

# Pregnancy during the evolving pandemic Coronavirus Disease 2019 (COVID-19): A rapid scoping review of evidence in the published literature

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## Systematic Review

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# Abstract

## Background

With more than 1 million confirmed cases of coronavirus disease 2019 (COVID-19) worldwide and more than 50,000 deaths, the pandemic of Severe Acute Respiratory Syndrome CoV (SARS-CoV-2) is rapidly evolving. SARS-CoV-2 can also pose a higher risk to pregnant women, due to their immunosuppression during pregnancy. This study investigates the emerging and most UpToDate published scientific literature on the clinical feature and management recommendations for pregnant women with COVID-19.

## Method

A wide range of published scientific literature was systematically searched from PubMed, Embase, Scopus, Web of Science, and "Global research on coronavirus disease (COVID-19)" managed by the World Health Organization, published between 1 January 2019 to 27 March 2020. No limitations were used for geographical location, and articles published in English were included in the review. Results for the eligible studies were charted, analyzed, and presented in a narrative format.

## Result

Our study identified 52 unique articles, and 29 of those articles were included in this review after fulltext screening. Participants were mostly in their third trimester and presented with fever, dry cough, myalgia, shortness, and difficulty in breathing. Ground-glass opacity in the computerized tomography scan of the chest was the cardinal feature of COVID-19 pneumonia. Except for two participants, severe pneumonia did not occur among pregnant women. Pregnant women with COVID-19 were treated with a wide range of antiviral drugs. Higher episodes of preterm birth and cesarean delivery were observed; however, it cannot be explicitly attributed to the SARS-CoV-2. There is no published evidence on the vertical transmission of SARS-CoV-2. Pregnancy with COVID-19 infection must be managed by a collaborative team of healthcare professionals during antenatal, delivery, or postnatal stage. Detailed contact tracing, investigating travel history, radiological assessment, and laboratory tests with regular fetal health monitoring must be done.

## Conclusion

The emerging evidence of higher perinatal complications puts pregnant women in a further vulnerable condition. Cautiousness is imperative during the clinical management of pregnant women with COVID-19, as there is no approved treatment regime available at this moment. More research is necessary to fill the gaps in the knowledge of the clinical spectrum of COVID-19 among pregnant women.

## Background

As of 3 April 2020, more than 1 million confirmed coronavirus disease 2019 (COVID-19) cases have been detected worldwide, and more than 50,000 deaths have been attributed to this pandemic (1). COVID-19 is caused by a novel mutation of a previously known coronavirus (CoV) and has been labeled as Severe Acute Respiratory Syndrome CoV (SARS-CoV-2), mostly spreads through respiratory droplets made by sneezing and coughing. This is also known as Wuhan CoV due to its first detection in Wuhan, the capital city of Hubei province in China. Now, this virus has been detected across all regions (195 countries) within the world. This is an enveloped and positive-sense single-stranded ribonucleic acid virus belonging to the 'Coronaviridae' family, 'Nidovirales' order, and 'Rivoviria' realm (2). CoV has also caused SARS (began in 2002) and the Middle East respiratory syndrome (began in 2012) epidemics before COVID-19 (3).

Although a large proportion of people infected with SARS-CoV-2 may suffer from asymptomatic infection to mild to moderate fever or respiratory illness and would recover without any special treatment, older people and people with underlying medical conditions or immunosuppression (e.g., cardiovascular disease, diabetes, and other chronic diseases) may demonstrate a severe form of pneumonia, including deaths (4,5). SARS-CoV-2 can also pose pregnant women at higher risk due to their immunosuppression during pregnancy (6); however, it remains unclear whether this virus is transmitted from mother to child during pregnancy (7). Although new data are coming regarding its origin, microbiological and clinical features, and severity, few previous studies reported its impacts during pregnancy.

Despite the dearth of existing studies, summarizing the existing case reports/series, expert consensus, correspondences, commentaries, opinions, editorials, research letters, original articles, and systematic reviews may help to understand the impacts of SARS-CoV-2 on pregnancy, including clinical management because of little knowledge about these. A scoping review of the existing literature may help identify not only available knowledge but also existing gaps and may direct future research (8). However, despite preliminary evidence and rationale suggesting that SARS-CoV-2 infection during pregnancy may severely impact its outcomes, to our knowledge, no previous studies conducted any scoping review by summarizing all existing studies. We aim to address these knowledge gaps by investigating the

most UpToDate published scientific literature to synthesize the growing body of evidence on the clinical feature of COVID-19 among pregnant women and recommendations around their clinical management.

## Methods

This rapid scoping review was conducted following the steps recommended by Arksey and O'Malley (9), and Levac and colleagues (10). Reporting of the result of the review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses' Extension for Scoping Reviews (PRISMA-ScR) (11). Development of search strategy and literature search was collaboratively done by MH and TA. Two investigators (MH and GMK) independently performed the study selection by title and abstract, and full-text screening. Due to the limitation of time, data extraction, and synthesis of the result was done collaboratively by MH and GMK. Fig. 1 presents the schematic diagram of the study selection process based on the guidelines of Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). Ethical approval was not obtained for the review, as all required information was obtained from publicly available literature, and no primary data was collected or generated during the review process.

## Search strategy and selection criteria

A rapid scoping review was conducted to identify the relevant scientific literature providing recent evidence on clinical features and management recommendations for COVID-19 among pregnant women. As part of the review process, a systematic and replicable search strategy was developed considering two concepts: (a) pregnant women, and (b) COVID-19. Relevant keywords and index terms associated with these two concepts were identified from the MeSH terms listed in PubMed and from Google Scholar.

The search strategy was implemented between 1 January 2019 to 27 March 2020 across four electronic databases: (a) PubMed ([ncbi.nlm.nih.gov/pubmed/](http://ncbi.nlm.nih.gov/pubmed/)), (b) Embase ([embase.com](http://embase.com)), (c) Scopus ([scopus.org](http://scopus.org)), and (d) Web of Science ([webofknowledge.com](http://webofknowledge.com)). Also, a hand search was conducted in the electronic database "Global research on coronavirus disease (COVID-19)" managed by World Health Organization (WHO) (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov>). Literature search from PubMed generated 28 records published between 01 January 2019 to 27 March 2020 (Dated 27 March 2020). The search strategy for PubMed is presented in Table 1, and the details of the individual search strategy for the other databases are provided in the supplementary material.

**Table 1: PubMed Search Strategy on pregnancy and Coronavirus Disease 2019 (COVID-19) implemented on 27 March 2020**

Database	Concept	Key Words	Results
PubMed	Pregnant women	Line (Pregnant Woman[MESH] OR Pregnant*[tw] OR Gestation[tw] OR Gravid*[tw] OR natal*[tw] OR Antenatal[tw] OR Perinatal[tw] OR Postnatal[tw] OR partum*[tw] OR Antepartum*[tw] OR peripartum*[tw] OR postpartum*[tw] OR puerperium[tw]) AND	28
	Coronavirus disease-19	Line Wuhan coronavirus"[tw] OR "Wuhan seafood market pneumonia virus"[tw] OR "COVID19 virus"[tw] OR "COVID-19 virus"[tw] OR "coronavirus disease 2019 virus"[tw] OR "SARS-CoV-2"[tw] OR "SARS2"[tw] OR "2019-nCoV"[tw] OR "2019 novel coronavirus"[tw] OR "2019 novel coronavirus infection"[tw] OR "2019-nCoV infection"[tw] OR "COVID-19 pandemic"[tw] OR "coronavirus disease-19"[tw] OR "2019-nCoV disease" OR "COVID19"[tw] OR "2019 novel coronavirus disease"[tw] OR "coronavirus disease 2019"[tw]) AND	
	Time frame	Line ("2019/01/01"[PDat] : "2020/03/27"[PDat])	
		3	

Search results from the five electronic databases resulted in 69 initially identified literature, which was imported into Covidence systematic review software ([covidence.org](http://covidence.org)) to implement the selection process. At this stage, 17 duplicates were removed. Next, titles and the abstracts of 52 uniquely identified studies were screened, and an additional 11 studies were found to be irrelevant based on the set of a priori inclusion and exclusion criteria (Table 2).

**Table 2: Inclusion and exclusion criteria for the record selection process associated with pregnancy and Coronavirus Disease 2019 (COVID-19)**

	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Theme	Evidence of Coronavirus disease-19 among pregnant women	Records which did not provide any findings or recommendation related to Coronavirus disease-19 among pregnant women
Evidence characteristics	Original research Case studies or case reports Expert consensus Correspondence, commentary, opinion or editorials Systematic, scoping or rapid review Research letter	Author's reply Research highlight News or media watch
Time frame	1 January 2019 to 27 March 2020	
Reporting characteristics	Records published in scientific journals	Records not published in English

For the eligible literature presenting the subject matter of the scoping review, full documents were obtained and imported into Covidence. For full-text screening, the same set of criteria was used by the investigators. Studies published in scientific journals and written in English were included. Due to the methodological plasticity of scoping review, a variety of published literature was included in the studies, which includes original research, case studies or reports, expert consensus, correspondence, reviews, etc. However, author's reply, research highlights, and news or media watches were excluded from the review.

## Charting the data and analysis

Investigator charted data on study characteristics (the type of study, location of the study), population characteristics (number of pregnant women, the clinical features of the women), and type of evidence presented in the study. The charted data was summarized by two thematic areas: (a) clinical feature of pregnant women with COVID-19, and (b) recommendations for clinical management of COVID-19 during pregnancy. The collated evidence is presented in a narrative format with the help of tables.

Due to the sparsity of data and the evolving nature of the evidence, the quality of the published literature was not assessed for robustness or generalizability in the rapid scoping review (9,12,13). While Levac and colleagues (10) recommended expert consultation, due to time limitation, it was not performed as a part of this scoping review. No patients or populations were included in the conception and conduct of the scoping review.

## Results

Out of the 69 extracted publications, 29 full-text publications were included for the scoping review (6,14–41) (Table 3). Among the included studies, 16 presented clinical findings of COVID-19 among pregnant women, which includes six original articles (15,16,23–25,41), three case reports (18,35,36), two case-reviews (32,39), two research letters (21,40), and one correspondence (37), rapid review (27) and systematic review and meta-analysis (17) each. Out of these 16 studies, only 13 reported original data (15,16,18,21,23–25,27,35–37,40,41) and three study (17,32,34) reviewed data from existing studies (Table 4). From the 16 studies which presented clinical findings of COVID-19, 15 articles were from China and only one from Honduras (40). Cumulatively clinical features of 229 pregnant women were reported in the studies included in this review – ranging from a single (21,35–37,40) to 41 pregnant women (17,24). One of the original articles from Zhu and colleagues (41) was originally presented the clinical findings from 10 neonates. However, we only included the relevant information on the pregnant COVID-19 cases from that study. It is possible that duplication of clinical cases presents between studies – however – we have actively tried to remove duplicate findings from the result.

**Table 3: Specifications of published studies (1 January 2019 to 27 March 2020) on pregnancy and Coronavirus Disease 2019 (COVID-19) between**

Reference	Study Type	Country	Number of Pregnant Woman	Original Finding Reported	Recommendation Reported
Chen et al.(14)	Expert consensus	..	..	No	Yes
Chen et al. (15)	Original article	China	9	Yes	No
Chen et al. (16)	Original article	China	17	Yes	Yes
Di Mascio et al. (17)	Systematic review & meta-analysis	China	41 <sup>a</sup>	No	Yes
Fan et al. (18)	Case report	China	2	Yes	Yes
Favre et al. (19)	Correspondence	..	..	No	Yes
Jiao(20)	Commentary	..	..	No	Yes
Li et al. (21)	Research letter	China	1	Yes	Yes
Liang & Acharya (22)	Special editorial	..	..	No	Yes
Liu et al. (23)	Original article	China	15	Yes	No
Liu et al. (6)	Review article	..	..	No	Yes
Liu et al. (24)	Original article	China	41 <sup>b</sup>	Yes	No
Liu et al. (25)	Original article	China	13	Yes	No
Moro et al. (26)	Correspondence	..	..	No	Yes
Mullins et al. (27)	Rapid review	..	32	Yes	Yes
Poon et al. (28)	Opinion	..	..	No	Yes
Qiao (29)	Comment	..	..	No	Yes
Rasmussen & Jamieson (30)	Commentary	..	..	No	Yes
Rasmussen et al. (31)	Expert review	..	..	No	Yes
Schwartz (32)	Case review	China	38	No	No
Schwartz & Graham (33)	Correspondence	..	..	No	No
Wang et al. (34)	Correspondence	China	..	No	Yes
Wang et al. (35)	Case report	China	1	Yes	No
Wang et al. (36)	Case report	China	1	Yes	No
Wen et al. (37)	Correspondence	China	1	Yes	No
Yang et al. (38)	Opinion	..	..	No	Yes
Yu et al. (39)	Case review	China	7	No	Yes
Zambrano et al. (40)	Research letter	Honduras	1	Yes	No
Zhu et al. (41)	Original article	China	9	Yes	Yes

Note: a = Out of the 79 pregnancies affected by Corona Virus infections, 41 were affected by SARS-CoV-2

b = Out of 59 patients with COVID-19, 41 were pregnant

**Table 4: Findings on pregnancy and Coronavirus Disease 2019 (COVID-19) reported in published literature (1 January 2019 to 27 March 2020)**

Reference	Study Type	Patients Characteristics	Findings
Chen et al. (15)	Original article	All nine pregnant women were confirmed COVID-19 were in their third trimester	<ul style="list-style-type: none"> <li>• Seven women were presented with fever without chill</li> <li>• Other symptoms included cough, myalgia, sore throat and malaise</li> <li>• None of the women developed severe pneumonia</li> <li>• Lymphopenia, elevated C-reactive protein, aminotransferase (ALT) and aspartate aminotransferase (AST) were observed among several patients</li> <li>• Eight out of nine pregnant women presented patchy ground-glass opacity in the lung in CT scan</li> <li>• All pregnant women underwent cesarean section</li> <li>• All deliveries resulted in live births with no evidence of vertical transmission of SARS-CoV-2</li> <li>• The SARS-CoV-2 virus was not present in amniotic fluid, cord blood, neonatal throat swab, and breastmilk</li> </ul>
Chen et al. (16)	Original article	All 17 pregnant women were tested positive by RT-PCR for SARS-CoV-2	<ul style="list-style-type: none"> <li>• Four women were presented with mild fever and chill</li> <li>• Other symptoms included cough, fatigue, chest distress, overt dyspnea, and diarrhea</li> <li>• Lymphopenia and elevated C-reactive protein were reported for some patients. However, all patients had a normal level of ALT, AST, creatinine and blood urea nitrogen</li> <li>• All pregnant women presented patchy ground-glass opacity in the lung in CT scan</li> <li>• All pregnant women underwent cesarean section</li> <li>• 14 pregnant women received epidural anesthesia, and 12 of them experienced intraoperative hypotension</li> <li>• Three patients received general anesthesia with tracheal intubation due to deteriorating clinical condition</li> <li>• All deliveries resulted in live births, and none of the newborns were tested positive for SARS-CoV-2</li> </ul>
Di Mascio et al. (17)	Systematic review and meta-analysis	All nine pregnant women were confirmed COVID-19 were in their third trimester	<ul style="list-style-type: none"> <li>• Most common symptoms of COVID-19 were fever, cough, and lymphopenia</li> <li>• Radiological findings of pneumonia were presented in most of the cases</li> <li>• No data were presented on miscarriage during the first trimester related to COVID-19 infection</li> <li>• While the sample size is very limited, compared to MERS and SARS, COVID-19 infection resulted in higher rates of miscarriage, preeclampsia and preterm birth</li> <li>• Preterm birth was reported most of the cases (41% before 37 weeks and 15% before 34 weeks)</li> <li>• Preterm rupture of membranes reported for 19%, whereas only one pregnant woman suffered from Pre-eclampsia and no fetal growth restriction were reported</li> <li>• No maternal death was reported</li> </ul>

Reference	Study Type	Patients Characteristics	Findings
			<ul style="list-style-type: none"> <li>Vertical transmission of SARS-CoV-2 was not reported for any newborns</li> </ul>
Fan et al. (18)	Case report	Both pregnant women were physicians with confirmed COVID-19 were in their third trimester	<ul style="list-style-type: none"> <li>Fever and nasal congestion were reported in both cases</li> <li>One of the patients presented a rash on her abdomen</li> <li>CT scan of the chest showed patchy consolidations indicating pneumonia</li> <li>Complete blood count was indicative of lymphopenia only in one of the cases</li> <li>Oseltamivir and Lianhua Qingwen capsules were prescribed for both cases. However, one of the pregnant women received Ceftazidime as antibiotic treatment - whereas - the other women received Azithromycin.</li> <li>One of the cases received methylprednisolone for pneumonia</li> <li>Both pregnant women underwent cesarean section</li> <li>Vertical transmission of SARS-CoV-2 was not reported, and the newborns or any products of conception was not tested positive for SARS-CoV-2</li> </ul>
Li et al. (21)	Research Letter	The pregnant women were in 35th week of pregnancy with confirmed COVID-19	<ul style="list-style-type: none"> <li>Clinical symptoms started with dry cough and fever</li> <li>Radiography of chest presented multiple patchy and scattered infiltrates in both lungs</li> <li>Antiviral drugs (Lopinavir and Ritonavir) and methylprednisolone were given to the patient.</li> <li>Emergency cesarean section was conducted on 36th week of the pregnancy, and the women delivered a live and healthy baby</li> <li>The newborn was not tested positive for SARS-CoV-2 in repeated testing during the postnatal period</li> </ul>
Liu et al. (23)	Original article	All 15 pregnant women were confirmed for COVID-19 pneumonia with gestational age ranging from 12-38 weeks	<ul style="list-style-type: none"> <li>Most prevalent clinical symptoms were fever and cough</li> <li>Fatigues, muscle ache, dyspnea, sore throat, and diarrhea were observed in fewer patients</li> <li>Lymphopenia and elevated C-reactive protein was observed among 12 and 10 patients accordingly, which were returned to normal</li> <li>Early CT scan of the chest indicated ground-glass opacities in the lungs which developed into crazy paving pattern and consolidations</li> <li>Among the 15 women, ten underwent cesarean section, and one delivered vaginally</li> <li>The 11 women, who delivered, received antiviral treatment after delivery. The other four women did not receive antiviral treatment. All 15 women received antibiotic treatment</li> <li>No neonatal complication was observed, and the newborns were not tested positive for SARS-CoV-2</li> </ul>
Liu et al. (24)	Original article	Among 41 pregnant women 16 were laboratory positive SARS-CoV-2, 25 were clinically-diagnosed COVID-19 cases. Their gestational age ranging from 22-40 weeks	<ul style="list-style-type: none"> <li>Initially, the pregnant women presented normal body temperature compared to the non-pregnant group</li> <li>Leukocytosis and elevated neutrophil ratio were also presented among pregnant women</li> </ul>

Reference	Study Type	Patients Characteristics	Findings
			<ul style="list-style-type: none"> <li>In the scan of the chest, a higher proportion of pregnant women presented mixed and complete consolidation compared to the non-pregnant group. However, pure ground-glass opacity was more common among the non-pregnant group</li> <li>Six laboratory-positive and 8 CT-confirmed pregnant women receive Antiviral therapy.</li> <li>Vertical transmission of SARS-CoV-2 was not reported for any newborns</li> </ul>
Liu et al. (25)	Original article	Among 13 pregnant women with SARS-CoV-2 positive, two women were less than 28 weeks of gestation, and 11 were in their third trimester	<ul style="list-style-type: none"> <li>Most of the patients reported fever and fatigue. Other less prevalent feature included dyspnea</li> <li>After treatment, three pregnant women were discharged.</li> <li>Ten pregnant women went through the cesarean section. Among them, five underwent emergency cesarean section due to complications (such as fetal distress [three], premature rupture of the membrane [10] and stillbirth [one])</li> <li>Six pregnant women experienced preterm birth</li> <li>One pregnant woman developed severe pneumonia with multiple organ failure, acute respiratory distress syndrome, acute hepatic failure, acute renal failure, and septic shock. Her respiration was supported by extracorporeal membrane oxygenation (ECMO) in the intensive care unit (ICU)</li> <li>No vertical transmission of SARS-CoV-2 was reported among the live births</li> </ul>
Mullins et al. (27)	Rapid review	32 pregnant women with confirmed SARS-CoV-2 infection	<ul style="list-style-type: none"> <li>fetal growth was not affected, and no information is available related to placental pathology</li> <li>Of the 32 pregnancies, 30 babies were delivered. Seven women were asymptomatic, and two were admitted to the intensive care unit. However, no maternal death was reported</li> <li>47% (15 out of 32) pregnant women delivered prematurely. And most of the delivery was conducted by cesarean section</li> <li>No vertical transmission of SARS-CoV-2 was reported among the live births</li> </ul>
Rasmussen et al. (31)	Expert review	--	<ul style="list-style-type: none"> <li>Currently, there is no evidence suggesting pregnant women are more susceptible to COVID-19</li> <li>Most common symptoms of COVID-19 are fever and cough, while lymphopenia was also common in several cases</li> <li>Premature birth and cesarean section were reported in several studies</li> <li>Any abnormality of fetal heart rate may indicate an early sign of the mothers' respiratory deterioration.</li> <li>There is limited information on perinatal or postnatal modes of transmission</li> </ul>
Schwartz (32)	Case review	All 38 pregnant women were in their third trimester in pregnancy, and 37 had confirmed SARS-CoV-2 infection	<ul style="list-style-type: none"> <li>Clinical features included fever, cough, myalgia, sore throat, malaise, gastrointestinal symptoms and shortness of breath</li> <li>Laboratory features were indicative of lymphopenia and elevated C-reactive protein, ALT, and AST.</li> <li>Patchy ground-glass opacity and pulmonary consolidation is observed in lung CT scan</li> <li>Premature rupture of membranes was observed most of the cases, which lead to premature birth by cesarean section was reported in most of the cases</li> </ul>

Reference	Study Type	Patients Characteristics	Findings
			<ul style="list-style-type: none"> <li>No vertical transmission of SARS-CoV-2 was reported</li> <li>One study from the review reported several newborns presented gastrointestinal (gastric bleeding, refusal to feed, bloating and food intolerance) and respiratory symptoms (abnormalities in chest radiography, respiratory distress syndrome, and pneumothorax). Two children developed thrombocytopenia. One premature newborn died on the 9th day due to multiple organ failure, refractory shock, and disseminated intravascular coagulation</li> </ul>
Wang et al. (35)	Case report	The pregnant women were in her 40th week of pregnancy with COVID-19	<ul style="list-style-type: none"> <li>The pregnant women developed low-grade fever two hours after having small vaginal bleeding and lower abdominal pain</li> <li>Chest CT scan indicated ground-glass opacities in the lung (left upper and lower lobes)</li> <li>Laboratory diagnostic presented lymphopenia, neutrophilia, elevated C-reactive protein</li> <li>Though there was no fetal distress, emergency cesarean delivery was performed, and meconium-stained liquor reported during the operative process</li> <li>Immediate after delivery, the mother was asymptomatic, but later developed a fever. She received antiviral (Interferon <math>\alpha</math>1b and Ganciclovir) and antibiotic (Abipenem and Moxifloxacin) and methylprednisolone.</li> <li>The newborn was separated from the mother after the delivery. The infant appeared to be healthy but presented lymphopenia, elevated AST, total bilirubin, indirect bilirubin, and creatine kinase</li> <li>The pharyngeal swab of the newborn was tested positive for SARS-CoV-2 at 36 hours after birth. However, the cord blood, placental specimens, and breast milk samples were tested negative for SARS-CoV-2.</li> <li>The CT scan of the infant's chest presented high-density nodular shadow which evolved into scattered with small pieces of patchy shadow in the upper lobe of the right lung</li> </ul>
Wang et al. (36)	Case report	A 30-week pregnant woman with COVID-19	<ul style="list-style-type: none"> <li>The pregnant women presented with fever for one week.</li> <li>Laboratory findings presented a low level of lymphocytes and albumin</li> <li>Chest CT scan of lung indicated ground-glass opacities (right side) and subpleural patchy consolidation (left side), which evolved into bilateral ground-glass opacities</li> <li>To prepare for emergency cesarean delivery, the mother was provided with antivirals (Arbidol, Lopinavir, and Ritonavir), antibiotic (Cefoperazone Sodium and Sulbactam Sodium), Human Serum Albumin, dexamethasone and magnesium sulfate</li> <li>Vertical transmission of SARS-CoV-2 was not reported, and the newborns or any products of conception was not tested positive for SARS-CoV-2</li> </ul>
Wen et al. (37)	Correspondence	A 30-week pregnant woman with COVID-19	<ul style="list-style-type: none"> <li>During the initial presentation, the pregnant women were presented with mild diarrhea; however, she was afebrile, breathing normally and without any cough or chest pain</li> <li>The chest CT scan of lung indicated ground-glass opacities and patchy consolidation in multiple regions. The lesions were "distributed along with the bronchial bundles or within the subpleural lung regions." A small collection of fluid found in the left pleural cavity</li> <li>The patient received interferon, antiviral (Lopinavir and Ritonavir)</li> </ul>

Reference	Study Type	Patients Characteristics	Findings
Yu et al. (39)	Original article	Seven pregnant women with COVID-19 between 37 weeks to 41 weeks of the gestational period	<ul style="list-style-type: none"> <li>The pregnant women were discharged after her nasopharyngeal swabs were negative for SARS-CoV-2 and clinical condition was improved</li> <li>The reported incubation period ranged from two to nine days.</li> <li>Major clinical feature of six out of seven patients was fever, with few patients reporting cough, shortness of breath and diarrhea</li> <li>Laboratory report indicated normal leukocyte count and elevated D-dimer for all patients. Five of the women had Neutrophilia, five had Lymphocytopenia, two had thrombocytopenia, and two had elevated ALT and AST.</li> <li>Chest CT scan of the lung of all seven women was indicative of pneumonia</li> <li>Antiviral medication (oseltamivir, ganciclovir, interferon, and arbidol) and antibiotic (cephalosporins, quinolones, and macrolides) were given to the patients, along with traditional Chinese medications. Five women were treated with methylprednisolone at the postpartum stage</li> <li>All patients underwent cesarean section with combined spinal and epidural anesthesia (six patients) or general anesthesia (one patient)</li> <li>Among the seven neonates four were not tested for SARS-CoV-2, three were tested for SARS-CoV-2, and one neonate was tested positive for SARS-CoV-2 after 36 hours of birth</li> </ul>
Zambrano et al. (40)	Research letter	Pregnant women with 31 weeks of gestation with COVID-19	<ul style="list-style-type: none"> <li>The initial presentation of the pregnant woman was fever, dry cough, myalgia, and headache. The patient also presented bilateral conjunctival hyperemia.</li> <li>There was no other clinical feature reported which was related to COVID-19</li> </ul>
Zhu et al. (41)	Original article	Nine pregnant women were confirmed with COVID-19 (gestational age 31-39 weeks)	<ul style="list-style-type: none"> <li>In most of the cases, fever and cough were the onsets of symptoms, with only one patient having diarrhea.</li> <li>CT scan of the chest indicated viral pneumonia with bilateral ground-glass opacities with patchy lung consolidation and blurred borders of the lungs. After treatment, the lesions resolved significantly.</li> <li>Several prenatal complications were reported which includes intrauterine distress (six women), premature rupture of membranes (three women), abnormality of amniotic fluid (two women) and umbilical cord (two women), and placenta previa (one woman)</li> <li>Five women received antiviral therapy (oseltamivir) after delivery. Among them, one received oseltamivir and interferon combination</li> <li>Seven women underwent cesarean sections, and two had vaginal deliveries.</li> <li>Vertical transmission of SARS-CoV-2 was not reported for any newborns</li> <li>Several newborns presented gastrointestinal (gastric bleeding, refusal to feed, bloating and food intolerance) and respiratory symptoms (abnormalities in chest radiography, respiratory distress syndrome, and pneumothorax). Two children developed thrombocytopenia. One premature newborn died on the 9th day due to multiple organ failure, refractory shock, and disseminated intravascular coagulation</li> </ul>

Most of the pregnant women suffering from COVID-19 cases were in their third trimester. Liu et al. (23) presented a case of early pregnancy in its 12<sup>th</sup> week. All the studies reported that COVID-19 confirmation had been done by real-time reverse transcription-polymerase chain reaction (RT-PCR) test; however, Liu and colleagues (24) included 25 participants (out of 41) who were laboratory negative SARS-CoV-2 but had clinical features of COVID-19.

Seven studies reported both clinical findings and recommendations for the management of COVID-19 during pregnancy, which included four original articles (15,16,24,41), two case-reports (18,36), and one correspondence (37). On the other hand, 12 studies exclusively discussed the recommendation of management of COVID-19 during pregnancy without providing any original findings. Among these studies, three were correspondences (19,26,34), two were commentaries (29,30), two were opinion pieces (28,38), one of case review (39), expert consensus (14), expert review (31), review article (6), and special editorial (22) each.

## Clinical presentation and diagnostics of COVID-19 among pregnant women

The most common and earliest clinical presentation of COVID-19 is fever, which is often accompanied by dry cough, myalgia, and malaise. Among initial respiratory symptoms, sore throat is most common; however, shortness and difficulty in breathing (dyspnea) and chest distress were reported by pregnant women. Four studies reported gastrointestinal symptoms such as diarrhea (16,23,37,39). Among the atypical findings, abdominal rash (18), and bilateral conjunctival hyperemia (40).

Apart from the RT-PCR result, computerized tomography (CT) scan of the chest was the primary mode of investigation used by the majority of the study to diagnose COVID-19 infection. Patchy ground-glass opacity (GGO) with or without consolidation was the most common feature of COVID-19 pneumonia, which resolved with time. Liu et al. (23) further elaborated on the progression of the lesion into paving patterns and consolidations. In addition to the lung parenchymal change, one of the atypical findings was found in a 30-week pregnant woman who presented with small pleural effusion on the left side.

Common laboratory finding among COVID-19 patients includes lymphopenia (lower-than-normal quantity of lymphocytes in the blood) and elevated C-reactive protein (indicator of inflammation) (15–18,23,31,32,35,36,39). Impaired liver function was also observed, which is reflected by increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (15,21,32,35,39). Among other laboratory findings, three studies reported neutrophilia (24,35,39); one study reported leukocytosis (24); one study stated a lower level of albumin (36); one study reported elevated D-dimer and thrombocytopenia (39) among the pregnant women.

## Medication prescribed to the COVID-19 cases

The antiviral drug was most commonly used to treat pregnant women with COVID-19, and the most frequently used four antiviral drugs were atomized inhalation of interferon-ALPHA (35,37,39,41), Oseltamivir (18,37,41), Lopinavir (21,37,37), and Ritonavir (21,36,37). Among other antiviral drugs, Ganciclovir (35) and Arbidol (36,39) were reported to be used in two studies each. The use of a wide range of antibiotics for the treatment of secondary bacterial pneumonia after the COVID-19 was also common, which included – Beta-lactam (35,36) (Abipenem and Sulbactam Sodium), Cephalosporins (18,36,39) (Cefoperazone Sodium and Ceftazidime), Macrolides(18,38) (Azithromycin), and Quinolones (35,38) (Moxifloxacin).

Besides, supportive treatment with methylprednisolone was provided for pneumonia (18,21,35,39). Two studies (18,39) reported the use of traditional Chinese medications along with antiviral and antibiotic treatment. In his case study, Wang et al. (36) reported a 30-week pregnant woman with COVID-19 was given Human Serum Albumin, dexamethasone, and magnesium sulfate to prepare her for an emergency cesarean delivery. The clinical condition of all the pregnant women – except two (25,27) – improved after the treatment. However, none of the studies commented on the efficacy or effectiveness of the medication given to the pregnant women for management of COVID-19.

## Maternal Outcomes

According to Rasmussen and colleagues (31), currently, there is no evidence suggesting higher susceptibility of COVID-19 among pregnant women, and no maternal death was reported in any study included in this scoping review. The incubation period among pregnant women ranges from two to nine days (39). The development of severe pneumonia was not reported by the majority of the studies. Two studies – Liu et al. (25) and Mullins et al. (27) – reported that two pregnant women developed severe pneumonia, which required mechanical ventilation support in the intensive care unit (ICU).

It is essential to mention that, except for one pregnant woman – in her 12 weeks of gestation (23) – most confirmed COVID-19 cases were in their third trimester of pregnancy. Therefore, little is known about COVID-19 in the earlier stages of pregnancy. In their systematic review, Di Mascio et al. (17) reported no evidence was obtained of miscarriage in the first trimester, which was related to COVID-19 infection.

However, with a limited number of cases and without proper controls, we cannot assume the association between miscarriages and SARS-CoV-2 infection.

Eight studies (15,18,21,27,32,36,39,41) specifically mentioned the duration of onset of symptoms to delivery which ranged from one (15,32,41) to 13 days (27). The duration of hospitalization was inconsistently mentioned across studies. Preterm births emerged to be a common feature among pregnant COVID-19 cases. Seven studies – including original articles (25,41), case review (32), research letter (21), and reviews(17,27) – reported preterm births. In some of the pregnancies, preterm births were also accompanied by other pregnancy-related complications – such as preterm rupture of membranes (17,32,41), abnormality of amniotic fluid (35,41), pre-eclampsia (17), intrauterine distress (41), abnormality of the umbilical cord (41), and placenta previa (41). While pregnancy-related complications may be an indication of the cesarean section, the majority of the pregnancies underwent cesarean section (15,16,18,21,23,25,27,32,35,36,39,41), and the indication of deliveries was not always reported. Two of the articles specified that type of anesthetic agent (either epidural or general) used in the cesarean sections, and Chen et al. (16) reported 12 out of 14 pregnant women who received epidural anesthesia experience intraoperative hypotension. Only three vaginal deliveries were reported (23,41), and no peripartum or postpartum complications were mentioned for them.

Except for one stillbirth (25) – from a 34 weeks pregnant woman with fever and sore throat – all pregnancies resulted in live births. The study conducted by Zhu et al. (41) – and this similar finding was reported by Schwartz (32) in his review – reported several newborns presented gastrointestinal (gastric bleeding, refusal to feed, bloating and food intolerance) and respiratory symptoms (abnormalities in chest radiography, respiratory distress syndrome and pneumothorax) afterbirths. Two children developed thrombocytopenia. One premature newborn died on the 9th day due to multiple organ failure, refractory shock, and disseminated intravascular coagulation, which was the only postnatal death of newborns reported in the studies (32,41). Vertical transmission of SARS-CoV-2 was not reported by any studies (15–18,21,23–25,27,31,32,36,39,41), as – after delivery – the newborns or any products of conception was not tested positive for SARS-CoV-2. Yu et al. (39) reported that one neonate was tested positive for SARS-CoV-2 after 36 hours of birth. However, it was also reported that the placenta and cord blood of the mother of the child tested negative for SARS-CoV-2 after delivery. Thus, it is not clear if this is a case of intrauterine vertical transmission.

## Management recommendations for COVID-19 during Pregnancy

While a wide range of management recommendation was given in these studies, we reported our findings across the following thematic area: prevention, isolation and screening, diagnostic procedures, management of suspected cases, management of confirmed cases, clinical monitoring of confirmed cases, antenatal stage, delivery stage, and postnatal stage. While the itemized recommendation and associated cautionary measures were listed in Table 5, the critical points of the findings of the scoping review were stated below.

**Table 5: Recommendation related to pregnancy and Coronavirus Disease 2019 (COVID-19) reported in the published literature (1 January 2019 to 27 March 2020)**

Recommendation	Caution	References
<u>Prevention</u>		
<ul style="list-style-type: none"> <li>It is recommended to maintain social distancing, refrain from unnecessary travel and crowds</li> </ul>		(22,31)
<ul style="list-style-type: none"> <li>Maintain personal and social hygiene</li> </ul>		(22,28,30)
<ul style="list-style-type: none"> <li>Provide pregnant women with necessary psychological support to prevent stress and anxiety</li> </ul>		(22)
<u>Isolation and screening</u>		
<ul style="list-style-type: none"> <li>The screening process should begin before the pregnant woman arrives in the facility. If possible, detailed of clinical features and respiratory signs and symptoms should be discussed and noted over the telephone or using any online portal</li> </ul>		(31,34)
<ul style="list-style-type: none"> <li>Immediate isolation of the suspected pregnant women in a single room for screening</li> </ul>		(14,22,28-31,34,41)
<ul style="list-style-type: none"> <li>Travel history, contact history, and patient's location in a known clustering occurrence need to be investigated during the initial assessment</li> </ul>		(14,28,31,34,41)
<ul style="list-style-type: none"> <li>Movement of the suspected pregnant women should be restricted throughout the facility</li> </ul>		(14,30,31)
<u>Diagnostic procedures</u>		
<ul style="list-style-type: none"> <li>Even if asymptomatic, a pregnant woman with a travel history within the previous 14 days or reported contact with a confirmed SARS-CoV-2 patient should be tested for SARS-CoV-2 as soon as possible using real-time polymerase chain reaction (RT-PCR) test</li> </ul>	<ul style="list-style-type: none"> <li>For diagnostic confirmation repeated testing may be required</li> </ul>	(14,19,22,23,28,31,34)
<ul style="list-style-type: none"> <li>X-ray and computed tomography (CT) with abdominal shielding can be performed.</li> </ul>	<ul style="list-style-type: none"> <li>May cause radiation exposure to the fetus</li> </ul>	(6,14,22,27,28,34)
<ul style="list-style-type: none"> <li>Imaging is particularly important as a pregnant woman with imaging characteristics of COVID-19 should be considered as a clinically diagnosed case even if laboratory confirmation of SARS-CoV-2 is negative</li> </ul>		(34)
<ul style="list-style-type: none"> <li>One study recommended application of lung ultrasound to identify pathological lesion indicative of COVID-19</li> </ul>		(26)
<ul style="list-style-type: none"> <li>The blood sample should be collected for microbial cultures to investigate any secondary bacterial infection for pneumonia and sepsis,</li> </ul>		(22,28,31)
<u>Management of suspected cases</u>		
<ul style="list-style-type: none"> <li>Supportive care (e.g., adequate rest, sleep and caloric intake; maintain electrolyte and fluid balance; and provide symptomatic medications such as antipyretic, antidiarrheal)</li> </ul>		(28,31)
<ul style="list-style-type: none"> <li>Monitor oxygen saturation and vital signs</li> </ul>		(28)
<ul style="list-style-type: none"> <li>Perform arterial blood gas analysis</li> </ul>		(28)
<ul style="list-style-type: none"> <li>Perform chest imaging for monitoring</li> </ul>		(28)
<ul style="list-style-type: none"> <li>Monitor fetal health using ultrasound or doppler assessment</li> </ul>		(28)
<u>Management of confirmed cases</u>		
<ul style="list-style-type: none"> <li>Treatment should be performed in a negative pressure room or in isolation ward</li> </ul>		(28) (14,22,28,31,41)
<ul style="list-style-type: none"> <li>Pregnant women with critical illness must be transferred to the intensive care unit with negative pressure</li> </ul>		(14,19,22,28)

Recommendation	Caution	References
<ul style="list-style-type: none"> <li>Management of the pregnant women must be done by a multidisciplinary team</li> </ul>		(28,31,34,39)
<ul style="list-style-type: none"> <li>Pregnant women need to be classified as  <u>Mild</u>: Symptomatic but vital signs are stable  <u>Severe</u>: Respiration rate is <math>\geq 30</math>/min, resting oxygen saturation is <math>\leq 93\%</math>, arterial blood oxygen partial pressure/oxygen concentration <math>\leq 300</math> mmHg  <u>Critical</u>: Respiratory failure with the need for mechanical ventilation, shock with organ failure or refractory hypoxemia</li> </ul>		(22)
<ul style="list-style-type: none"> <li>Supportive care (e.g., adequate rest, sleep and caloric intake; respiratory support by oxygen supplement; maintain electrolyte and fluid balance)</li> </ul>		(14,22,28,30,31)
<ul style="list-style-type: none"> <li>Suggest lateral-decubitus position for better oxygenation of the fetus</li> </ul>		(14,28)
<ul style="list-style-type: none"> <li>Broad-spectrum antibiotic (Ceftriaxone) was suggested to prevent community-acquired pneumonia.</li> </ul>	<ul style="list-style-type: none"> <li>Bacterial culture and sensitivity results need to be performed</li> </ul>	(14,22,28)
<ul style="list-style-type: none"> <li>Antiretroviral agents (e.g., Alpha-interferon, Lopinavir/ritonavir) were recommended in some studies. Traditional Chinese medicines were prescribed in some studies from china</li> </ul>	<ul style="list-style-type: none"> <li>It is necessary to understand the teratogenic effect, impact on fetal growth and development before prescribing any specific drug. No safety data was available for the traditional Chinese medicines</li> </ul>	(14,22,23,27,28,34)
<ul style="list-style-type: none"> <li>Clinical trials are currently ongoing for Remdesivir (nucleotide analog) and chloroquine (an antimalarial drug). However, there is no conclusive evidence on their effectiveness at this moment</li> </ul>		(22,27)
<ul style="list-style-type: none"> <li>Short term methylprednisolone may be used to reduce dyspnea and hypoxemia during pneumonia; however, the evidence is not conclusive</li> </ul>	<ul style="list-style-type: none"> <li>Use of long-term corticosteroids treatment is not recommended</li> </ul>	(22)
<ul style="list-style-type: none"> <li>Hemodialysis for sepsis-induced severe acute renal failure</li> </ul>		(14)
<ul style="list-style-type: none"> <li>in case of reparatory failure, beyond mechanical ventilation, extracorporeal membrane oxygenation (ECMO) was suggested by some literature</li> </ul>		(25,31)
<ul style="list-style-type: none"> <li>"If the temperature reverts to normal for more than three days, the respiratory symptoms improve significantly, the lung imaging shows obvious absorption of inflammation, and the nucleic acid test for respiratory pathogens shows negative for two consecutive times (sampling interval at least one day), the patient could discharge from the hospital or be transferred to the appropriate department for treatment according to other illnesses."</li> </ul>		(34)
<u>Clinical monitoring of confirmed cases</u>		
<ul style="list-style-type: none"> <li>Monitor oxygen saturation and vital signs</li> </ul>		(14,22)
<ul style="list-style-type: none"> <li>Perform arterial blood gas analysis</li> </ul>		(14)
<ul style="list-style-type: none"> <li>Perform chest imaging for monitoring</li> </ul>		(14)
<ul style="list-style-type: none"> <li>Monitor organ functions using complete blood count, metabolic panel, C-reactive protein, lactate, renal function, liver function, and cardiac enzymes, etc.</li> </ul>		(14,22)

Recommendation	Caution	References
<ul style="list-style-type: none"> <li>Monitor fetal health using ultrasound or Doppler assessment</li> </ul>		(14,28)
<ul style="list-style-type: none"> <li>Amniocentesis is not recommended</li> </ul>		(14)
<u>Management during the antenatal stage</u>		
<ul style="list-style-type: none"> <li>Due to the evolving pandemic, very little is known about the effect of COVID-19 on during first and second trimester of the pregnancy. Regular monitoring and further research are needed.</li> </ul>		(20,6)
<ul style="list-style-type: none"> <li>Asymptomatic pregnant woman with laboratory-confirmed SARS-CoV-2 infection must self-monitor herself at home for 14 days</li> </ul>		(19,28,31)
<ul style="list-style-type: none"> <li>Routine antenatal care should be provided in a negative pressure room by healthcare providers using proper personal protection equipment</li> </ul>		(14,28-30,34)
<ul style="list-style-type: none"> <li>Regular ultrasounds and doppler assessment were recommended to monitor fetal growth</li> </ul>		(19,22,28,34)
<u>Management during the delivery stage</u>		
<ul style="list-style-type: none"> <li>COVID-19 is not an indication of pregnancy termination</li> </ul>	<ul style="list-style-type: none"> <li>For Severe and critical cases or for obstetric indications needs to be evaluated by physicians and care, management team</li> </ul>	(14,34)
<ul style="list-style-type: none"> <li>COVID-19 alone should not be an indication of early delivery. Mother's clinical status, gestational age and fetal well-being needs to be prioritized</li> </ul>	<ul style="list-style-type: none"> <li>Deteriorating fetal condition may warrant early delivery</li> </ul>	(14,17,19,22,28,31,39)
<ul style="list-style-type: none"> <li>The mode of delivery should be based on obstetric indications. While there is no indication of cesarean section, complications (such as acute organ failure, septic shock or fetal distress) may prompt for emergency cesarean section</li> </ul>		(14,19,22,28,38)
<ul style="list-style-type: none"> <li>The anesthesiology team should indicate the mode of analgesia. Though during cesarean delivery epidural or general anesthesia can be safely used, neuraxial anesthesia may reduce pulmonary complications due to intubation</li> </ul>	<ul style="list-style-type: none"> <li>Hypotension needs to be managed during epidural anesthesia</li> </ul>	(14,16,28)
<ul style="list-style-type: none"> <li>Endotracheal intubation may be used for poor maternal status</li> </ul>		(14)
<ul style="list-style-type: none"> <li>Use of steroids (dexamethasone or betamethasone) for lung maturation of the fetus needs to be evaluated by physicians</li> </ul>	<ul style="list-style-type: none"> <li>Use of antenatal steroid can worsen the disease condition</li> </ul>	(28)
<ul style="list-style-type: none"> <li>Tocolysis is not recommended to delay spontaneous preterm labor for administering antenatal steroids</li> </ul>		(28)
<ul style="list-style-type: none"> <li>Pregnancy-related by-product needs to be treated as biohazardous waste and disposal of them needs to abide by the proper biosafety regulation of the country</li> </ul>		(14,28)
<ul style="list-style-type: none"> <li>Delivery should be performed in a negative pressure room with proper biosafety precautions for medical staff</li> </ul>		(14,16,21,22,28,38)
<u>Management during the postnatal stage</u>		
<ul style="list-style-type: none"> <li>Delayed cord clamping is not recommended. However, recommendation varies across studies</li> </ul>		(14,22,27,28)
<ul style="list-style-type: none"> <li>Newborns should be isolated from suspected or diagnosed COVID-19 mothers for 14 days</li> </ul>		(14,22,28,29,31,38,41)

Recommendation	Caution	References
<ul style="list-style-type: none"> <li>Any recommendation for breastfeeding is not conclusive. However, to prevent human-to-human transmission (via direct contact, fomites, or potential aerosol), direct breastfeeding is discouraged.</li> </ul>	<ul style="list-style-type: none"> <li>Pumping breast milk can be an alternative option considering proper hygiene is maintained. Breastfeeding is not recommended when the mother is taking antiviral drugs (Lopinavir/ritonavir)</li> </ul>	(14,18,27-29,31,34)
<ul style="list-style-type: none"> <li>Provide the mother with necessary psychological support to prevent stress and anxiety</li> </ul>		(28)

### Prevention (22,28,30,31)

Maintaining personal and social hygiene is the main recommendation for preventing COVID-19. Due to the long incubation period, an asymptomatic individual can infect an unaware pregnant woman. Thus, maintaining the social distancing measures (such as limiting unnecessary travel, avoiding the crowd and public transport), frequently washing hands using soap, using hand sanitizer, and avoid touching face (the areas around the mouth, chins, nose, and eyes) are extremely necessary. Also, it is crucial to take care of the mental health of pregnant women by providing her necessary psychological support to prevent stress and anxiety.

### Isolation and screening (14,22,28-31,34,41)

Innovative use of technology can greatly help the screening of suspected pregnant women with COVID-19 infection. Initial screening and triage of the probable cases using telephone or mobile or online portal – whenever possible – can reduce the chance of limiting the exposure or reducing the spread of the infection. Within a healthcare facility, it is paramount to immediately isolate any suspected pregnant women in a single room – if possible, with negative pressure – for screening, contact tracing, and history taking.

### Diagnostic procedures (6,14,19,22,26-28,31,34)

Even if asymptomatic, a pregnant woman with a travel history within the previous 14 days or reported contact with a confirmed SARS-CoV-2 patient should be tested for SARS-CoV-2 as soon as possible using an RT-PCR test. As indicated from the clinical findings, CT scan is providing more diagnostic support for COVID-19 cases. Imaging is particularly important as a pregnant woman with imaging characteristics of COVID-19 should be considered as a clinically diagnosed case even if laboratory confirmation of SARS-CoV-2 is negative. Proper precautions need to be taken while using the CT scan, and radiation exposure need to at its lowest achievable limit. It is also important to assess the risk-benefit for each CT examination, and informed consent must be acquired after proper communication(42). The blood sample should be collected and analyzed for microbial cultures to investigate any secondary bacterial infection for post-viral infection pneumonia and sepsis.

One study recommended the application of lung ultrasound to identify pathological lesion indicative of COVID-19 (26). While this is a novel idea and Moro and colleagues (26) provided details description where obstetricians/gynecologists can perform lung ultrasound of the pregnant women. While the RT-PCR test is yet not available everywhere, the existing infrastructure for ultrasound tests can significantly improve the accessibility of the diagnostic and treatment of COVID-19.

### Management of suspected cases (28,31)

Management of probable cases of COVID-19 among pregnant women mostly includes supportive treatment and monitoring of the health status while keeping her in isolation. Supportive treatment must ensure adequate rest, sleep, and caloric intake; maintain electrolyte and fluid balance; and provide symptomatic medications such as antipyretic, and antidiarrheal. In addition, oxygen saturation and vital signs need to be assessed, and arterial blood gas analysis, chest imaging, and fetal ultrasound or doppler assessment need to be performed as monitoring purposes.

### Management of confirmed cases (6,14,19,22,25,27,28,31,34,39,41)

Treatment of pregnant women with COVID-19 needs to be performed in a negative pressure room – if possible – or in the isolation ward. Worsening cases of COVID-19 pneumonia must be transferred to the intensive care unit with mechanical ventilation support. Integrating the support from an obstetrician, intensive care medicine specialist, microbiologist, pathologist, anesthetist, and neonatologist, a multidisciplinary team should provide the care for pregnant women with COVID-19 infection. Apart from providing supportive treatment, when providing antiviral and antibiotic therapy to a pregnant woman, it is necessary to understand the teratogenic effect of the drugs, which may impact on fetal growth and development.

#### **Clinical monitoring of confirmed cases (14,22,28)**

Based on the limited data available, it appears that preterm delivery and associated obstetric complications are more prevalent among pregnant women with COVID-19 infection. Also, existing comorbidity of COVID-19 patients may lead to life-threatening conditions (43). Thus, clinical monitoring of the patient during pregnancy is critical. Monitoring fetal health using ultrasound or Doppler assessment may also provide warning for the maternal condition. Any abnormality of fetal heart rate may indicate an early sign of the mother's respiratory deterioration (31). Amniocentesis is not recommended at this stage as it can lead to intrauterine transmission of the infection.

#### **Management during antenatal stage (6,14,19,20,22,28–31,34)**

Due to the evolving pandemic, very little is known about the effect of COVID-19 during the first and second trimester of the pregnancy. Thus, asymptomatic pregnant women with laboratory-confirmed SARS-CoV-2 infection are recommended to self-monitor their health by isolating themselves at home for 14 days. One should not stop receiving routine antenatal care due to COVID-19. Moreover, special attention must be given to monitor fetal health and growth.

#### **Management during delivery stage (14,16,17,19,21,22,28,31,34,38,39)**

COVID-19 is not an indication of pregnancy termination or conducting an emergency cesarean section. Here, the mother's clinical status, gestational age, and fetal well-being need to be prioritized, and the mode of delivery should be based on obstetric indications. Delivery should be performed in a negative pressure room – whenever possible – with proper biosafety precautions for medical staff. While COVID-19 alone is not an indication of cesarean section, new and emerging obstetric or health complications (such as acute organ failure, septic shock, or fetal distress) may prompt for emergency cesarean section. The anesthesiology team should indicate the mode of analgesia. Evidence suggests, either epidural or general anesthesia can be safely used during cesarean delivery. The use of neuraxial anesthesia may reduce pulmonary complications due to intubation.

As preterm births appear to be more prevalent among COVID-19 patients, the use of steroids (dexamethasone or betamethasone) for lung maturation of the fetus needs to be evaluated by physicians as it can worsen the maternal disease condition. Tocolysis is not recommended to delay spontaneous preterm labor for administering antenatal steroids. No records included in this scoping review indicated vertical transmission of the SARS-CoV-2. All pregnancy-related by-product needs to be treated as biohazardous waste, and disposal of them needs to abide by the proper biosafety regulation.

#### **Management during postnatal stage (14,18,22,28,29,31,34,38,41)**

Though recommendation varies across studies, several studies did not recommend delayed cord-clamping to prevent potential vertical transmission of SARS-CoV-2. Newborns should be isolated from suspected or diagnosed COVID-19 positive mother for 14 days. Recommendation on breastfeeding is not also conclusive. However, to prevent human-to-human transmission (via direct contact, fomites, or potential aerosol), direct breastfeeding is discouraged. Pumping breast milk can be an alternative option considering proper hygiene is maintained. However, the use of mother's milk for feeding neonates is not recommended if the mother is taking antiviral drugs. Last but not least, it is imperative to provide psychological support for the mother to prevent stress and anxiety.

## **Conclusion**

In summary, with the limited evidence reported until now (27 March 2020), it is evident that pregnant women with COVID-19 infection present similar clinical features as others. The majority of the cases develop pneumonia, which is overtly diagnosed with radiological findings. Pregnant women with COVID-19 were treated with a wide range of antiviral drugs – mostly in China – however, to date, there is no official guideline from World Health Organization (44) or Center for Disease Control (45) (dated 1 April 2020). Several of these drugs are under clinical trial (46). Pregnant women with COVID-19 presented higher episodes of preterm birth and cesarean delivery, though, it cannot be explicitly attributed to the SARS-CoV-2. There is no published evidence on the vertical transmission of SARS-CoV-2.

Pregnancy – being an immunocompromised physiological state – with COVID-19 infection needs to be treated as a priority case and needed to be treated in a higher level healthcare facility. Management of pregnant women during antenatal, delivery, or postnatal stage must be conducted in isolation or negative pressure room whenever possible. A collaborative team of intensive care medicine specialists, obstetricians, anesthetists, neonatologist, microbiologist, and pathologist is necessary to manage critical COVID-19 patients. Healthcare professionals should protect themselves using proper personal protection equipment. Detail history taking (especially for contact tracing and travel history), radiological assessment, and laboratory testing with regular monitoring of fetal health need to be done at every stage of the pregnancy during COVID-19. Though reported only once (26), the effectiveness of lung ultrasound should be evaluated as a more accessible and cost-effective measure of investigation.

The literature did not suggest early termination or use of cesarean section for uncomplicated cases of COVID-19. While vertical transmission of SARS-CoV-2 was not reported, every effort should be made to prevent mother to child transmission of SARS-CoV-2 or iatrogenic infection, during and after the delivery. At the postnatal stage, infants need to be isolated from suspected or confirmed COVID-19 mother. More evidence is needed to conclude the safety of breastfeeding at this stage.

As the COVID-19 pandemic is evolving across the world, more and more evidence is being generated. As a part of this scoping review, we have included a wide range of published literature. This literature – which is mostly observational studies – with a small number of cases and mostly without proper control, quality of the evidence considered to be variable. However, it is essential to acknowledge the contribution of the physicians and researchers who went above and beyond their capacity to produce these initial sets of evidence to highlight critical findings for pregnant women with COVID-19 cases. “Standing on the shoulders of giants” – our rapid scoping review is an effort to collate and report the existing evidence on clinical findings and management recommendations of published scientific literature (dated 27 March 2020). We have tried to use a mostly narrative form of synthesis to connect the results across the literature.

There are several limitations of this scoping review. Due to the methodological design of the scoping review, a quality appraisal of the evidence was not conducted as a part of the review. The time frame of the study was bounded between 1 January 2019 to 27 March 2020, as most of the COVID-19 related literature was published between this timeframe. All study which presented clinical findings of pregnant COVID-19 patients were based on hospital and mostly in their late stage of the pregnancy. Thus, very little is known about the patients who had mild/no clinical symptoms or in their early stages of pregnancy. Except for one study from Honduras (40), all study was based in China. Therefore, the outcomes of pregnancy may be different in other settings.

The selection of the study question was limited to pregnant women, and we did not extend our research questions and search criteria to include neonatal clinical presentation and management recommendations for them. We felt an over encompassing review of maternal, neonatal, and infantile findings would not be feasible at this stage. Thus, we recommend further research and systematic synthesis of the data.

## **Abbreviations**

COVID-19 = Coronavirus disease 2019; CoV = Coronavirus; SARS-CoV-2 = Severe Acute Respiratory Syndrome CoV; PRISMA = Preferred Reporting Items for Systematic reviews and Meta-Analyses; RT-PCR = real-time reverse transcription-polymerase chain reaction; CT = computerized tomography; GGO = ground-glass opacity, ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; ICU = Intensive care unit;

## **Declarations**

### **Ethical Approval**

No ethical approval is required for the study.

### **Availability of data and materials**

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

### **Competing interests**

All authors declare no competing interests.

### **Funding**

None.

### Authors' contributions

MH conceptualized the research question and led to the development of the methodology. Development of literature search strategy, and implementation of the literature search was performed by MH and TA. MH and GMK independently performed the study selection by title and abstract and full-text screening. MH and GMK equally contributed to the analysis and interpretation of the data. MH took the lead to develop the first draft. Both MH and GMK finalized the manuscript and the abstract. All authors contributed to the manuscript revision and read and approved the submitted version of the manuscript.

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## Figures

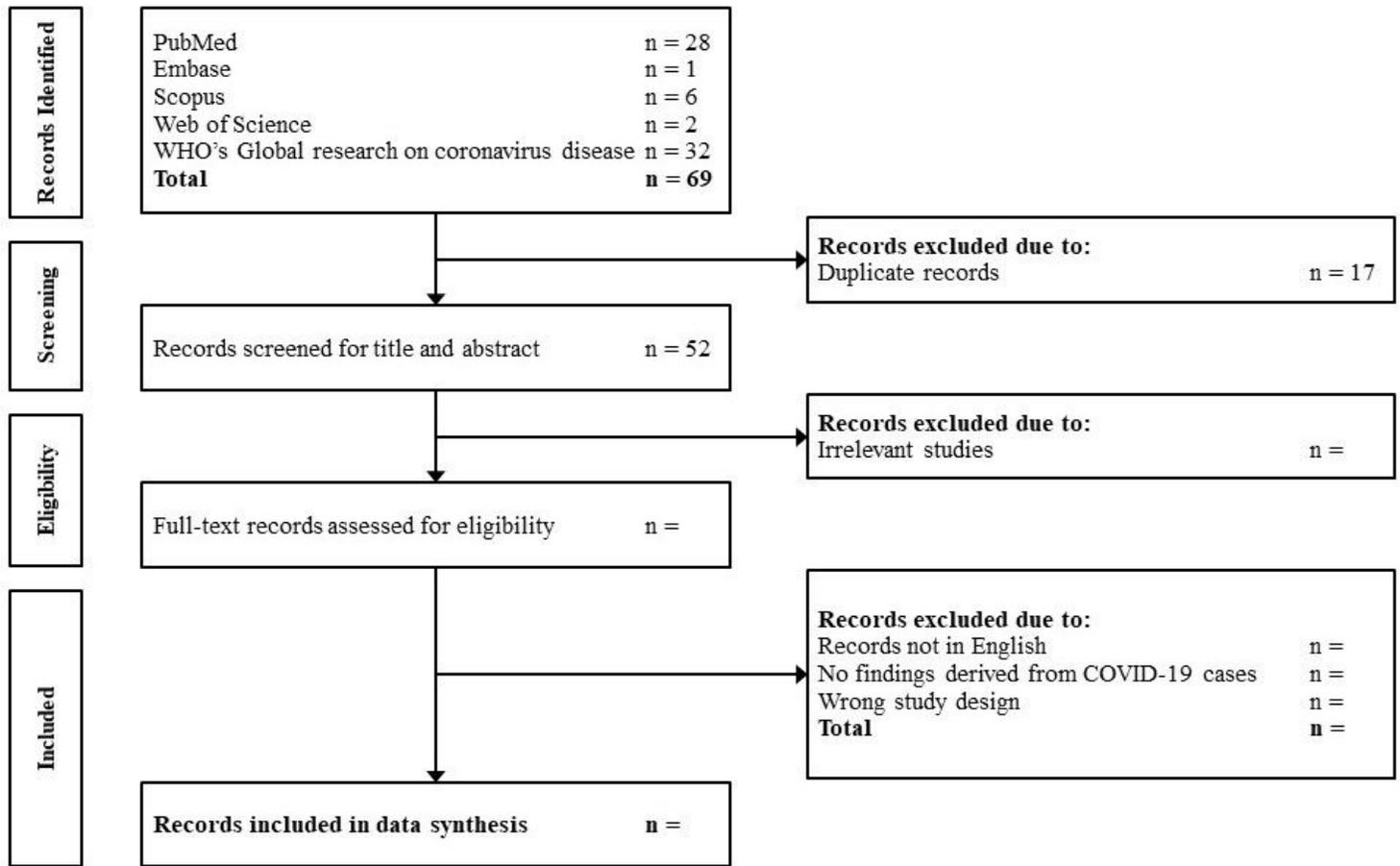


Figure 1

Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Diagram

## Supplementary Files

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