

Impact of COVID-19 on Pregnancy and Childbirth: A Systematic Review of Recent Evidence

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ABSTRACT

Background and Objective: There is a high suspicion that SARS-CoV-2 might be transmitted vertically from mother to fetus and causes clinically significant infection. This review evaluates the pathogenesis, risk factors, diagnosis and management strategies in pregnant women suspected or confirmed with COVID-19 infection.

Methods: A literature review of published articles was carried out using keywords of corona virus (and its root derivatives), pregnancy, vertical transmission and childbirth in Medline, Cochrane, CINAHL and Web of Sciences. Clinical articles including case-control, case reports, case series and reviews published between 2019 and 2020, in English language were included. Editorials and Letter to Editors were not included. Two independent authors reviewed title and abstract and another set of two independent authors screened full text. A total of 22 articles were shortlisted for addition into the final manuscript.

Results: A total of 403 pregnancies were considered in the study with most of the patients in the third trimester of pregnancy. There was no maternal mortality reported in the literature, however 1.49% fetal mortality has been reported.

Conclusion: Extensive care should be taken to determine the timing and mode of delivery, preparation of a safe-to-deliver labor room and the choice of anesthesia with detailed newborn observation.

KEYWORDS: COVID-19, PRISMA guidelines, Pregnant females, Vertical transmission.

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INTRODUCTION

In December, 2019, a number of cases resembling viral pneumonia of unknown cause emerged in the city of Wuhan (Hubei, China). Deep and rapid

sequencing analysis from lower respiratory tract samples revealed the presence of a novel Coronavirus species that was later named severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2).¹ As of 13th April 2020, there's been a total of 1,866,654 verified cases around the globe with 115,269 deaths and 434,054 patients recovering from the infection.²

SARS-CoV-2, severe acute respiratory syndrome Coronavirus (SARS-CoV) and Middle East respiratory syndrome Coronavirus (MERS-CoV), belongs to the Beta Coronavirus genus. Although initial reports suggest SARS-CoV-2 to be less virulent than the two previous zoonotic corona-viruses infections SARS-CoV and MERS-CoV, it has proved to be far more efficient in terms of transmission between close contacts.^{3,4} Over the last two decades, SARS-CoV and MERS-CoV infected > 10 000 persons worldwide. The mortality rate of SARS-CoV infection was 10%, of which the mortality rate in pregnant women was 25%, and the mortality rate of MERS-CoV infection till November 2019 was 34.4% of which the mortality rate in pregnant women was up to 37%.⁵⁻⁷

The recent viral Ebola epidemic and SARS pandemics showed that pregnant women suffer worse outcomes than non-pregnant individuals. This is attributed to the increased oxygen consumption and decreased functional residual capacity during pregnancy, hence COVID-19 may levy a greater risk in pregnant women as compared to the non-pregnant adult cohort. Moreover, pregnancy is an immunosuppressive state, and a weakened immune system makes women more susceptible to adverse infection outcomes. Even though there's no evidence yet, however there's a high suspicion that SARS-CoV-2 might be transmitted vertically from mother to fetus and cause clinically significant infection.⁸⁻¹⁰

This systematic review analyzes the recent literature in an attempt to help clinicians in making decisions on treating pregnant females who are suspected or a confirmed case of COVID-19. With the evolving situation and scarcity of literature, it's imperative to bring together authentic published literature on the pathogenesis of the infection, maternal and external risk factors, diagnosis and management of such patients.

METHODS

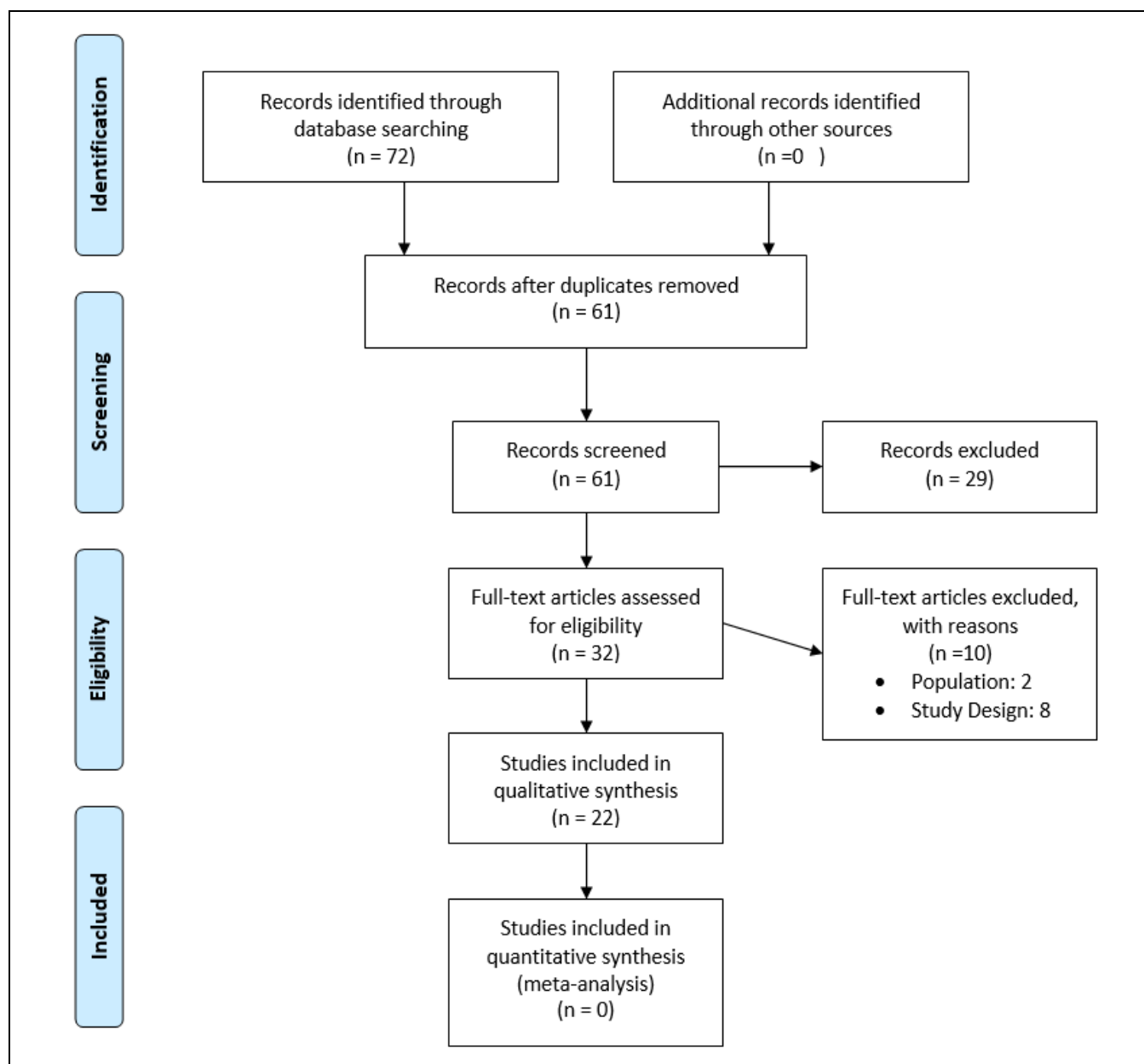
A literature review of published articles was carried out by two independent authors using the keywords: Corona Virus (and its derivatives to expand the search pool: COVID-19, n-CoV, novel corona virus), Pregnancy, Childbirth and Vertical Transmission. This search was carried out on Medline, Cochrane Database, Web of Sciences and CINAHL. Articles were filtered according to years (2019 – 2020) and articles in English language were kept. Editorials and Letter to Editors were not included in the initial search; however, Case Reports and Case Series were included to increase the number of cases and variety of presentation. Various guidelines and expert perspective reports were also included to enhance the content of the manuscript as being efficient resource for readers and clinical practitioners.

Two independent reviewers initially screened the articles on the basis of title and abstract. The shortlisted articles then underwent full text review by two independent authors. Any discrepancies were resolved by a third author. Risk bias analysis and quality of non-randomized studies such as case-control and cohort studies were judged using Newcastle Ottawa Score (NOS), case reports/series using "Methodological Quality of Case Reports and Case Series" (MQC): a validated scale published in BMJ¹¹ and systematic reviews using AMSTAR reporting guidelines.¹²

Data from the manuscript was then extrapolated on a pre-structured worksheet. Due to limitation of time, the review was not registered in any registry however all the corresponding authors have been kept in loop with respect to every aspect of manuscript preparation. Due to time constraints, the systematic review couldn't have been registered in PROSPERO. PRISMA guidelines for conduction of systematic review was followed to ensure accuracy and consistency.¹³

RESULTS

A total of 22 articles were shortlisted for addition into the final manuscript. The PRISMA flow diagram of study selection at all stages can be visualized in Figure 1. Two of the full texts were excluded due to wrong population: discussing Middle Eastern Respiratory Syndrome (MERS) and



eight articles were excluded because they were either editorials or commentaries.

The accepted articles can be visualized in Table-1 below. NOS measures the risk bias and quality of the cohort and case control manuscripts on bases of three variables: selection (scored out of 4 stars, represented in the first row of table), comparability (scored out of 2 stars, represented in the second row of the table) and exposure (measured out of 3 stars, represented in the third row of the table). A score of 7 or more is expected to be a good score. MQC measures the quality of

methodology using selection (scored out of one plus sign), ascertainment (scored out of 2 plus signs), causality (scored out of 4 plus signs), and reporting (scored out of 1 plus sign). A score of 6 or more was considered a good score. AMSTAR score was used in reviewing the methodology of included systematic reviews. AMSTAR marks on 11 components with yes, partial yes and no. To make the evaluation brief, these three scores are grouped together and the final score is given in the table. The guidelines were not evaluated because of the exhaustive process and time constraints.

Table 1: Characteristics of Included Studies.

Author Names	Study Type	1) Paper Published 2) Paper in Press	Risk Bias Assessment (New-Castle Ottawa Score) for Case-Control and Cohort Studies	Methodological Quality of Case Reports and Case Series*	AMSTAR Assessment of systematic Reviews
Chen D et al.	Perspective Report	2			
Poon LC et al.	Guideline Document	2			
Chen Y et al.	Case Series	2		+	
				++	
				++	
				+	
Chen S et al.	Retrospective Cohort	2	**** - ***		
Poon LC et al.	Guidelines	2			
Moro F et al.	Technical Report	2			
				+	
				++	
				+++	
				+	
Zaigham M et al.	Review Article	2			5
Liu D et al.	Retrospective Cohort	1	**** * ** ****		
Shwartz DA et al.	Retrospective Cohort	2	* ***		
Panah L et al.	Review Article	1			6
				+	
				++	
				+++	
				+	
Mullins E et al.	Review Article	2			3
Li N et al.	Case Control Study	2	**** * **		
				+	
				++	
				+++	
				+	
Wang S et al.	Case Report	1	**** ** *** ****		
Chen H et al.	Retrospective Cohort	1	* **		
Yu N et al.	Retrospective Cohort	1			
				+	
				++	
				+++	
				+	
Fan C et al.	Case Series	2			
Rasmussen et al.	Perspective Report	1			
Dashraath P et al.	Perspective Report	2			
Wang SS et al.	Perspective Report	1			

Liu H et al.	Retrospective Cohort	2	* **		

Perspective reports and technical documents were subjectively screened for risk bias assessment.

The demographics of patients in terms of

trimester of pregnancy in which diagnosis is made, the geographical location of patient(s) and symptoms warranting screening and testing are included in the studies are shown in Table-2 below. A total of 403

Table 2: Patient Demographics of Included Studies.

Author Names	Sample Size (Pregnancies)	Trimester of Pregnancy+	Geographical Location*	Fever at Presentation	Cough	Respiratory Distress	Contact History
Chen D et al.	-	-	China	-	-	-	-
Poon LC et al.	56	2 nd and 3 rd	China	In majority of patients	In majority of patients	-	Yes
Chen Y et al.	3	2 (1 st), 1 (3 rd)	China	-	-	-	Yes
Chen S et al.	5	3 rd	China	In majority of patients	In majority of patients	Present	-
Poon LC et al.	-	-	Hong Kong	Yes	In majority of patients	Present	Yes
Moro F et al.	-	-	Italy	-	-	-	-
Kalafat E et al.	1	3 rd	Turkey	No	No	Present	-
Zaigham M et al.	22	20% (1 st) 80% (3 rd)	China, USA, Korea, Honduras	68% reported fever	34% reported cough	12% reported distress	-
Liu D et al.	15	1 st -3 rd	-	87% reported fever	60% reported cough	7% reported distress	13% reported contact
Shwartz DA et al.	38	3 rd	China	78% reported fever	44% reported cough	11% reported distress	None
Panah L et al.	37	-	-	In majority of patients	In majority of patients	-	-
Lee DH et al.	1	3 rd	Korea	Yes	Yes	-	Yes
Mullins E et al.	32	3 rd	-	-	-	6% reported distress	-
Li N et al.	121	-	China	Very few had fever	Very few had cough	-	-
Wang S et al.	1	3 rd	China	Yes	No	-	No
Chen H et al.	3	3 rd	China	78% reported fever	44% reported cough	-	No
Yu N et al.	7	3 rd	China	86% reported fever	14% reported cough	-	No
Fan C et al.	2	3 rd	China	50% reported fever	50% reported cough	-	No
Rasmussen et al.	-	-	-	-	-	-	-
Dashraath P et al.	-	-	-	-	-	-	-
Wang SS et al.	-	-	China	Yes	-	-	-
Liu H et al.	59	-	China	44% reported fever	-	-	-

(-) indicates a missing information in the manuscript

(*) in places where geographical location of patients hasn't been explicitly mentioned, the publishing institute's city is cited

(+) implies trimesters stated in the manuscript, with multiple cases, the most reported trimester has been stated

pregnancies were considered in the study with most of the patients in the third trimester of pregnancy. Due to high volumes of data from China, most of the studies either originates from mainland China or are published by Chinese authors. In the cohort sampled, there was no maternal mortality reported and only 6 fetal mortalities have been reported by Schwartz et al,¹⁴ Zaigham et al,¹⁵ Panah et al,¹⁶ and Mullins et al,¹⁷ of which there was 1 intrauterine, 1 still birth and the other 4 neonates expired shortly after birth.

Risk Factors

Maternal Risk Factors

Pregnant women are usually considered a high-risk group for viral infections, such as SARS-CoV-2. The

pregnancy induces physiological immunosuppression in women, making the mother more vulnerable to severe infections. The anatomical changes in mothers such as an increase in the transverse diameter of the thoracic cage and an elevated level of the diaphragm decreases maternal tolerance to hypoxia. The changes in lung volume and physiological vasodilation can lead to mucosal edema and increased secretions in the upper respiratory tract. In addition, alterations in cell-mediated immunity contribute to the increased susceptibility of pregnant women to be infected by intracellular respiratory pathogens like COVID-19 and cause severe pneumonia.^{14,18-20}

This immunosuppressive alteration in pregnancy may result due to the attenuation in cell-

mediated immunity by Th-1 cells due to the physiological shift to a Th2 dominant environment, which contributes to overall infectious morbidity by increasing maternal susceptibility to intracellular pathogens like viruses. However Dashraath et al.²¹ postulated that changes in the hormonal levels during pregnancy which influence immunological activity against viral pathogens, in addition to physiological shift to a predominant Th-2 response, may favor the expression of anti-inflammatory cytokines (IL - 4 and IL - 10) and other unknown immune adaptations which may serve as the predominant immune response to SARS-CoV-2, thereby resulting in a lesser severity of COVID-19 infection as compared to the non-pregnant cohort.²²⁻²³

Changes in the cardiovascular and respiratory systems, including increased heart rate, stroke volume, oxygen consumption, and decreased lung capacity, as well as the development of immunologic adaptations that allow a mother to tolerate an antigenically distinctive fetus, increases the risk for pregnant women to develop severe respiratory disease. It is significant that these comorbid maternal conditions, which included preeclampsia, pregnancy-induced hypertension, uterine scarring, gestational diabetes, and uterine atony, does not appear to be significant risk factors for intrauterine transmission of SARS-CoV-2 to the fetus.¹⁷

Other Risk Factors

Among the other risk factors which can influence the infectious disease process are summarized in Table-3b. These risk factors include but are not limited to environmental, occupational and health care associated exposure to COVID-19. Most of these patients had an environmental exposure to already SARS-CoV-2 confirmed patients, while others had been exposed to an infected person without knowing it otherwise.

Table 3: *Identifying Other Risk Factors in COVID-19 Pregnant Mothers.*

Author Names	Key Findings
Wang S et al.	More than 15 patients in the same community had been diagnosed with COVID-19 unrelated to a common person's contact, thereby expressing concerns of environmental exposure. ⁵

Chen H et al.	All 9 patients had confirmed epidemiological exposure to COVID-19 with 5 of the patients having exposure to the similar infected person. ²⁴
Yu N et al.	All the 7 patients reported an epidemiological exposure to COVID-19 infected person. ¹
Fan C et al.	One of the patients was a physician who was in contact with a COVID-19 positive patient and patient 2 was in unprotected exposure with her husband who was tested positive for COVID-19. ⁸

Pathogenesis

Mechanism of Materno-Fetal Transmission

Possible discussion on the vertical transmission have been discussed by many authors with most of them believing there's insufficient data on vertical transmission from the mother to her fetus.²⁵⁻²⁸ Scientists have run SARS-CoV-2 RT-PCR analysis on COVID-19 positive mothers' breastmilk samples and specimens of amniotic fluid, blood from the umbilical cord and throat swabs from the neonates. All of these tests have found a negative presence of the viral antigen in the abovementioned specimens, thereby making the physicians unsure of materno-fetal transmission.¹⁶

A possible vertical transmission was reported in a 34 weeks gestational mother who presented with respiratory difficulties, had patchy-ground-glass opacities on Chest CT and had a positive RT-PCR on nasopharyngeal swabs. Her infant girl was delivered by caesarian section in a negative pressure isolation room and had no symptoms, but was immediately quarantined in the neonatal intensive care unit. After 2 hours of birth, her the SARS-CoV-2 IgG level were reported to be 140.32 IU/mL and the IgM level were recorded at 45.83 IU/mL. Immunological cytokines such as IL-6 and IL-10 were raised at 28.26 pg/mL and 153.60 pg/mL respectively with an elevated white blood cell count of $18.08 \times 10^9/L$. Her SARS-CoV-2 IgM and IgG level remained above normal limits at the time of discharge 15 days after birth. This too was consistent with abovementioned findings of negative SARS-CoV-2 breastmilk RT-PCR.²⁹

Among other plausible ways of SARS-CoV-2 infection, in addition to vertical transmission are: close contact transmission, droplet transmission from family members & family visitors and nosocomial infections. If the mother does get tested

positive, the newborn should be isolated and observed as soon as possible, and nucleic acid tests should be carried out, too. In addition, breast feeding should not be performed if the mother was infected by SARS-CoV-2³⁰, even though WHO strictly doesn't prohibit breastfeeding, it does recommend caution.

Outcomes in mothers who develop COVID-19 pneumonia

There is a significant understanding that the signs and symptoms of COVID-19 infection are similar in the pregnant female and their counterpart cohort. Studies have evaluated that pregnant mothers may develop postpartum fever and chest radiography similar to non-pregnant females. The common symptoms include fever, dry cough, myalgia, fatigue, dyspnea and anorexia.^{1,24,25,27} Liu D et al.²⁰ evaluated if the pneumonia aggravated in mothers after giving birth to their off-springs. The authors obtained chest CT-scan images before and after delivery and concluded that there was no significant difference between the two radiographs.

However, some believe that mothers who develop SARS-CoV-2 during pregnancy are more predisposed to complications for themselves and their fetus. These include, but are not limited to rupture of membranes, preterm delivery, respiratory distress, fetal distress, coagulopathy accompanied by liver dysfunction and in severe cases, the death of the mother.¹⁵ Hyperpyrexia can cause miscarriage in first and early second trimester and cause intrauterine death in late second and the third trimester. Hence fever control is very important during the infection and can be achieved by paracetamol or cold sponging or both.

Effects on Fetus & Neonates of COVID-19

Despite many authors not reporting adverse neonatal outcomes, Zhu et al.³¹ reported one neonatal death among six neonates who were tested positive for COVID-19 at their neonatal intensive care unit. The first symptom in all the newborns was shortness of breath, followed by fever, thrombocytopenia accompanied by abnormal liver function, tachycardia, vomiting, and pneumothorax. The authors reported that 6 out of 10 neonates admitted to their center were born

prematurely and 8 out of 10 were delivered by Cesarean section, the two important predictors of adverse outcomes, as per the authors.³¹

Shwartz et al.¹⁷ reported extensive neonatal outcomes in children born to COVID-19 positive mothers. Authors reported cases of 10 children who were evaluated using the Pediatric Critical Illness Score (PCIS). Six of the newborns had a PCIS of less than 90 (the lesser the scores, the worse the predicted outcomes) with 6 infants developing shortness of breath, two were febrile and one of them had a significant tachycardia. Gastrointestinal symptoms such as gastric bleeding, refusal to feed, feeding intolerance and abdominal bloating was observed in 4 infants. The chest radiograph abnormalities in 7 newborns at the time of admission comprised of infection in 4, neonatal respiratory distress syndrome in 2 and pneumothorax in 1 infant. Two infants had the onset of thrombocytopenia associated with liver dysfunction. One premature infant developed shortness of breath and fluctuations of oxygenation with decreased platelets and was treated with respiratory support and transfusions accordingly. There was one neonatal fatality among the cohort, that of a premature child. Pharyngeal swab specimens were collected from 9 of the neonates between 1- and 9-days following delivery and tested for SARS-CoV-2, and all were negative.

Diagnosis

What is a Suspected Case?

A person is labelled as a 'suspected case' if she meets either of the following criteria:²⁵

- A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness of breath) AND with no other etiology that fully explains the clinical presentation AND a history of travel to or residence in a country/area or territory reporting local transmission of COVID-19 infection during the 14 days prior to symptom onset.
- A patient with any acute respiratory illness AND who has been in contact with a confirmed or probable COVID-19 case (see definition of contact below) in the 14 days prior to onset of symptoms.

- A patient with severe acute respiratory infection (fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness breath) AND requiring hospitalization AND with no other etiology that fully explains the clinical presentation.

What is a Probable Case?

A person is labelled as a 'probable case' if she has non-specific symptoms and for whom laboratory testing for COVID-19 is inconclusive.²⁵

What is a Confirmed Case?

A person is labelled as a 'confirmed case' of COVID-19 if she has a laboratory confirmation of SARS-CoV-2 infection, irrespective of clinical signs and symptoms.²⁵

Chest Radiography in Diagnosis of COVID-19 in Pregnant Women

Chest imaging including Chest X-rays and CT scan can supplement and augment the diagnosis of the viral infection but cannot replace molecular confirmation of COVID-19 by RT-PCR. The predominant findings are peripheral airspace shadowing on a plain chest radiograph. However, CT scan has a higher sensitivity and efficiency than chest X-ray. The classical findings are bilateral, multi-lobar ground-glass opacities (GGO) or consolidation on CT scan of the chest. Perhaps the most specific CT scan finding is the presence of ground-glass opacification in either one field or bilaterally. These opacifications can occur as a single patchy consolidation or as multiple patchy infiltrates.^{1,5,8,15,21,32,33}

Liu H et al,³² however remarked that the consolidation lesions were more prevalent in the pregnant cases. They showed that even though the non-pregnant and the pregnant groups shared the same peripheral lung lesion distribution, the consolidation was significantly more frequent in the pregnant adult's group. This shows that the pregnant cohort was more predisposed to pulmonary involvement in CT scan. Common CT scan presentations included: pure GGO, GGO with consolidation or reticulation, and complete consolidation with predominantly peripheral

distribution and bilateral lung involvement. The abovementioned features will facilitate the diagnosis of COVID-19 pneumonia.

Ultrasound in Diagnosis of COVID-19 in Pregnant Women

Moro et al,³⁴ devised pathological ultrasound patterns in pregnant females when compared to those expected in a normal lung, with particular emphasis on those more indicative of COVID-19 infection. The normal lung ultrasound will show A-Lines which are hyperechoic, repetitive reverberations, at regular intervals of the pleural line. The authors discuss 4 different presentations:

- 1) B-Lines: These occur when the lung loses normal aeration, but is not completely consolidated, it creates vertical artifacts of varying lengths and shapes, referred to as the B-Lines. These can occur in the setting of interstitial lung disease, pulmonary fibrosis etc. and have to be clinically correlated. With early stages of COVID-19, the pleural line is usually irregular, thickened, and have a characteristic distribution (multifocal, monofocal, patchy etc.) surrounded by normal lung field and no gravitational distribution.
- 2) White Lung: When the density of the peripheral lung parenchyma is increased as in the settings of SARS-CoV-2 acute respiratory distress syndrome (ARDS), ultrasound examination shows a white area which has no visible A or B lines.
- 3) Consolidation: This presentation occurs in the setting of pneumonia or atelectasis, when the lung is almost completely collapsed. In pathology such as COVID-19 pneumonia, advanced ARDS, or bronchiolitis, the lung may present only small subpleural, hypoechoic consolidations.
- 4) Pleural Effusion: In general, pleural effusion can be simple and uniformly anechoic or complicated by the presence of hyperechoic spots due to blood, pus, fibrin and/or septa.

Hematological Workup in Diagnosis of COVID-19 in Pregnant Women

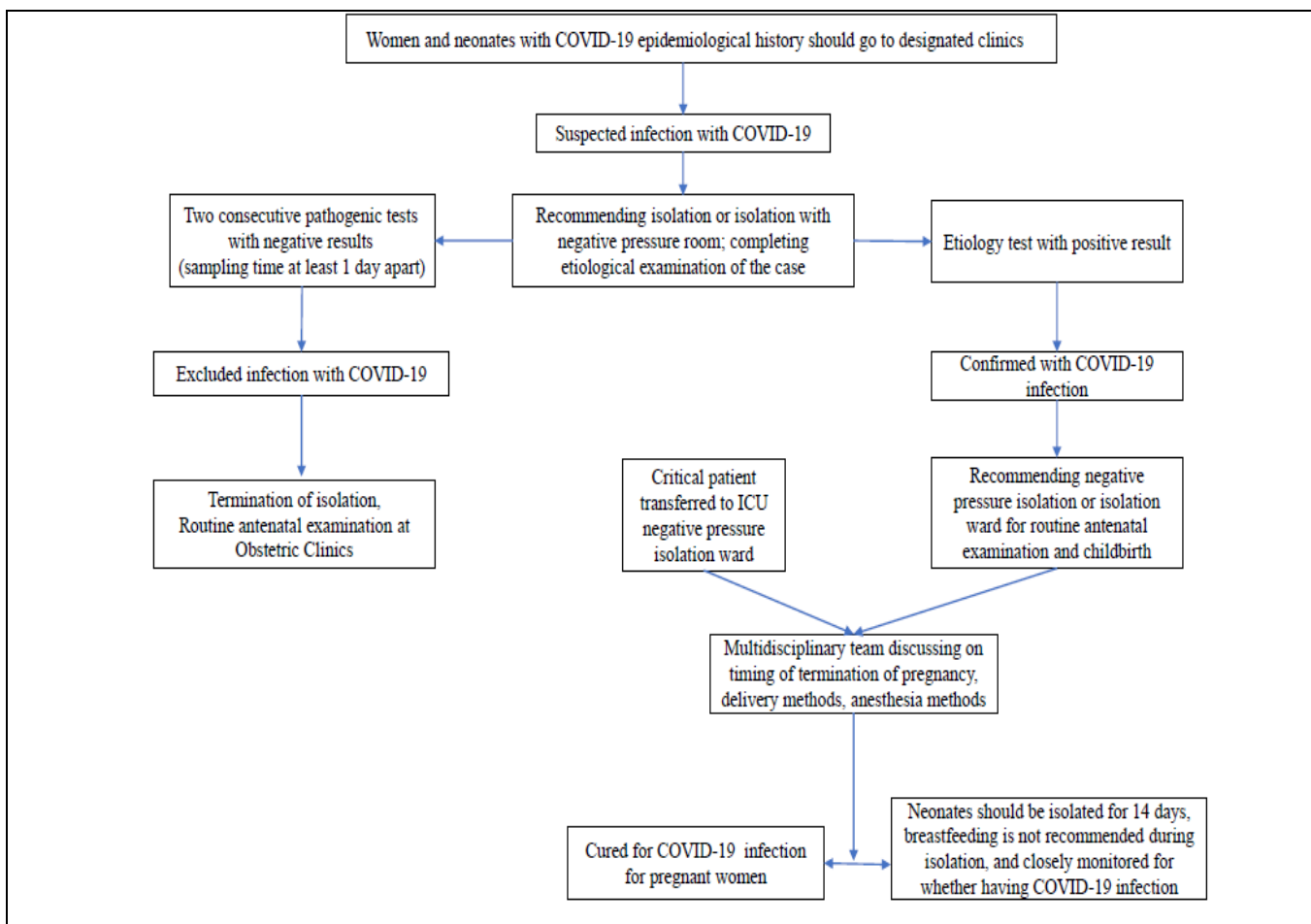
The most common SARS-CoV-2 hematological disturbances noted are lymphopenia, lowered

counts of neutrophils, C-reactive protein (CRP) and alanine aminotransferase (ALT) with a mildly increased D-dimer count.^{1,14,15,17} Levels of AST and eosinophils are either similar to the control population or higher. However, some authors have reported higher ALT, AST and CRP levels in their patients, along with lymphopenia.^{5,20} A consistent finding is a raised WBC, neutrophils, eosinophils, and CRP count in postpartum blood tests of pneumonia patients.^{3,17}

Management

Management of Patient in COVID-19 Designated Clinics

A flowchart to designate the procedures to be followed when a patient who suspects COVID-19 comes to a designated clinic is shown in the flowchart below Adapted from Chen D et al.³⁵ The chart focuses on getting rapid testing to confirm the diagnosis of the infection, isolation in a timely fashion, and developing multi-disciplinary strategies to mitigate the risk of maternal or fetal morbidity and mortality.



Management of Suspected and Confirmed Cases

The management of suspected and confirmed cases can be evaluated in the box below. These strategies have been formulated using the guidelines proposed by CDC and principles suggested by Rasmussen et al.³⁶

Table 4: Strategies to Deal with Suspected and Confirmed Cases of COVID-19.

- Patients who develop respiratory symptoms should practice strict respiratory hygiene including coughing and sneezing on a tissue paper or a bent elbow. These patients should be wearing facemask and wait in a designated area, at least six feet from other patients.

- Pregnant females should be isolated in a negative pressure room, regardless whether they are suspected or confirmed
- Healthcare providers should take special care in wearing CDC instructed personal protective equipment including N-95 respirators, facial shields, gloves and gowns. The hospital's infectious disease department should be kept in loop at all times.
- Patient's nasopharyngeal or oropharyngeal swabs should be collected and sent to institutes running the SARS-CoV-2 RT-PCR testing. Contact the designated COVID-19 government helpline for further information
- Make sure that the patient has limited access to relatives and irrelevant staff in the isolation room
- Close monitoring of mother's vital signs and diagnostic testing should be done, since pregnancy itself is a high-risk condition
- Fetal monitoring should be carried out regularly to ensure the wellbeing of the fetus. It's suggested to regularly to check fetal heart rate and rate of contractions.
- In case the mother is in respiratory distress, consider the use of early oxygen therapy with the goal of maintaining O₂ saturation $\geq 95\%$ and pO₂ ≥ 70 mmHg. In setting of advancing respiratory failure, consider mechanical ventilation
- Use intravenous fluids conservatively unless cardiovascular instability is present
- Screen for any other respiratory infection: viral and bacterial
- Consider empiric antimicrobial therapy (because of risk for superimposed bacterial infections).
- Judicious use of corticosteroids should be done to promote fetal maturity in the setting of an anticipated preterm delivery
- If septic shock is suspected, institute prompt, targeted management.
- Delivery and pregnancy termination decisions should be based on gestational age, maternal condition, and fetal stability, and maternal wishes. The clinical judgement should be done by multidisciplinary team of obstetrics, neonatologists, intensive care specialists, anesthetists and nursing staff.

Among other recommendations to deal with confirmed cases are:

- 1) Kalafat et al: The authors commenced the treatment of their patient with azithromycin, hydroxychloroquine and oseltamivir as per Turkish national COVID-19 treatment guidelines. Favipiravir and steroids were added to her treatment regimen later.³⁷
- 2) Mullins et al. recommends that the decision regarding the mode of delivery should be an obstetric indication and not on presumed protection of the infant.¹⁶
- 3) Li N et al. recommend the use of regional anesthesia because it is known to be safer for both mother and fetus than general anesthesia. The authors also recommended to limit the aerosols generated during the procedure. It's also recommended to ensure that the patient has donned adequate facial mask to protect her from nosocomial infection.³
- 4) Wang S et al: Treated the mother with 40 µg of

recombinant human interferon $\alpha 1b$ -atomized inhalation with 2 mL of sterilization injection water twice daily and ganciclovir (0.25 g every 12 hours, intravenously). They also added Abipenem (0.3 g every 12 hours, intravenously) and moxifloxacin (0.4 g once daily, intravenously) to the treatment regime. The child was treated with methylprednisolone (40 mg once daily, intravenously).⁵

Indications for Terminating Pregnancy

The guidelines on deciding termination of pregnancy have been suggested by Wang SS et al.³⁰ and they are based on:

- 1) Obstetric Indications: judging according to the specific situation and indications for termination of pregnancy
- 2) Severe and Critically ill cases of COVID-19 pneumonia: in which cases continuing pregnancy may endanger the life of the mother and the fetus. The severe and critical states refer to:
 - Severe cases refer to respiratory distress (respiratory rate ≥ 30 beats/min); or oxygen saturation $\leq 93\%$ at rest; or arterial blood oxygen pressure (PaO₂)/oxygen concentration (FiO₂) ≤ 300 mmHg.
 - Critically ill patients refer to cases with respiratory failure and requirement for mechanical ventilation; or shock; or complications of other organ failure requiring ICU monitoring and treatment.

The termination can then be carried out vaginally when the illness is mild, there are favorable cervical conditions, mother is already in labor and there are no contraindications present to SVD. Surgical termination is reserved for severe and critical cases as mentioned above.

Precautions

Precautionary measures for mothers and fetus

The following precautionary measures, although mentioned above, should be taken for and by the pregnant patient infected with SRS-CoV-2:

- 1) Wearing facial masks or appropriate N-95 respirators.
- 2) Negative pressure isolations.

- 3) Quarantine and maintaining social distancing.
- 4) Practicing good hand and respiratory hygiene.
- 5) Avoid breastfeeding the newborn until neonatologists and gynecologists deem suitable.
- 6) Avoid the unnecessary use of corticosteroids.
- 7) Make sure that before any CT examination, the patient's lower abdomen and pelvis is covered with a lead blanket to prevent harm to the fetus.
- 8) Triage pregnant females to avoid unnecessary exposure in hospital settings.

Precautionary Measures for Newborns

The following recommendations, although mentioned above, have been suggested for the care of the newborn:

- 1) Isolate for 14 days if mother is tested COVID-19 positive or if the child itself has been proven infected with the viral illness.
- 2) Transfer to a neonatal intensive care unit for close monitoring of respiratory compromise.
- 3) Avoid breastfeeding and prefer the use of formula milk.

Precautionary Measures for OBGYN Healthcare Providers

It is imperative that the healthcare providers themselves stay vigilant and monitor themselves daily for signs and symptoms of COVID-19. Proper PPE for contact, droplet and airborne precautions should be used as mentioned above to ensure risk of cross contamination with the patients. Where possible, extra staff should not be present in the labor room to prevent overcrowding. Institute's infectious diseases department and state health department should be notified of any patient who is suspicious or a confirmed case of COVID-19.²¹

Vaccinations

No vaccinations have been proposed for the management of SARS-CoV-2 in pregnant females at the time of writing this manuscript.

CONCLUSION

Efficient obstetric treatment is the key in

optimizing the prognosis of both: the mother and the child. Extensive care should be taken to determine the timing and mode of delivery, preparation of a safe-to-deliver labor room and the choice of anesthesia with detailed newborn observation. Regular follow-up visits should be scheduled to monitor the health of the mother and her newborn.

CONFLICT OF INTEREST

None to declare.

FINANCIAL DISCLOSURE

None to disclose.

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Author's Contribution

MIS: Acquisition of the published data, drafting of manuscript.

SA: Conception and design of study.

KS: Final approval of the manuscript.

MS: Critical revision of manuscript for important intellectual content.

SA: Drafting of manuscript.

NK: Final approval of the manuscript.

ZP: Critical revision of manuscript for important intellectual content.