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Review Article

A Narrative Review of Recent Descriptive Studies of COVID Pregnant Patients

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Received: October 30, 2022; **Published:** November 10, 2022

Abstract

On December 1st, 2019 a case of pneumonia of unknown cause is first found in Wuhan-China. Early data show association between infected patients and wholesale seafood market. On December 31st 2019, China notified WHO of the novel outbreak and few days later a novel strain of Coronavirus family is linked to this outbreak. On January 10th 2020, scientists were able to identify the genetic sequence of the virus for the first time. On January 21st 2020, the first case was identified in USA which activated the operative process in CDC. SARS-COV 2 is RNA, single positive stranded, linear, non-segmented virus which belongs to family of Coronaviridae and subfamily Orthocoronaviridae. In this review, we are analyzing and comparing data from different studies to have a broad-spectrum view of the impact of SARS-COV 2 on the clinical practice during pregnancy and postpartum. Data analysis shows that Covid infected pregnant patients showed potential similar course and outcome to general population and pregnancy associated physiological changes do not seem to exacerbate the presentation of the novel COVID 19 in pregnancy. Studies found no enough evidence to confirm vertical or perinatal transmission. Neonates of COVID 19 mothers showed similar outcomes to non-infected mothers.

***Keywords**: COVID-19; Pregnancy; Postpartum*

Introduction

On December 1st 2019, a case of pneumonia of unknown cause is first found in Wuhan-China [1]. Early date show association between infected patients and wholesale seafood market [2]. On December 31, China notified WHO of the novel outbreak and few days later a novel strain of Coronavirus family is linked to this outbreak [3]. On January 10th, scientists were able to identify the genetic sequence of the virus for the first time [2]. On January 21st, the first case was identified in USA which activated the operative process in CDC [2]. Other subtypes of Coronavirus are well known to have significant morbidity and mortality in pregnant patients like severe acute respiratory syndrome (SARS-COV) and Middle East respiratory syndrome (MERS-COV) [4]. WHO confirm the new name of this disease as COVID-19 and the causative agent is SARS-COV 2 [5]. This virus can be transmitted through respiratory droplets or oral or contact with infected surfaces [6]. On January 30th 2020, WHO declared public health emergency of international concern (PHEIC) and on the following day (January 31st 2020, USA declared public health emergency all over the country [2]. On March 1st, the first case is diagnosed in New York which was considered the epicenter of this virus in USA [7].

SARS-COV 2 is RNA, single positive stranded, linear, non-segmented virus which belongs to family of Coronaviridae and subfamily Orthocoronaviridae [8]. It also belongs to Beta genus which shows polymorphism in its envelope and protein structure [9]. It is believed that it may be a zoonotic infection because the virus shows 85% similarity to bat coronavirus [9,10]. Bats appear to be the natural reservoirs of both SARS-COV and MERS-COV as well, the incidence of these viruses in humans has been explained as host switching which happened when the virus jumped from an intermediary host e.g. cats or camels to human [2]. There are seven coronaviruses can infect human and SARS-COV 2 is the third to cause major pandemic after SARS and MERS [8]. The viral envelope consists of bilaminar lipid and transmembrane protein, and the projections outside the membrane are spine like under the microscope [8]. SARS- CoV-2 attacks the host cell by binding its S proteins to ACE2 receptors on the surface of the host cells [8].

Clinically, the virus causes a severe respiratory disease manifested as pneumonia with a specific features in chest CT and CXR [11]. In pregnancy, most of the recent data are reassuring for both maternal and neonatal outcomes besides having poor evidence of vertical transmission [12,13]. Although, more studies are needed to confirm these data keeping in mind that this is a novel emerging virus and its potential ability to affect the perinatal outcomes [4,14,15]. On the other hand, patients with preexisting chronic debilitating disease seem vulnerable to complications like intubation, clots, and stroke [16-18]. As result, universal screening and meticulous follow up of infected patients are critical for the obstetric practice during this pandemic [7,19]. In this review, we are analyzing and comparing data from different studies to have a broad-spectrum view of the impact of SARS-COV 2 on the clinical practice during pregnancy and postpartum.

Why pregnant patients may be more susceptible to complications of COVID-19?

Viruses affecting the respiratory tract, such as SARS, MERS and influenza, have been shown to have higher complication rates in pregnant women. In SARS, pregnant women were more intubated, admitted to intensive care and had a higher risk of mortality [20]. Pregnant women were shown to have a higher mortality risk in the 2009 H1N1 influenza A epidemic [21]. Although the case fatality rate of MERS in pregnant women does not have a statistically significant difference compared to of non-pregnant women, fetal demise rate was higher [22].

The vulnerability can be partly explained by pregnancy-related changes of the immune system and respiratory system. Pregnant women appear to be more vulnerable to respiratory illnesses in the event of maternal hypoxemia due to elevation of diaphragm by gravid uterus, reduction of the functional residual volume, and increase in oxygen demand [23,24]. As for the immune system, suppression in cell-mediated immunity has been demonstrated due to pregnancy-related adaptation. Changes in the immune system is also thought to cause uncontrolled proliferation of viruses.

Materials and Methodology

This study is a narrative review in which we collect published articles that analyzed the demographics of COVID pregnant women, maternal and fetal outcomes. In this review, we searched for all articles published in PUBMED using MeSH compliant keywords including COVID-19, Pregnancy, Coronavirus 2019 and SARS-CoV-2 from January 2020 to May 2020 then reviewed them. The title and abstract of all published articles were analyzed separately using specific keywords. the relevant articles were collected, and their results were summarized and reported.

Results

The novel COVID 19 has variable clinical presentations which range from asymptomatic carriers up to stroke, multiorgan failure and thromboembolic manifestations [11,26]. In our studies we did not find enough data about the percent of asymptomatic carriers in pregnancy. Data from 79 patients show that 66 patients had fever (83.5%). 45 patients out of 141 reported cough (31.9%). Data from 119

patients showed 14 patients had shortness of breath (11.8%). Data from 91 patients showed 8 patients had shortness of breath (8.8%). See table 1.

Study	sample size	Demographics		Clinical presentations				
		Mean age	Gestational age	Asymptomatic	Fever	Cough	Shortness of breath	Diarrhea
Chen et al	5	28.8 (25-31)	NA	4	NA	1	NA	NA
Feraazi et al	42	32.9 (21-40)	NA	NA	26	18	8	2
Liu et al	15	32 (23-40)	32	NA	13	9	1	2
Yu et al	7	32	39	NA	6	1	1	1
Hui Yang et al	23	29.9	38	NA	NA	NA	NA	NA
Doria et al	12	31.9		11	NA	NA	NA	NA
Khan et al	17	29	37.8	NA	3	6	2	3
Qianch-eng X	28	30	38	NA	5	7	2	NA
TOTAL				15	66	45	14	8
SS-included				17	79	141	119	91
PERCENTAGE			36.7	88.2	83.5	31.9	11.8	8.8

Table 1: *SS included = sample size included.*

The imaging workup like X ray and CT are more likely to show abnormal findings (88% of the reported cases). CRP is high in 57.7% of the reported cases. leukocytosis is reported in 41.6% of cases while leucopenia and lymphopenia are reported in 50.6% and 52% respectively. thrombocytopenia and high liver enzymes are reported in 10.7% and7.8% respectively. See table 2.

Study	sample size	Work up						
		Leukocytosis	Leucopeniaor normal	Lymphopenia	Thrombocytopenia	Elevated CRP	High AST/ALT	Abnormal CT/CXR
Chen et al	5	3	2	4	0	4	0	5
Feraazi et al	42	16	NA	NA	6	17	5	NA
Liu et al	15	NA	NA	13	NA	10	NA	NA
Yu et al	7	NA	NA	NA	NA	NA	NA	NA
Hui Yang et al	23	14	4	8	NA	19	2	26
Doria et al	12	NA	NA	NA	NA	NA	NA	NA
Khan et al	17	8	9	4	NA	NA	2	5
Qianch-eng X	28	10	18	8	2	17	0	26
TOTAL		52	42	39	8	71	9	88
SS-included		125	83	75	75	123	115	100
PERCENTAGE		41.6	50.6	52.0	10.7	57.7	7.8	88.0

Table 2: *SS included = sample size included.*

Regarding management plans, our data showed that 102 patients received antibiotics and 78 patients received antiviral medications out of 107 patients (95.3% and 72.9% respectively). Out of 104 patients, 51 received oxygen therapy (49%). Steroids were administered in 10 patients out of 75 patients (13.3%). See table 3.

Study	sample size	Treatment			
		Antibiotics	Antiviral	Oxygen	Steroids
Chen et al	5	NA	NA	NA	NA
Feraazi et al	42	NA	NA	7	NA
Liu et al	15	15	11	14	NA
Yu et al	7	7	7	7	5
Hui Yang et al	23	23	19	23	1
Doria et al	12	NA	NA	NA	NA
Khan et al	17	17	16	NA	NA
Qianch-eng X	28	24	21	NA	4
TOTAL		102	78	51	10
SS-included		107	107	104	75
PERCENTAGE		95.3	72.9	49.0	13.3

Table 3: *SS included = sample size included.*

Fortunately, both maternal and neonatal outcomes of COVID infected pregnant patients are reassuring. Vertical transmission is not proved yet according to recent upcoming data [1,18,27,28]. Testing of 144 neonates showed only 7 positive cases. In these studies, researchers could not rule of risk of postpartum infection [29]. One of these cases showed positive serology but negative PCR twice [30]. The placenta, cord and amniotic fluids were not tested in 2 cases to confirm perinatal transmission [31]. 9 preterm labors were reported [13,30-32]. 2 of them were associated with premature rupture of membrane [13,33] and one case is related to placental abruption [13]. No risk factors were associated with the rest of the preterm cases [31]. 6 neonates had low birth weight, 2 of them were twins pregnancy, one case was preterm, other 3 were not associated with other risk factors [13,32,33]. Apgar score was assessed in 126 neonates and 94 neonates had score 9 or 10. 3 neonates were admitted to neonatal care unit due to mild respiratory symptoms, one of the three cases is positive [34]. All of the three cases were discharged 2 weeks later and were healthy on 1 month follow up visit [34]. 5 neonates had pneumonia, all of them have been reported in one study [31]. 2 of the 5 cases were positive throat swab within 24 hours of delivery but placenta, cord, and amniotic fluid were not tested to confirm vertical or perinatal transmission [31]. No neonatal deaths have been reported in the studies. See table 4 and 5.

Study	sample size	Maternal outcomes				
		Hospitalization	Death	Discharge	Vaginal delivery	C-section
Chen et al	5	0	0	5	2	3
Feraazi et al	42	0	0	42	24	18
Liu et al	15	0	0	15	1	10
Yu et al	7	0	0	7	0	7
Hui Yang et al	23	0	0	23	5	18
Doria et al	12	0	0	12	4	6
Khan et al	17	0	0	17	0	17
Qianch-eng X	28	7	0	21	5	17
TOTAL		8	0	158	43	110
SS-included		45	0	166	164	164
PERCENTAGE		17.8	0.0	95.2	26.2	67.1

Table 4: *SS included = sample size included.*

Neonate Number	Neonatal outcomes							
	Number tested	Number positive	Preterm labor	Low birth weight	APGAR 9 or 10	Neonatal unit admission	Neonatal death	Neonatal pneumonia
5	5	0	0	0	5	0	0	0
42	42	3	NA	NA	NA	NA	NA	NA
11	11	0	0	NA	11	NA	0	0
7	5	1	0	0	7	5	0	NA
24	23	0	1	2	23/24	0	0	0
13	11	0	0	NA	11	NA	0	NA
17	17	2	3	NA	16	0	0	5
22	22	0	1	1	22	0	0	0
168	144	6	9	6	94	3	0	5
	188	159	126	115	126		126	106
	85.7	4.3	7.1	5.2	74.6		0.0	4.7

Table 5: *SS included = sample size included.*

Conclusion

Covid infected pregnant patients showed potential similar course and outcome to general population and pregnancy associated physiological changes do not seem to exacerbate the presentation of the novel COVID 19 in pregnancy. Studies found no enough evidence to confirm vertical or perinatal transmission. Neonates of COVID 19 mothers showed similar outcomes to non-infected mothers.

Limitations of the Study

Because of the novel nature of COVID 19, data are still preliminary. Sample size is inadequate and not representing the general population in the obstetric field [15,19,29,34]. Most of the patients who were included in the study are in the third trimester. So, we do not have enough data about early pregnancy complications nor risk of early vertical transmission [29,34]. Some of the studies could not have accurate testing of the placental tissues, amniotic fluid nor umbilical cords so intrauterine transmission of COVID 19 can be confirmed or excluded [31,33]. The outcomes in some studies are incomplete because data were published so early, or some patients did not come back for follow up [15,29].

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Volume 11 Issue 12 December 2022