-	-	6/8(75)
X.Wu, et al. 2020 [24]	-	-	23/23 (100)

Khan, et al. 2020a [26]	-	3/3 (100)	-
Fan, et al. 2020 [27]	2/2(100)	-	-
Y.Chen, et al. 2020 [28]	-	4/4 (100)	-
Cao, et al. 2020 [34]	4/10 (40)	6/10 (60)	-

Table 7: Treatment

Authors	Treatment				
	Steroid	Antibiotic	Antiviral	High throughput O2	ECMO
Na Li et al. 2020 [11]					
Confirmed Case (16)	-	16/16 (100.0)	4/16 (25.0)	-	-
Suspected Case (18)	-	18/18 (100.0)	-	-	-
Control 2020 (121)	-	-	-	-	-
Control 2019 (121)	-	-	-	-	-
H.Chen, et al. 2020 [12]	-	9/9(100)	6/9(67)	9/9(100)	-
Yu, et al. 2020 [15]	-	7/7(100)	7/7(100)	7/7(100)	-
D.Liu, et al. 2020 [19]	-	15/15(100)	11/15(73)	14/15(93)	-
Yan, et al. 2020 [20]	37/116 (31.9)	109/116 (94.0)	63/116 (54.3)	6/116 (5.2)	1/116 (0.9)
C.Wu, et al. 2020 [23]	-	8/8(100)	-	-	-
Pierce-Wiliams, et al. 2020 [25]					
Severe (44)	4/44 (9%)	22/44 (50%)	3/44 (7%)	5/44 (11%)	-
Critical (20)	11/20 (55%)	14 /20 (70%)	13/20 (65%)	11/20 (55%)	-
Khan, et al. 2020a [26]	-	3/3 (100)	3/3 (100)	-	-
Fan, et al. 2020 [27]	2/2(100)	2/2(100)	2/2(100)	-	-
Khan, et al. 2020b [31]	-	17/17 (100)	16/17 (94)	-	-
Xu, et al. 2020 [35]	4/5 (80)	5/5 (100)	5/5 (100)	-	-
Hantoushzadeh, et al. 2020 [36]	-	9/9 (100)	9/9 (100)	-	-
Hirshberg, et al. 2020 [37]	5/5 (100)	-	5/5 (100)	-	-
Qiancheng, et al. 2020 [38]	-	24/28 (85.7)	20/28 (71.4)	-	-
Hu, et al. 2020 [39]	-	-	1/7 (14)	-	-
Savasi, et al. 2020 [43]	-	27/77 (35)	25/77 (32)	20/77 (26)	-

Table 8: Maternal comorbidities and maternal outcome

Authors	Chronic Illness	Pregnancy Complications	Maternal ICU Admission	Maternal Mortality
Na Li et al. 2020 [11]				
Confirmed Case (16)	2/16 (12.5)	11/16 (68.8)	-	-
Suspected Case (18)	1/18 (5.6)	13/18 (72.2)		
Control 2020 (121)	5/121 (4.1)	38/121 (31.4)		
Control 2019 (121)	-	32/121 (33.3)		
H.Chen, et al. 2020 [12]	-	7/9(77)	-	-
S.Chen. et al. 2020 [13]	-	3/5(60)	-	-
Zhu et al. 2020 [14]	-	4/9(44)	-	-
Yu, et al. 2020 [15]	2/7(29)	3/7(43)	-	-
R.Chen, et al. 2020 [16]	-	8/17 (47)	-	-
H.Liu, et al. 2020 [17]	-	7/41 (17)	-	-

Yan, et al. 2020 [20]	-	18/116(15.5)	8/116(6.9)	-
Breslin, et al. 2020a [21]	-	-	2/29 (4.7)	-
Pierce-Williams, et al. 2020 [25]				
Severe (44)	20/44 (45)	9/44 (20)	-	-
Critical (20)	7/20 (35)	3/20 (15)	-	-
Khan, et al. 2020b [31]	-	5/17 (29.4)	-	-
Zheng, et al. 2020 [32]	-	3/33 (9)	-	-
Cao, et al. 2020 [34]	-	3/10 (30)	-	-
Hantoushzadeh, et al. 2020 [36]	3/9 (33)	-	7/9 (77)	7/9 (77)
Hirshberg, et al. 2020 [37]	5/5 (100)	-	-	-
Qiancheng, et al. 2020 [38]	6/28 (21.4)	4/28 (14.3)	-	-
Cooke, et al. 2020 [40]	2/2 (100)	-	2/2 (100)	-
Lokken, et al. 2020 [42]	17/46 (37)	-	8/46 (17)	-
Savasi, et al. 2020 [43]	-	-	14/77 (18)	-
London, et al. 2020 [44]	-	4/68 (6)	-	-
Ferrazi, et al. 2020 [46]	-	6/42 (14)	4/42 (10)	-

Table 9: Neonatal outcomes

Authors	Intrauterine Fetal Death	Intrauterine Fetal Distress	Mean Birth Weight	Low Birth Weight	APGAR score at 1 minute after birth	APGAR score at 5 minutes after birth
Na Li et al. 2020 [11]						
Confirmed Case (16)	-	2/16 (12.5)	3066.7 ± 560.2	3/16 (17.6)	9.6 ± 0.5	10.0 ± 0.0
Suspected Case (18)		1/18 (6.0)	3198.7 ± 522.6	2/18 (11.0)	9.6 ± 0.5	10.0 ± 0.0
Control 2020 (121)		6 /121(5.0)	3317.1 ± 455.3	3/121 (2.5)	9.8 ± 0.4	10.0 ± 0.0
Control 2019 (121)		6/121 (5.0)	3307.9 ± 419.3	3/121 (2.5)	9.9 ± 0.3	10.0 ± 0.0
H.Chen, et al. 2020 [12]	-	-	3011 grams	2/9(22)	9	10
S.Chen. et al. 2020 [13]	-	-	3691 grams	-	10	10
Zhu et al. 2020 [14]	-	6/9(67)	2423 grams	6/9(67)	9	9.4
Yu, et al. 2020 [15]		-	3264 grams	-	9	10
R.Chen, et al. 2020 [16]	-	-	3030 grams	-	9	10
Yang, et al. 2020 [18]						
Confirmed (13)	-	-	3063.2 ± 536.4	-	-	-
Control (42)	-	-	3317.1 ± 522.5	-	-	-
D.Liu, et al. 2020 [19]	-	-	-	-	8	9
Yan, et al. 2020 [20]	-	9 /99(10.6)	3108 ± 526	-	9	10
Pierce-Williams, et al. 2020 [25]						
Severe (44)	-	-	2945.8±509.2	-	-	8.8±0.8
Critical (20)	-	-	1924.6±846.6	-	-	7.2±2.0
Khan, et al. 2020a [26]	-	-	3373	-	8.6	9.6
Fan, et al. 2020 [27]	-	-	3145	-	9	10
Y.Chen, et al. 2020 [28]	-	-	3400	-	8	8
Campbell, et al. 2020 [29]	-	-	3370	-	-	-
Baergen ,et al. 2020 [30]	-	-	3309	3/17 (18)	8	9

Khan, et al. 2020b [31]	-	-	3104	-	9	9
Zheng, et al. 2020 [32]	-	-	-	-	-	-
W.Liu, et al. 2020 [33]	-	-	3293	-	8	9
Cao, et al. 2020 [34]	-	-	3003	2/10 (20)	9	10
Xu, et al. 2020 [35]	-	-	2992	1/5 (20)	8	9
Hantoushzadeh, et al. 2020 [36]	3/11(27)	3/11 (27)	2464	5/11 (45)	8	9
Hirshberg, et al. 2020 [37]	-	-	1818	3/3 (100)	6	7
Qiancheng, et al. 2020 [38]	-	1/23 (4)	-	1/23 (4)	10	10
Hu, et al. 2020 [39]	-	-	3331	-	8	9
Cooke, et al. 2020 [40]	-	-	1450	2/2 (100)	4	6
Doria, et al. 2020 [41]	-	-	2960	3/10 (30)	9	10
Savasi, et al. 2020 [43]	-	-	3160	-	-	10
London, et al. 2020 [44]	-	1/55 (2)	-	-	-	-
Govind, et al. 2020 [45]	-	-	3155	1/9 (11)	7	9
Ferrazi, et al. 2020 [46]	-	-	3018	-	-	9

Discussion

Clinical Manifestations and Complications during Pregnancy

Based on the earlier evidence of Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) the clinical manifestation of these infections during pregnancy varies from asymptomatic presentation to severe respiratory illness and mortality. A recent retrospective study presented the clinical profile of nine pregnant women diagnosed with COVID-19 during the third trimester. The authors reported that the clinical presentation of COVID-19 positive pregnant women was comparable with the non-pregnant female patients, and the frequent symptoms were fever (78%), cough (44%), myalgia (33%), sore throat and malaise (22% each). Lymphopenia was reported in five patients and none of them had developed severe pneumonia that requires mechanical ventilation and all survived. All women had a caesarean section and the Apgar score was 8-9 at 1 minute and 9-10 at 5 minutes. Four out of nine deliveries had pre-term labour but after 36 gestational weeks and seven patients developed pregnancy related-complications [12].

Another series of nine COVID-19 positive pregnant women with ten infants (one had twins) by Zhu et al., reported onset of symptomatic presentation prior to delivery (1-6 days) in four, on the day of delivery in two, and post-delivery (1-3 days) in three cases [14]. Similar to the earlier report, the clinical presentation of COVID-19 cases was comparable to non-pregnant patients. Of the nine pregnancies, six patients had intrauterine foetal distress, seven had a caesarean section, six were preterm deliveries and four had pregnancy-related complications [14].

Yu et al. studied seven pregnant COVID-19 patients with a mean age of 32 (range 29–34 years) admitted during early 2020 [15]. The average gestational age was over 39 weeks. Six patients had a fever as their chief clinical manifestation, shortness of breath, and cough and diarrhoea in one patient each. Caesarean sections were performed in all patients within three days of clinical presentation. All women had good maternal and neonatal outcomes but one neonate was tested positive for COVID-19 36 hours after birth [15]. Wu et al. reported eight pregnant patients aged 26 to 35 years [24]. Six of these women were laboratory-confirmed and two were highly suspected SARS-CoV-2 infection cases. Six had caesarean sections because of premature rupture of membrane, preeclampsia, fetal distress, or the history of caesarean section. Notably, intensive care or mechanical ventilation was not required in any patients. Four out of eight pregnant women remained asymptomatic prior to delivery, but later developed symptoms post-partum [24]. Breslin et al. reported seven confirmed COVID-19 cases in pregnancy in the USA, presented with symptoms such as cough, fevers, myalgia, chest pain, and headache. Two patients required supportive care with intravenous hydration [22]. Another study from the USA described 43 patients, 14 (32.6%) were asymptomatic, later on, ten patients developed symptoms during the hospital course or early after postpartum discharge [21]. Three required antenatal admission for viral symptoms of the other 29 (67.4%) symptomatic patients. The disease was mild in 86%, severe in 9.3%, and critical in 4.7%. Wu et al. demonstrated a significant difference in the median time for hospitalisation among asymptomatic and symptomatic patients (14 vs. 25.5 days, $p < 0.05$) [24]. This study was conducted retrospectively among

23 pregnant patients diagnosed with COVID-19 and admitted to the hospital in Wuhan [24].

Chen and colleagues [13] reported five young pregnant COVID-19 patients aged 25 to 31 years, gestational age from 38 to 41 weeks, who were admitted to the hospital. The women developed low-grade fever within 24 hours post-partum. The renal and liver function profile was unremarkable for all patients. CT scan images revealed abnormal bilateral ground-glass opacity (three cases) or unilateral lobe (two cases). Three had normal births and two underwent caesarean sections; all labours were smoothly processed with no maternal or newborn complications. The Apgar scores were 10 points at 1 and 5 minutes after delivery [13]. Liu et al. reported clinical differences among pregnant and non-pregnant. The laboratory-confirmed and clinically diagnosed COVID-19 pregnant women had higher initial body temperature, leukocytosis and elevated neutrophil ratio, and lymphopenia as compared to laboratory-confirmed non-pregnant patients [17]. The CT imaging revealed lesions with peripheral (98%) and bilateral (67%) distributions. For the non-pregnant adults, pure ground-glass opacity (72%) was the most frequent finding [17].

A retrospective study by Zhang et al. compared the pregnancy outcomes among COVID-19 positive and negative women having similar gestational age and delivered by caesarean section [49]. The authors suggested no additional risk of intra-operative blood loss during delivery with a comparable birth weight in both groups. In addition, the two groups were comparable for meconium-stained amniotic fluid, foetal distress, preterm birth, and neonatal asphyxia between COVID-19 patients and controls. Based on ten neonates in this study, there was no evidence of mother-to-fetal vertical transmission of COVID-19 infection [49]. Yang et al. tested the throat swab samples within 24 h after birth for COVID-19 which revealed no evidence of SARS-CoV-2 transmission from infected mother to newborn babies [18].

A case-control study conducted by Li et al. [48] included 16 pregnant women positive for COVID-19 and 18 suspected cases in the third trimester admitted to the hospital. Notably, two patients were presented with respiratory symptoms (fever and cough) on admission. Most of the patients had chest CT (computed tomography) scan images suggesting typical COVID-19 pneumonia. Similar to other studies, these patients had lower white blood cells and neutrophils counts, with deranged alanine aminotransferase (ALT) and C-reactive protein (CRP) levels on admission compared to controls. Postpartum blood investigations revealed increased eosinophils, white blood cells, neutrophils and CRP. Three women with confirmed COVID-19 and three in the control group developed pneumonia and had preterm delivery secondary to maternal complications. None of the subjects had

a respiratory failure in the hospital, all newborns were negative for infection, and none had severe neonatal complications [48]. Zaigham et al. conducted a systematic review to evaluate the maternal and perinatal outcomes in pregnancies with COVID-19 [50]. The authors included all case reports and series from December 8, 2019 and April 1, 2020 and identified a total of 108 pregnancies. During their third trimester of pregnancy, most studies observed women mostly presented with fever (68%) and coughing (34%). Lymphocytopenia (59%) with elevated CRP (70%) was also common. Most (91%) deliveries were by caesarean section and three pregnant women required ICU admissions. Overall, there was one neonatal and intrauterine death with no maternal mortality [50]. The authors concluded that most pregnant women were discharged without significant complications, but there are some cases with severe maternal morbidity and perinatal deaths secondary to COVID-19 infection. Also, vertical transmission of the COVID-19 infection from mother to foetus could not be ruled out [50].

The emerging evidence also indicates that vertical transmission of SARS-CoV-2 infection is unlikely, but still considering the smaller proportion of pregnant cases, the mode of transmission of COVID-19 needs further exploration. Two published reports have evidence of IgM antibodies for SARS-CoV-2 in neonatal serum after birth [23,51]. Since, IgM antibodies are not known to cross the placenta, the presence of these antibodies indicates the neonatal immune response to maternal in-utero infection. Although conflicting results were published in previous case reports from China, we must remember that case reports are the lowest form of evidence in the hierarchy of evidence [52]. These reports found that the samples of amniotic fluid, placenta and neonatal throat swabs, cord blood, genital fluid, and breast milk were negative for COVID-19 infection, indicating no vertical transmission evidence [12, 14, 29, 48]. This also suggests that breastfeeding should be encouraged if at all possible, with precautions such as washing hands before holding the baby and the mother wearing a face mask during breastfeeding.

Previous studies have reported that SARS-CoV-2 has more genetic proximity (88% sequence homology) with two SARS-like coronaviruses derived from bat i.e. bat-SL-CoVZC45 and bat-SL-CoVZXC21, as compared to SARS-CoV-1 (79% sequence identity) and MERS-CoV (about 50% identity). However, modelling studies using bioinformatics tools showed that receptor binding domain structure of SARS-CoV-2 and SARS-CoV-1 are similar, which suggests a similar course of pathogenesis among the two infections [53-55]. Hence, there is a lower possibility of vertical transmission of COVID-19 infection similar to that of SARS-CoV-1. The pooled clinical records of 116 pregnant women with COVID-19 from China concluded no evidence of SARS-CoV-2 vertical transmission

of infection among pregnant women during the third-trimester [20].

Clinical Management

Pregnant women are considered high risk, so those with suspicion of COVID-19 must be isolated, clinically assessed, and investigated for the infection [56]. Zeng et al. reported that all six COVID-19 pregnant women in their study had caesarean deliveries in their third trimester in negative pressure isolation rooms [23]. All mothers should wear masks and medical staff should use protective suits and double masks. The infants were isolated immediately post delivery, and throat swabs and blood specimens were found to be found negative by RT-PCR test [23]. The COVID-19 Obstetrics Task Force, from Italy stressed the need to isolate newborns from COVID-19-positive and symptomatic mothers and use pumps to express breast milk [47].

Pregnant patients who tested positive for infection must be immediately shifted to an isolation ward, ideally an isolation ward in a tertiary care hospital equipped with appropriate medical facilities and multi-disciplinary team to manage severely ill pregnant women. Such patients should be triaged and clinically evaluated for risk stratification from the beginning. Patients with mild symptoms often have stable vital signs, while those with severe pulmonary distress have respiratory rate $\geq 30/\text{min}$, resting oxygen saturation $\leq 93\%$, and the ratio of arterial blood oxygen partial pressure (PaO_2)/oxygen concentration (FiO_2) to be $\leq 300 \text{ mmHg}$ [7]. Importantly, those with critical illness may develop shock with organ dysfunction, a respiratory failure requiring mechanical ventilation, extra-corporal membrane oxygenation (ECMO) to manage refractory hypoxemia [57]. Universal COVID-19 testing for all pregnant women closer delivery time will help in triaging for hospital isolation, bed assignment, personal protective equipment (PPE) by healthcare providers and improved neonatal care [58].

A multispecialty team of obstetricians, midwives, intensivists, microbiologists, anaesthetists and neonatologist should be available to manage pregnant women with COVID-19 primarily to manage severe and critical cases [59]. Importantly, physiological adaptations in pregnancy should be given higher consideration while treating pregnant females with confirmed diagnosis of COVID-19 infection. For appropriate patient care and infection prevention among healthcare workers, the clinical staff involved in the care of COVID-19 patients should properly use PPE such as N95 masks, gowns, gloves, and goggles [60]. However, we need to remember that all pregnant women, irrespective of COVID-19 infections, deserve the best quality of care pre and post-partum, should be treated with respect and dignity; and have an attendant of choice available during delivery [61].

Pregnant women with infection should rest, and be closely monitored for adequate nutritional support, hydration, electrolyte balance, vital signs and oxygen saturation to maintain good physiological status [56]. In patients with acute respiratory distress, supplemental oxygen through a high-flow nasal cannula should be inspired with 60%-100% concentration at a flow rate of 40 L/min, depending upon the severity of hypoxemia [62]. In critically ill patients, mechanical ventilatory support or extra-corporal membrane oxygenation should be considered to maintain oxygen saturation. The other complications more common in COVID-19 patients may include sepsis and septic shock, acute kidney injury, and virus-induced cardiac injury [63]. Therefore, in severe cases it is crucial to closely monitor the derangement of arterial blood gases, serum lactate, renal and liver function profile and cardiac enzymes as clinical indicators of physiologic deterioration.

In China, the antiviral treatment has been administered routinely to manage COVID-19 patients which some recommended even for pregnant patients [56]. Particularly, combination therapy of antiproteases namely Lopinavir/Ritonavir is preferred and considered a relatively safer drug regimen in pregnant COVID-19 patients. It is recommended to have oral administration of Lopinavir/Ritonavir (200 mg/50 mg per capsule) two capsules orally twice a day along with the inhalation of nebulised α -interferon (5 million IU in 2 mL of sterile water for injection) twice daily [64]. The World Health Organization (WHO) suggested taking precautions and judicious risk-benefit assessment prior to administering of any therapeutic drug among pregnant females except for clinical trials. Interestingly, Remdesivir a nucleotide analogue, and chloroquine/hydroxychloroquine, a known antimalarial drug, are emerging potential therapeutic agents against COVID-19 which inhibit the SARS-CoV-2 virus replication in in-vitro studies [65]. In-vitro studies demonstrated inhibition activity of Chloroquine against SARS-CoV-2 virus and potentially minimised the duration of viral shedding. However, we are waiting for the outcomes of various clinical trials to assess the therapeutic implication of these drugs in human subjects. More recently the ISIDOG guidelines reminded us that anti-retrovirals are not indicated in pregnancy unless there are no other treatment options available to manage severe illness [7].

The SARS-CoV-2 virus is known to cause extensive pulmonary damage that eventually enhances the possibility of secondary bacterial pneumonia [66]. Therefore, the administration of antibiotics prophylaxis is primarily recommended, if there is a diagnosis of secondary bacterial infection. Moreover, antibiotic treatment should be initiated immediately if bacterial sepsis is suspected [62]. Mainly, intravenous administration of

Ceftriaxone can be initiated even before the availability of culture and sensitivity results.

To date, there is no available standard treatment for COVID-19, so novel or off-labelled drug should be considered experimental, and a detailed explanation has to be provided to the patients and partner prior to administration. For instance, Corticosteroids can be used to prevent neonatal lung hypoplasia, necrotic enterocolitis and interventricular haemorrhage due to prematurity. Although, (Hydro) chloroquine is considered a safe drug for pregnant women, all precautions must be considered before administration in COVID-19 patients.

Prevention

Evidence suggested that the incubation period of COVID19 ranges from 2-14 days, but the infected individual can also transmit the virus despite being asymptomatic during this period. Therefore, pregnant women should avoid public transport, crowds, contact with sick people, unnecessary travel, maintain appropriate social and personal hygiene, including proper washing of hands as per recommendation [20]. Moreover, pregnant women with symptoms of cough, fever, myalgia, fatigue, sore throat or shortness of breath should seek immediate medical consultation. Women with a clinical suspicion of COVID-19 infection and travel history must be isolated and investigated [67]. Also, there is a need to provide professional psychological support to overcome mental health illness among pregnant women at risk of developing severe anxiety and depression [68].

As per the current guidelines of the UK's Royal College of Obstetricians and Gynaecologists (RCOG), the Royal College of Midwives (RCM), and the Royal College of Paediatrics and Child Health (RCPCH), health workers exceeding 28 weeks of pregnancy must avoid direct patients contact whether they are infected with COVID-19 or not [69, 70]. However, healthcare professionals with less than 28 weeks of pregnancy, can directly deal with the patients using appropriate PPEs. It is advisable to have a more precautionary approach for pregnant women completed 28 weeks' gestation, or those with underlying comorbidities such as heart or lung diseases working in clinical services. If possible, such females should work from home, stay away from infected individuals, and avoid unnecessary social contact. Moreover, under these circumstances the healthcare workers have opportunities for flexible working capacity and newer approaches such as telephone or video conference consultations, or assigned administrative duties [70].

With this outbreak, there is a realisation to strengthen our healthcare capacity to tackle the emergent novel outbreaks, propose stringent regulations to contain the spread of infectious diseases and implement public education among families,

communities and other religious groups to avoid further outbreak and preparedness through transparency and solidarity. In order to avoid delayed responses to an outbreak by the administration, timely reporting of emergent infectious agents is of paramount importance [71]. Proper infection control and preventive measures should be implemented in the healthcare facilities through isolation of confirmed cases and recommended PPE to protect medical professionals and other healthcare staff from exposure to communicable diseases [72]. It is worth noting that this extensive systematic review only cover papers published in 2020, and hence studies conducted in or before 2020. This was before the emergence of variants of COVID-19, especially the delta and omicron variants.

Conclusion

The COVID-19 outbreak is exponentially increasing worldwide. A better understanding of the disease transmission, major risk factors, vulnerable population, and the outcome is crucial for prevention and management. At present, limited information is available for pregnant women with COVID-19 to propose best practices for specialised care. However, the current literature suggests that pregnant women with COVID-19 infection may develop severe clinical manifestations. Therefore, surveillance systems for COVID-19 positive patients are being established to analyse the maternal and foetal outcomes during pregnancy. Also, awareness about the management of COVID-19 positive pregnancies and prevention of neonatal infection is vital for healthcare professionals. Proper vigilance and monitoring of the disease spread and rapid implementation of preventive measures are crucial to containing the spread of infection in the community. The ready availability of standard respiratory support to manage severe COVID-19 infection in pregnancy is crucial and should be implemented rigorously by a multidisciplinary team. For better understanding it is essential to have systematic data reporting for evidence based clinical assessment, management, and pregnancy outcomes in infected females that will guide the healthcare facilities with limited resources to manage the vulnerable population in an outbreak.

Acknowledgements

None

Authors' contribution

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Competing interests

There is no conflict of interest for any author of this manuscript.

Source of Support:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector.

Authors' affiliations:

^{1,7,11}Geriatrics and long term care Department, Rumailah Hospital, Hamad Medical Corporation, Doha, Qatar

²Sir Seewoosagur Ramgoolam Medical College, Mauritius

^{3,6}Trauma Surgery, Hamad General Hospital, Doha, Qatar

^{1,4,9}Bournemouth University, Bournemouth, England, United Kingdom

⁵Clinical Research Center, Fundación Valle del Lili. Cali, Colombia

⁸School of Allied Health, Faculty of Health, Education, Medicine, and Social Care, Anglia Ruskin University, Chelmsford, United Kingdom

⁹University of Huddersfield, United Kingdom

¹⁰University Hospital and School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

¹¹Medical Director, Rumailah Hospital (RH) & Qatar Rehabilitation Institute (QRI), Doha, Qatar.

References

1. COVID-19 Coronavirus Pandemic. [Online] 2020 [Cited 2020 Apr 27]. Available from: URL https://www.worldometers.info/coronavirus/?utm_campaign=homeAdvegas1?%22%20%5C%20%22countryss/
2. Rasmussen SA, Hayes EB. Public health approach to emerging infections among pregnant women. *Am J Public Health*. 2005;95:1942-4. <https://doi.org/10.2105/AJPH.2004.054957> PMID:16195518 PMCID:PMC1449464
3. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA*. 2010;303:1517-25. <https://doi.org/10.1001/jama.2010.479> PMID:20407061 PMCID:PMC5823273
4. Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA Pediatr*. 2017;171:288-95. <https://doi.org/10.1001/jamapediatrics.2016.3982> PMID:27812690 PMCID:PMC5561417
5. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects--Reviewing the evidence for causality. *N Engl J Med*. 2016;374:1981-7. <https://doi.org/10.1056/NEJMSr1604338> PMID:27074377
6. Dashraath P, Wong JIJ, Lim MXK, et al. Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy. *Am J Obstet Gynecol*. 2020:S0002-9378:30343-4. <https://doi.org/10.1016/j.ajog.2020.03.021>

PMid:32217113 PMCID:PMC7270569

7. Donders F, Lonnee-Hoffmann R, Tsiakalos A, et al. ISIDOG recommendations concerning COVID-19 and pregnancy. *ISIDOG Recommendations Concerning COVID-19 and Pregnancy*. *Diagnostics*. 2020;10:243.

<https://doi.org/10.3390/diagnostics10040243>

PMid:32338645 PMCID:PMC7235990

8. Haddad LB, Jamieson DJ, Rasmussen SA. Pregnant women and the Ebola crisis. *N Engl J Med*. 2018;379:2492-3.

<https://doi.org/10.1056/NEJMp1814020>

PMid:30485156

9. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Latin American Network of Coronavirus Disease 2019-COVID-19 Research (LANCOVID-19). Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis*. 2020:101623.

<https://doi.org/10.1016/j.tmaid.2020.101623>

PMid:32179124 PMCID:PMC7102608

10. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507-13.

[https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)

11. Li N, Han L, Peng M, et al. Maternal and Neonatal Outcomes of Pregnant Women With Coronavirus Disease 2019 (COVID-19) Pneumonia: A Case-Control Study. *Clin Infect Dis*. 2020 Nov 19;71(16):2035-2041.

<https://doi.org/10.1093/cid/ciaa352>

PMid:32249918 PMCID:PMC7184430

12. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020 Mar 7;395(10226):809-815. Erratum in: *Lancet*. 2020 Mar 28;395(10229):1038.

[https://doi.org/10.1016/S0140-6736\(20\)30360-3](https://doi.org/10.1016/S0140-6736(20)30360-3)

PMid: 32151335; PMCID: PMC7159281.

13. Chen S, Liao E, Cao D, Gao Y, Sun G, Shao Y. Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia. *J Med Virol*. 2020 Sep;92(9):1556-1561.

<https://doi.org/10.1002/jmv.25789>

PMid:32222119 PMCID:PMC7228212

14. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020 Feb;9(1):51-60.

<https://doi.org/10.21037/tp.2020.02.06>

PMid:32154135 PMCID:PMC7036645

15. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis*. 2020 May;20(5):559-564

[https://doi.org/10.1016/S1473-3099\(20\)30176-6](https://doi.org/10.1016/S1473-3099(20)30176-6)

PMid: 32220284; PMCID: PMC7158904.

16. Chen R, Zhang Y, Huang L, Cheng BH, Xia ZY, Meng QT. Safety and efficacy of different anesthetic regimens for parturients with COVID-19 undergoing Cesarean delivery: a case series of 17 patients. *Can J Anaesth*. 2020 Jun;67(6):655-663.

- <https://doi.org/10.1007/s12630-020-01630-7>
PMid:32180175 PMCID:PMC7090434
17. Liu H, Liu F, Li J, Zhang T, Wang D, Lan W. Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children. *J Infect.* 2020 May;80(5):e7-e13.
<https://doi.org/10.1016/j.jinf.2020.03.007>
PMid:32171865 PMCID:PMC7156118
18. Yang H, Sun G, Tang F, et al. Clinical features and outcomes of pregnant women suspected of coronavirus disease 2019. *J Infect.* 2020 Jul;81(1):e40-e44.
<https://doi.org/10.1016/j.jinf.2020.04.003>
PMid:32294503 PMCID:PMC7152867
19. Liu D, Li L, Wu X, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. *AJR Am J Roentgenol.* 2020 Jul;215(1):127-132.
<https://doi.org/10.2214/AJR.20.23072>
PMid:32186894
20. Yan J, Guo J, Fan C et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. *Am J Obstet Gynecol.* 2020 Jul;223(1):111.e1-111.e14.
<https://doi.org/10.1016/j.ajog.2020.04.014>
PMid:32335053 PMCID:PMC7177142
21. Breslin N, Baptiste C, Gyamfi-Bannerman C, et al. Coronavirus disease 2019 among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM* 2020a;2:100118.
<https://doi.org/10.1016/j.ajogmf.2020.100118>
PMid:32292903 PMCID:PMC7144599
22. Breslin N, Baptiste C, Miller R, et al. Coronavirus disease 2019 in pregnancy: early lessons. *Am J Obstet Gynecol MFM.* 2020b May;2(2):100111.
<https://doi.org/10.1016/j.ajogmf.2020.100111>
PMid:32518902 PMCID:PMC7271091
23. Wu C, Yang W, Wu X, et al. Clinical Manifestation and Laboratory Characteristics of SARS-CoV-2 Infection in Pregnant Women. *Virol Sin.* 2020 Jun;35(3):305-310.
<https://doi.org/10.1007/s12250-020-00227-0>
PMid:32314274 PMCID:PMC7167538
24. Wu X, Sun R, Chen J, Xie Y, Zhang S, Wang X. Radiological findings and clinical characteristics of pregnant women with COVID-19 pneumonia. *Int J Gynaecol Obstet.* 2020 Jul;150(1):58-63.
<https://doi.org/10.1002/ijgo.13165>
PMid:32270479
25. Pierce-Williams RAM, Burd J, Felder L, et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. *Am J Obstet Gynecol MFM.* 2020 Aug;2(3):100134.
<https://doi.org/10.1016/j.ajogmf.2020.100134>
PMid:32391519 PMCID:PMC7205698
26. Khan S, Peng L, Siddique R, Nabi G, Nawsherwan, Xue M, Liu J, Han G. Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth. *Infect Control Hosp Epidemiol.* 2020a Jun;41(6):748-750.
<https://doi.org/10.1017/ice.2020.84>
PMid:32279693 PMCID:PMC7156579
27. Fan C, Lei D, Fang C, et al. Perinatal Transmission of 2019 Coronavirus Disease-Associated Severe Acute Respiratory Syndrome Coronavirus 2: Should We Worry? *Clin Infect Dis.* 2021 Mar 1;72(5):862-864.
<https://doi.org/10.1093/cid/ciaa226>
PMid:32182347 PMCID:PMC7184438
28. Chen Y, Peng H, Wang L, et al. Infants Born to Mothers With a New Coronavirus (COVID-19). *Front Pediatr.* 2020 Mar 16;8:104.
<https://doi.org/10.3389/fped.2020.00104>
PMid:32266184 PMCID:PMC7098456
29. Campbell KH, Tornatore JM, Lawrence KE, et al. Prevalence of SARS-CoV-2 Among Patients Admitted for Childbirth in Southern Connecticut. *JAMA.* 2020 Jun 23;323(24):2520-2522.
<https://doi.org/10.1001/jama.2020.8904>
PMid:32453390 PMCID:PMC7251498
30. Baergen RN, Heller DS. Placental Pathology in Covid-19 Positive Mothers: Preliminary Findings. *Pediatr Dev Pathol.* 2020 May-Jun;23(3):177-180.
<https://doi.org/10.1177/1093526620925569>
PMid:32397896 PMCID:PMC7252218
31. Khan S, Jun L, Nawsherwan, et al. Association of COVID-19 with pregnancy outcomes in health-care workers and general women. *Clin Microbiol Infect.* 2020b Jun;26(6):788-790.
<https://doi.org/10.1016/j.cmi.2020.03.034>
PMid:32278081 PMCID:PMC7141623
32. Zeng L, Xia S, Yuan W, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr.* 2020 Jul 1;174(7):722-725.
<https://doi.org/10.1001/jamapediatrics.2020.0878>
PMid:32215598 PMCID:PMC7099530
33. Liu W, Wang J, Li W, Zhou Z, Liu S, Rong Z. Clinical characteristics of 19 neonates born to mothers with COVID-19. *Front Med.* 2020 Apr;14(2):193-198.
<https://doi.org/10.1007/s11684-020-0772-y>
PMid:32285380 PMCID:PMC7152620
34. Cao D, Yin H, Chen J, et al. Clinical analysis of ten pregnant women with COVID-19 in Wuhan, China: A retrospective study. *Int J Infect Dis.* 2020 Jun;95:294-300.
<https://doi.org/10.1016/j.ijid.2020.04.047>
PMid:32335338 PMCID:PMC7179499
35. Xu L, Yang Q, Shi H, et al. Clinical presentations and outcomes of SARS-CoV-2 infected pneumonia in pregnant women and health status of their neonates. *Sci Bull (Beijing).* 2020 Sep 30;65(18):1537-1542.
<https://doi.org/10.1016/j.scib.2020.04.040>
PMid:32346493 PMCID:PMC7186128
36. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, et al. Maternal death due to COVID-19. *Am J Obstet Gynecol.* 2020 Jul;223(1):109.e1-109.e16.
<https://doi.org/10.1016/j.ajog.2020.04.030>
PMid:32360108 PMCID:PMC7187838
37. Hirshberg A, Kern-Goldberger AR, Levine LD, et al. Care

- of critically ill pregnant patients with coronavirus disease 2019: a case series. *Am J Obstet Gynecol.* 2020 Aug;223(2):286-290. <https://doi.org/10.1016/j.ajog.2020.04.029> PMID:32371056 PMCID:PMC7252050
38. Qiancheng X, Jian S, Lingling P, et al. Coronavirus disease 2019 in pregnancy. *Int J Infect Dis.* 2020 Jun;95:376-383. = <https://doi.org/10.1016/j.ijid.2020.04.065> PMID:32353549 PMCID:PMC7185021
39. Hu X, Gao J, Luo X, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers With Coronavirus Disease 2019 (COVID-19) Pneumonia. *Obstet Gynecol.* 2020 Jul;136(1):65-67 <https://doi.org/10.1097/AOG.0000000000003926> PMID:32332320 PMCID:PMC7219851
40. Cooke WR, Billett A, Gleeson S, et al. SARS-CoV-2 infection in very preterm pregnancy: Experiences from two cases. *Eur J Obstet Gynecol Reprod Biol.* 2020 Jul;250:259-260. <https://doi.org/10.1016/j.ejogrb.2020.05.025> PMID:32425297 PMCID:PMC7227538
41. Dória M, Peixinho C, Laranjo M, Mesquita Varejão A, Silva PT. Covid-19 during pregnancy: A case series from an universally tested population from the north of Portugal. *Eur J Obstet Gynecol Reprod Biol.* 2020 Jul;250:261-262 <https://doi.org/10.1016/j.ejogrb.2020.05.029> PMID:32425298 PMCID:PMC7227580
42. Lokken EM, Walker CL, Delaney S, et al. Clinical characteristics of 46 pregnant women with a severe acute respiratory syndrome coronavirus 2 infection in Washington State. *Am J Obstet Gynecol.* 2020 Dec;223(6):911.e1-911.e14. <https://doi.org/10.1016/j.ajog.2020.05.031> PMID:32439389 PMCID:PMC7234933
43. Savasi VM, Parisi F, Patanè L, et al. Clinical Findings and Disease Severity in Hospitalized Pregnant Women With Coronavirus Disease 2019 (COVID-19). *Obstet Gynecol.* 2020 Aug;136(2):252-258. <https://doi.org/10.1097/AOG.0000000000003979> PMID:32433453
44. London V, McLaren R Jr, Atallah F, et al. The Relationship between Status at Presentation and Outcomes among Pregnant Women with COVID-19. *Am J Perinatol.* 2020 Aug;37(10):991-994. <https://doi.org/10.1055/s-0040-1712164> PMID:32428964 PMCID:PMC7416203
45. Govind A, Essien S, Karthikeyan A, Fakokunde A, Janga D, Yoong W, Nakhosteen A. Re: Novel Coronavirus COVID-19 in late pregnancy: Outcomes of first nine cases in an inner city London hospital. *Eur J Obstet Gynecol Reprod Biol.* 2020 Aug;251:272-274. <https://doi.org/10.1016/j.ejogrb.2020.05.004> PMID:32402627 PMCID:PMC7204671
46. Ferrazzi EM, Frigerio L, Cetin I, et al. COVID-19 Obstetrics Task Force, Lombardy, Italy: Executive management summary and short report of outcome. *Int J Gynaecol Obstet.* 2020 Jun;149(3):377-378. <https://doi.org/10.1002/ijgo.13162> PMID:32267531
47. Li N, Han L, Peng M, et al. Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study. *Clin Infect Dis.* 2020;pii: ciao352. <https://doi.org/10.1093/cid/ciaa352> PMID:32249918 PMCID:PMC7184430
48. Zhang L, Jiang Y, Wei M, et al. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. *Zhonghua Fu Chan Ke Za Zhi.* 2020 Mar 7;55(0):E009. <https://doi.org/10.3760/cma.j.cn112141-20200218-00111>. PMID: 32145714
49. Zaigham M, Andersson O. Maternal and Perinatal Outcomes with COVID-19: a systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand.* 2020 Apr 7. <https://doi.org/10.1111/aogs.13867> PMID:32259279 PMCID:PMC7262097
50. Dong L, Tian J, He S, , et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.4621> PMID:32215581 PMCID:PMC7099527
51. Murad MH, Asi N, Alsawas M, Alahdab F. New evidence pyramid. *Evid Based Med.* 2016;21:125-7. <https://doi.org/10.1136/ebmed-2016-110401> PMID:27339128 PMCID:PMC4975798
52. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet.* 2020;395(10224):565-74. [https://doi.org/10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8) PMID: 32007145 PMCID: PMC7159086
53. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol* 2004;203: 631-7. <https://doi.org/10.1002/path.1570> PMID:15141377 PMCID:PMC7167720
54. To KF, Lo AW. Exploring the pathogenesis of severe acute respiratory syndrome (SARS): the tissue distribution of the coronavirus (SARS-CoV) and its putative receptor, angiotensin-converting enzyme 2 (ACE2). *J Pathol* 2004;203:740-3. <https://doi.org/10.1002/path.1597> PMID:15221932 PMCID:PMC7167902
55. Liang H, Acharya G. Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow? *Acta Obstet Gynecol Scand*, 99: 439-42. <https://doi.org/10.1111/aogs.13836> PMID:32141062
56. Zeng H, Xu C, Fan J, et al. Antibodies in Infants Born to Mothers With COVID-19 Pneumonia. *JAMA.* 2020 May 12;323(18):1848-1849. <https://doi.org/10.1001/jama.2020.4861> PMID: 32215589; PMCID: PMC7099444.
57. Critical Care Protocols for COVID-19 Patients. <http://www.med.umich.edu/surgery/mcccn/documents/Covid->

[Critical-Care-Protocols-v2.pdf](#).

58. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. *N Engl J Med*. 2020.

<https://doi.org/10.1056/NEJMc2009316>

PMid:32283004 PMCID:PMC7175422

59. Queensland Clinical Guidelines Perinatal care of suspected or confirmed COVID-19 pregnant women. Guideline No. MN20.63-V2-R25. Queensland Health. 2020. Available from: <http://www.health.qld.gov.au/qcg>.

60. Infection prevention and control during health care when novel coronavirus (CAUVID-19) infection is suspected Interim guidance. Available at: [https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected).

61. WHO 2020. Q&A on COVID-19, pregnancy, childbirth and breastfeeding 18 March 2020. Available at: <https://www.who.int/news-room/q-a-detail/q-a-on-covid-19-pregnancy-childbirth-and-breastfeeding>

Accessed: 14 April 2020

62. Clinical management of severe acute respiratory infection when Novel coronavirus (2019-nCoV) infection is suspected: Interim Guidance. WHO/nCoV/Clinical/2020.3 January 28 2020.

63. Matos R, Chung KK. DoD COVID-19 practice management guide. Clinical Management of 2019;COVID-19:23. Available at:

<http://www.med.umich.edu/surgery/mcccn/documents/DoD-COVID-19-Practice-Management-Guide-V10>

Accessed: 16 April 2020

64. Song Y, Zhang M, Yin L, et al. COVID-19 treatment: close to a cure? A rapid review of pharmacotherapies for the novel coronavirus (SARS-CoV-2). *Int J Antimicrob Agents*. 2020 Aug;56(2):106080.

<https://doi.org/10.1016/j.ijantimicag.2020.106080>.

PMiD: 32634603 PMCID: PMC7334905

65. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020;30:269-71.

<https://doi.org/10.1038/s41422-020-0282-0>

PMid:32020029 PMCID:PMC7054408

66. Coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK - seventh update, 25 March 2020. Stockholm: ECDC; 2020.

67. Asadi L, Tabatabaei R S, Safinejad H, Mohammadi M. New Corona Virus (COVID-19) Management in Pregnancy and Childbirth. *Arch Clin Infect Dis*. Online ahead of Print ; 15(COVID-19):e102938.

<https://doi.org/10.5812/archcid.102938>

68. Rashidi Fakari F, Simbar M. Coronavirus Pandemic and Worries during Pregnancy; a Letter to Editor. *Arch Acad Emerg Med*. 2020 Mar 16;8(1):e21.

PMiD: 32185371; PMCID: PMC7075675.

69. Rimmer Abi. Covid-19: doctors in final trimester of pregnancy should avoid direct patient contact. *BMJ*. 2020;368:m1173.

<https://doi.org/10.1136/bmj.m1173>

PMid:32205356

70. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) infection in pregnancy: information for healthcare professionals (version 2). 13 March 2020. www.rcog.org.uk/globalassets/documents/guidelines/2020-03-21-covid19-pregnancy-guidance-2118.pdf.

71. Bonačić Marinović A, Swaan C, van Steenberg J, Kretzschmar M. Quantifying reporting timeliness to improve outbreak control. *Emerg Infect Dis*. 2015;21:209-16. doi:10.3201/eid2102.130504

<https://doi.org/10.3201/eid2102.130504>

PMid:25625374 PMCID:PMC4313625

72. Guidance on Preparing Workplaces for COVID-19. Occupational Safety and Health Administration 2020. <https://www.osha.gov/Publications/OSHA3990.pdf>