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Comparison of maternal and neonatal outcomes between COVID-19 positive and negative parturients who delivered in a tertiary hospital: A retrospective cohort study

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Abstract:

INTRODUCTION: The coronavirus disease 2019 (COVID-19) is a respiratory disease caused by novel coronavirus named Severe Acute Respiratory Syndrome Coronavirus 2. Its growing number of cases with a very limited number of studies in the country is quite alarming, especially to the vulnerable populations, such as pregnant women.

OBJECTIVE: To determine and compare the maternal and neonatal outcomes of COVID-19 positive versus negative parturient.

MATERIALS AND METHODOLOGY: This is a retrospective cohort study of 131 parturient in a tertiary hospital.

RESULTS: We analyzed a total of 131 patients, of whom 65 (49.6%) were COVID positive. At the time of testing, more than half were at their early term of pregnancy (64.89%) and at term (14.5%). Based on disease severity, 45 women (69.2%) exhibited mild disease, 39 were asymptomatic and 6 symptomatic, 19 (29.2%) moderate disease, and 1 (1.5%) severe disease. Among those symptomatic, the most common signs and symptoms were cough (33.85%), myalgia (10.77%), and a radiographic finding of localized or multilobar infiltrates (30.76%). Those who had laboratory examinations, the c-reactive protein (CRP) and D-dimer were found to be elevated. Based on maternal outcomes, there was a higher incidence of preterm birth (21.54%, $P = 0.048$) and longer length of hospital stay ($P = 0.005$) in the COVID-19-positive group. While the neonatal outcomes were similar in both groups, except for longer hospital stay, and delayed institution of breastfeeding among the COVID-19-positive group.

CONCLUSION: In this study, there was no evidence that the presence of COVID-19 infection during pregnancy causes increased morbidity and mortality in mothers and their neonates. Close surveillance should be done on this population, especially if detected before term, as these patients are predisposed to having preterm labor. Further research is needed to understand the true extent of the risks to improve the management of these special population.

Keywords:

COVID-19, novel coronavirus, pregnancy

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Introduction

The coronavirus disease 2019 (COVID-19) is a respiratory disease caused by novel coronavirus named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The very first case was identified last December 2019 at Wuhan, China, and since then COVID-19 has spread to almost every country in the world and

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was declared a global pandemic on March 11, 2020, by the World Health Organization.[8,9] As of August 2, 2021, approximately, there are 198 million confirmed cases worldwide, with 4.2 million deaths reported.[3]

Currently, the Philippines is among the top 24 countries worldwide, with the greatest number of cases of COVID-19 disease.[3] The first-ever case of COVID-19 in the country was confirmed last January 2020 and as of August 2, 2021, confirmed cases escalated to 1,605,762.[3,4]

With the alarming rate of COVID-19 cases rapidly increasing, studies being currently carried out cater more to the general population leaving high-risk populations, such as pregnant women vulnerable. Despite lockdown measures, the pandemic continues to surge and has added another challenge in caring for pregnant patient. This group of patients is physiologically more susceptible to respiratory infection, which could evolve to respiratory collapse if left unrecognized and untreated. Two previous coronavirus outbreaks have perpetuated this pattern before, namely. the SARS-CoV and the Middle East respiratory syndrome coronavirus.[7,10,12] To date, there is insufficient good quality data internationally and locally, to draw an unbiased conclusion with regard to the severity of COVID-19 disease and its complications in the mother, as well as vertical transmission, perinatal, and neonatal complications.

The main purpose of this study is to determine whether COVID-19 infection will increase the risk for maternal or neonatal complications in the local setting. Given the current knowledge and patient data, the association of COVID-19 between maternal and perinatal outcomes aims to be established. The virus' novelty is a call for a more comprehensive clinical maternal care in the evolving pandemic scenario.

Objectives

i. General objective
   To determine and compare the maternal and neonatal outcomes of COVID-19-positive versus COVID-19-negative parturient.
ii. Specific objective
   1. To compare the clinical profiles of COVID-positive versus COVID-19-negative parturient in terms of:
      a. Age, gravidity, parity
      b. Comorbidities
      c. Age of gestation at testing
      d. Age of gestation at birth
      e. Respiratory symptoms
      f. Occupation, history of travel, history of exposure to COVID-19
      g. Residence.
   2. To compare the maternal outcomes of COVID positive versus COVID-19 negative parturient in terms of:
      a. Mode of delivery
      b. Length of hospital stay
      c. Intensive care unit (ICU) admission
      d. Postpartum complications:
         i. Mortality
         ii. Worsening of symptoms/condition
         iii. New symptoms
         iv. Hemorrhage.
   3. To compare neonatal outcomes of COVID-positive versus COVID-19-negative parturient in terms of:
      a. Birthweight and appropriateness of weight
      b. Appearance, Pulse, Grimace, Activity, and Respiration at 1, 5, 10 min
      c. Breastfeeding
      d. Neonatal ICU (NICU) admission and indications
      e. Respiratory symptoms/neonatal distress
      f. Length of hospital stay
      g. Amniotic fluid staining
      h. Mortality/stillbirth.
   4. To determine the incidence of neonatal COVID-19 infection among those delivered to COVID-19-positive patients.

Methodology

Study design

This is a retrospective single-center cohort study.

Setting of the study

The study was conducted at a Tertiary Hospital.

Study subject and target population

Inclusion criteria

Subjects with positive and negative results in Reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2, either for screening before admission or symptom-based

- Age 19–45-year-old
- Primipara or multipara
- Confirmed intrauterine pregnancy
- Preterm parturient (<37 weeks) or term parturient (>37)
- With or without co-morbidities
- Delivered from March 1, 2020 to July 31, 2021.

Exclusion criteria

- Presence of pulmonary and cardiac diseases resulting in poor maternal and fetal outcomes (cardiac disease Class III and IV)
- TORCH-positive cases.

Study outcomes are shown in Figure 1.

Sample size

A minimum of 130 mothers, or 65 each for positive and negative groups were included in the study based on a level of significance of 5% and a power of 80% [Table 1].

The proportions of neonates with low birthweight are 18% and 3% for COVID-positive and COVID-negative groups, respectively. These values are based on the study by Hulley *et al*., 2020.[11] Sample size formula and computation are shown in Figure 2.

Data collection procedure

The data collection was conducted at a Tertiary hospital, from March 1, 2020, to July 31, 2021, both private and service divisions. The review of charts included patients who were admitted from March 1, 2020, to July 31, 2021.

Data management and statistical tools

Maternal and neonatal clinical profiles and outcomes were compared for parturients classified as COVID positive versus COVID negative. Categorical variables were reported as frequency and percentage. Shapiro–Wilk test and Levene's test were used to determining the normality distribution and homogeneity of variance of continuous variables, respectively. Continuous quantitative data that met the normality assumption was summarized using mean and standard deviation, while those that do not was described using median and range.

Continuous variables which are normally distributed were compared using the independent *t*-test. Otherwise, the nonparametric Mann–Whitney *U*-test was used. Chi-square test was used to compare categorical variables. If the expected percentages in the cells are <5%, Fisher's Exact Test was used instead.

All analyses were conducted using STATA version 15.0 (StataCorp LLC, USA). Two-sided $P < 0.05$ indicated statistical significance.

Results

We analyzed the demographics and clinical profiles of 131 mothers [Figure 3], of whom 65 (49.6%) were COVID positive, among which nine (13.85%) had a known history of exposure to a COVID-19 case [Table 2]. Their overall mean age was 30.47 (±5.19) years and at the time of testing more than half were in their early term (37–38 6/7 weeks age of gestation) of pregnancy (64.89%) and at term (39–406/7 weeks age of gestation) (14.5%). Based on comorbidities, there were more pregnant women with gestational diabetes among COVID negative group (16.67% vs. 1.54%, $P = 0.003$). As to gravidity and parity, there was more multigravida in the COVID positive group ($P < 0.001$).

Based on disease severity, 45 women (69.2%) exhibited mild disease, 39 of which were asymptomatic and 6 symptomatic, 19 (29.2%) moderate disease and 1 (1.5%) severe disease. Among those who were symptomatic, the most common signs and symptoms presentation were cough (33.85% vs. 4.55%, $P < 0.001$), myalgia (10.77% vs. 1.52%, $P = 0.033$), and a radiographic finding of localized or multilobar infiltrates (30.76% vs. 0, $P < 0.001$).

Among the COVID-19-positive mothers who had laboratory exams done, the median values of laboratories

Name of outcome	Metric/measurement
Maternal outcomes	Mode of delivery
	Preterm labor
	Length of hospital stay
	ICU admission
	Postpartum complications
Neonatal outcomes	Birthweight and appropriateness of weight
	APGAR at 1,5,10 minutes
	Breastfeeding
	NICU admission and indications
	Respiratory symptoms
	Length of hospital stay
	Mortality/ Stillbirth

Figure 1: Study outcomes

$$N \geq \frac{\left[z_{\alpha}\sqrt{P(1-P)\left(\frac{1}{q_1}+\frac{1}{q_2}\right)} + z_{\beta}\sqrt{\left(\frac{P_1(1-P_1)}{q_1}\right)+\left(\frac{P_2(1-P_2)}{q_2}\right)} \right]^2}{(P_1-P_2)^2}$$

$$N \geq \frac{\left[1.96\sqrt{0.105(1-0.105)\left(\frac{1}{0.5}+\frac{1}{0.5}\right)} + 0.842\sqrt{\left(\frac{0.18(1-0.18)}{0.5}\right)+\left(\frac{0.03(1-0.03)}{0.5}\right)} \right]^2}{(0.18-0.03)^2}$$

$N \geq 130$

Where:
q1 = proportion of COVID-positive mothers = 0.50
q2 = proportion of COVID-negative mothers = 0.50
Z α/2 = specified size of the critical region (5%) = 1.960
Z β/2 = chosen level of power (80%) = 0.842
P1 = proportion of neonates with low birthweight among COVID-positive mothers = 18%
P2 = proportion of neonates with low birthweight among COVID-negative mothers = 3%
P = q1P1 + q2P2 = 0.105
N = minimum total number of subjects

Figure 2: Sample size formula and computation

Table 1: Minimum sample size at 0.05 level of significance

	COVID-positive (%)	COVID-negative (%)	80% power	90% power
Cesarean delivery	88	47	40	52
Complications in pregnancy	69	31	52	70
Low birth weight	18	3	130	172
Premature birth	24	6	122	162

COVID: Corona virus disease

Table 2: Demographic and clinical profiles of corona virus disease positive versus negative parturients (*n*=131)

	Mean±SD; Frequency (%); Median (range)			*P*
	Overall (*n*=131)	COVID-positive (*n*=65)	COVID-negative (*n*=66)	
Age	30.47±5.19	30.63±5.37	30.30±5.04	0.719*
Age of gestation at testing				
Early preterm (<33 6/7)	5 (3.82)	3 (4.62)	2 (3.03)	0.564†
Late preterm (34-36 6/7)	21 (16.03)	13 (20)	8 (12.12)	
Early term (37-38 6/7)	85 (64.89)	41 (63.08)	44 (66.67)	
Term (39-40 6/7)	19 (14.5)	8 (12.31)	11 (16.67)	
Age of gestation at birth	5 (3.82)	3 (4.62)	2 (3.03)	
Early preterm (<33 6/7)	14 (10.69)	10 (15.38)	4 (6.06)	0.321†
Late preterm (34-36 6/7)	78 (59.54)	37 (56.92)	41 (62.12)	
Early term (37-38 6/7)	34 (25.95)	15 (23.08)	19 (28.79)	
Term (39-40 6/7)	33 (25.38)	14 (21.88)	19 (28.79)	
Comorbidities				
Hypertension	16 (12.21)	7 (10.77)	9 (13.64)	0.616‡
Diabetes	12 (9.16)	1 (1.54)	11 (16.67)	0.003‡
Bronchial asthma	7 (5.34)	1 (1.54)	6 (9.09)	0.115†
Gravidity				
G1	57 (43.51)	15 (23.08)	42 (63.64)	<0.001‡
G2	42 (32.06)	27 (41.54)	15 (22.73)	
≥G3	32 (24.43)	23 (35.38)	9 (13.64)	
Parity				
P0	61 (46.56)	16 (24.62)	45 (68.18)	<0.001‡
P1	41 (31.3)	28 (43.08)	13 (19.7)	
≥P2	29 (22.14)	21 (32.31)	8 (12.12)	
Symptoms				
Fever	7 (5.34)	6 (9.23)	1 (1.52)	0.062†
Cough	25 (19.08)	22 (33.85)	3 (4.55)	<0.001‡
Dyspnea	3 (2.29)	3 (4.62)	0	0.119†
Malaise/fatigue	14 (10.69)	10 (15.38)	4 (6.06)	0.084‡
Myalgia	8 (6.11)	7 (10.77)	1 (1.52)	0.033†
Sore throat	4 (3.05)	3 (4.62)	1 (1.52)	0.365†
Nasal congestion	8 (6.11)	5 (7.69)	3 (4.55)	0.492†
Diarrhea	1 (0.76)	1 (1.54)	0	0.496†
Signs				
Lymphocytosis	38 (29.01)	17 (26.15)	21 (31.82)	0.475‡
CXR findings				
None	110 (84.62)	44 (68.75)	66 (100)	<0.001†
Localized infiltrates	8 (6.15)	8 (12.5)	0	
Multilobar infiltrate	12 (9.23)	12 (18.75)	0	
Occupation				
Nonworking	78 (59.54)	39 (60)	39 (59.09)	0.064†
Healthcare worker	6 (4.58)	4 (6.15)	2 (3.03)	
Nonhealthcare worker	42 (32.06)	17 (26.15)	25 (37.88)	
Others	5 (3.82)	5 (7.69)	0	
History of travel				
Within NCR	124 (94.66)	60 (92.31)	64 (96.97)	0.274†
Outside NCR but within Luzon	7 (5.34)	5 (7.69)	2 (3.03)	
History of exposure to COVID-19	10 (7.63)	9 (13.85)	1 (1.52)	0.008‡
Residence				
NCR	125 (95.42)	61 (93.85)	64 (96.97)	0.440†
Outside NCR	6 (4.58)	4 (6.15)	2 (3.03)	

*Independent *t*-test, †Fisher's exact test, ‡Chi-square test. SD: Standard deviation, NCR: National capital region, COVID-19: Coronavirus disease-2019, CXR: Chest xray

requested are shown in Table 3. Ferritin was requested in 12 patients, serum creatinine in 10 patients, and Serum glutamic pyruvic transaminase in eight patients. Serum glutamic oxaloacetic transaminase, high sensitivity CRP (hs-CRP), D-dimer, serum potassium, serum lactate dehydrogenase, and procalcitonin were requested

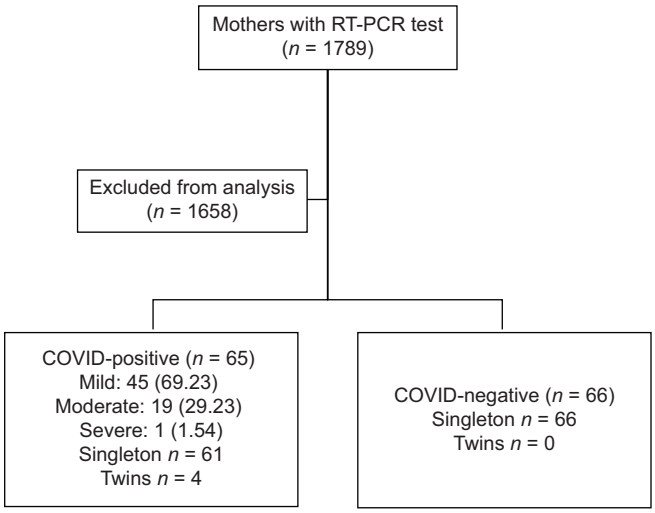

Figure 3: Sample size distribution

in <10 patients. Among the laboratories requested CRP (median 7.32 ng/mL) and D-dimer (median 1.26 ug/mL) were elevated.

In both groups, more than half of the patients were nonworkers at the time of delivery in both groups. There were four mothers in the COVID-positive group who were healthcare workers, and two among the COVID-negative group. There was no significant difference between the two groups based on their occupational status ($P = 0.064$).

Based on travel history, only 5.34% had a history of travel within greater Luzon, and the majority of patients in both groups reside within National Capital Region (92.31% vs. 96.97%) However, more patients in the COVID positive group had a history of exposure to COVID infection ($P = 0.008$).

Based on the maternal outcomes, there was no significant difference between the two groups except for preterm labor and length of hospital stay. There was a higher incidence of preterm labor (21.54% vs. 9.09%, $P = 0.048$) and longer median length of hospital stay (4 [ranges 1–35] vs. 3 [ranges 2–8] days, $P = 0.005$) [Table 4] in the COVID-19 positive group.

In this study, the neonatal outcomes varied as shown in Table 5, a total of 135 neonates were included in the study since 4 of the COVID positive mothers had twin deliveries. There was no statistical difference in the birthweight ($P = 0.177$) with the median weight of both groups computed at 2885 g. In the COVID-19 positive mothers had a median range of neonatal birthweight was 2810 g, while in COVID-19 negative mothers had a median birthweight of their neonates were 2910 g. Taking into account for appropriateness of weight, there was no significant difference between the groups ($P = 0.065$).

Table 3: Laboratory profile of coronavirus disease-2019 positive mothers

	n	Median (range)
SGPT, IU/L (15-41)	8	19.5 (12-59)
SGOT, IU/L (14-54)	3	22 (21-42)
Serum creatinine, umol/L (53-97)	10	48.5 (24-144)
hs-CRP, ng/mL (high risk >3.0)	5	7.32 (0.7-80)
D-Dimer, ug/mL (0-0.5)	5	1.26 (0.96-2.52)
Ferritin, ng/mL (4.63-204)	12	86.10 (17.13-276)
Serum potassium, mmol/L (3.6-5.5)	7	4.1 (2.9-5.1)
SLDH, U/L	5	390 (360-576)
Procalcitonin, ng/mL (0-0.5)	9	0.07 (0.03-1.35)

SGPT: Serum glutamic pyruvic transaminase, SGOT: Serum glutamic oxaloacetic transaminase, hs-CRP: High-sensitivity C-reactive protein, SLDH: Serum lactate dehydrogenase

Although it was not significant, there were more (small for gestational age) deliveries in the COVID-19 positive group versus in the COVID negative group (9 vs. 3). There was also no significant difference in the APGAR scores of the neonates as well ($P = 0.114$ and $P = 0.489$ for the first and 5th min respectively) between the two groups.

All the neonates born to COVID-19 positive mothers were tested for reverse transcriptase-polymerase chain reaction (RT-PCR) and none tested positive nor became symptomatic. Based on this study, the only 2 neonatal outcomes that showed statistically significant differences are the length of hospital stay and the breastfeeding status of the neonates. None of the neonates in COVID-19 positive mothers were breastfed, this is due to the isolation of the neonates for the COVID-19 positive mother upon delivery.

There was no significant difference in the NICU admission. Indications for NICU admissions include respiratory symptoms at birth amniotic fluid and staining, still birth, and neonatal mortality. Neonates of COVID-19-positive mothers stayed longer in the hospital, ranging from 2 to 32 days in hospital duration as compared to the 2–15 days of neonates of COVID-negative mothers ($P = 0.017$).

There was one occurrence of mortality/stillbirth in the COVID-19-negative group, which was not statistically significant ($P = 0.489$).

Discussion

Within the timeframe of this study, a total of 1789 patients were admitted for delivery at our Institution. We found that on admission, 3.6% of women were screened as a confirmed case of COVID-19, 9 of which had significant exposure through either family or close contact at the workplace. More than half (39 out of 65) of confirmed COVID-19 pregnant women were asymptomatic and

Table 4: Maternal outcomes of coronavirus disease positive versus negative parturients (*n*=131)

	Frequency (%)			*P*
	Overall (*n*=131)	COVID-positive (*n*=65)	COVID-negative (*n*=66)	
Mode of delivery				
NSD	74 (56.49)	35 (53.85)	39 (59.09)	0.263‡
Repeat CS	25 (19.08)	16 (24.62)	9 (13.64)	
Primary CS	32 (24.43)	14 (21.54)	18 (27.27)	
Preterm labor	20 (15.27)	14 (21.54)	6 (9.09)	0.048‡
Length of hospital stay	3 (1-35)	4 (1-35)	3 (2-8)	0.005§
≤14	130 (99.24)	64 (98.46)	66 (100)	
<14	1 (0.76)	1 (1.54)	0	
ICU admission	0	0	0	-
Postpartum complication				
Worsening of symptoms/condition	1 (0.76)	1 (1.54)	0	0.496†
New symptoms	2 (1.53)	1 (1.54)	1 (1.52)	0.999†
Hemorrhage	3 (2.29)	1 (1.54)	2 (3.03)	0.999†
Mortality	0	0	0	-

†Fisher's exact test, ‡Chi-square test, §Mann-Whitney *U* test. COVID: Corona virus disease, ICU: Intensive care unit, NSD: Normal spontaneous delivery, CS: Cesarean section

predominantly fell within the mild (6 symptomatic and 39 asymptomatic) and moderate (19 out of 65) classification, with an isolated case of 1 severe COVID-19 infection. Among those symptomatic (26 out of 65), the most common COVID-19 related symptoms were cough (33%), myalgia (15%), and fever (9%). Those with laboratory investigations showed lymphocytosis, elevated CRP and D-dimer. Those who had chest X-ray, their radiographic findings revealed localized or multilobular infiltrates. Maternal outcomes showed a higher incidence of preterm labor on the COVID-19 positive group. Due to the COVID-19 infection, both mother and neonate had a longer hospital stay. The mode of delivery was not influenced by the presence of COVID-19 infection, since most of parturient on the positive group were multiparous and underwent normal spontaneous delivery. There were no postpartum complications observed, such as worsening of symptoms, hemorrhage, and death associated with COVID-19, and none required emergent critical care for both mother and neonate.

The presence of COVID-19 infection among parturients did not have an effect on the neonatal outcomes, such as birthweight, appropriateness of weight, and APGAR score of neonates. Breastfeeding was not immediately instituted among the positive group because of quarantine and safety protocols. None of the neonates born to pregnant women with COVID-19 tested positive 24 h after delivery, which may imply the absence of vertical transmission.

There are several studies published that showed similar findings with the data acquired in this study. Breslin *et al.* conducted a study on pregnant and nonpregnant women with COVID-19 and observed similar disease severity of COVID-19 on the populations.[2,7] Pregnant COVID-19 patients admitted for obstetrical care were often asymptomatic on molecular testing, wherein, 86% are mild cases, while severe and critical cases were at 9.3% and 4.7%, respectively. Most common symptoms reported were fever and cough,[2,6] which was comparable to the study done where the majority of the COVID-19 positive patients appeared asymptomatic. The most common laboratory findings are lymphopenia and elevated CRP levels.[2] Notable maternal outcomes included in the study done by Breslin *et al*. and Di Toro *et al.*, showed higher rates of preterm birth in pregnant women with COVID-19, with an overall rate of 17% and 23%, respectively.[2,18] It was postulated that an increasing viral load, along with worsening maternal and fetal conditions would lead to early delivery. In our study, there was a higher incidence of preterm delivery (21.5%) on the COVID-19 positive group. According to Breslin *et al.*, majority of the pregnant women with COVID-19 infection underwent cesarean section (60%) but was not statistically significant.[2] Similarly, in our study, there was no increase in the rate of cesarean delivery in the COVID-19 positive group. In the studies of Breslin *et al.*, Chen *et al*., and Liu *et al.*, neonates, whose mothers tested positive for COVID-19, had no serious adverse outcomes observed. None of these neonates required critical care intervention such as mechanical ventilation and ICU admission, which was also found in our study.[2,17,14]

In contrast to the study done by Hassan *et al.*, Zambrano *et al.*, Wastnedge *et al.*, COVID-19 infection during pregnancy increases the risk of several adverse pregnancy outcomes, including higher rates of cesarean section, hospitalization, and ICU admission.[5,13,16] This was further supported by a systematic review study done by Allotey *et al.*, which showed an association of COVID-19 in pregnancy with maternal obesity, preexisting comorbidities, asthma, history of COVID-19

Table 5: Neonatal outcomes of coronavirus disease positive versus negative parturients (*n*=131 mothers, 135 neonates)

	Mean±SD; Median (range); Frequency (%)			*P*
	Overall (*n*=135)	Neonates born to COVID-positive mothers (*n*=69)	Neonates born to COVID-negative mothers (*n*=66)	
Birth weight	2885 (1000-3965)	2810 (1400-3965)	2910 (1000-3660)	0.177§
Appropriateness of weight				
SGA	12 (8.89)	9 (13.04)	3 (4.55)	0.065†
AGA	121 (89.63)	58 (84.06)	63 (95.45)	
LGA	2 (1.48)	2 (2.9)	0	
APGAR				
1 min				
<7	3 (2.22)	0	3 (4.55)	0.114†
≥7	132 (97.78)	69 (100)	63 (95.45)	
5 min				
<7	1 (0.74)	0	1 (1.52)	0.489†
≥7	134 (99.26)	69 (100)	65 (98.48)	
10 min				
<7	0	0	0	-
≥7	135 (100)	69 (100)	66 (100)	
Neonatal COVID-19	0	0	0	-
Breastfeeding	59 (43.7)	0 (0)	59 (89.39)	<0.001‡
NICU admission	48 (35.56)	26 (37.68)	22 (33.33)	0.598‡
NICU indication				
RDS	26 (19.26)	17 (24.64)	9 (13.64)	0.105‡
Jaundice	2 (1.48)	2 (2.9)	0 (0)	0.497†
Sepsis	26 (19.26)	12 (17.39)	14 (21.21)	0.574‡
Any respiratory symptoms	31 (22.96)	19 (27.54)	12 (18.18)	0.196‡
Alar flaring	5 (3.7)	4 (5.8)	1 (1.52)	0.366†
Tachypnea	7 (5.19)	4 (5.8)	3 (4.55)	0.999†
Apnea	1 (0.74)	1 (1.45)	0 (0)	0.999†
Retractions	31 (22.96)	20 (28.99)	11 (16.67)	0.089‡
Amniotic fluid				
Clear	106 (78.52)	54 (78.26)	52 (78.79)	0.857†
Thin	11 (8.15)	7 (10.14)	4 (6.06)	
Moderate	9 (6.67)	4 (5.8)	5 (7.58)	
Thick	9 (6.67)	4 (5.8)	5 (7.58)	
Length of hospital stay	4 (2-32)	4 (2-32)	3 (2-15)	0.017§
Mortality/stillbirth	1 (0.75)	0	1 (1.52)	0.489†

§Mann-Whitney *U* test, †Fisher's exact test, ‡Chi-square test, There were 4 COVID-positive mothers who had twin pregnancies. SD: Standard deviation, COVID-19: Coronavirus disease-2019, SGA: Small for gestational age, NICU: Neonatal intensive care unit, RDS: Respiratory distress syndrome, AGA: Appropriate for gestational age, LGA: Large for gestational age, APGAR: Appearance, Pulse, Grimace, Activity, and Respiration

in the support person and gestational diabetes.[1,7] Villar *et al.* demonstrated a substantially increased risk of severe pregnancy complications with COVID-19 infection, including preeclampsia/eclampsia/HELLP syndrome, ICU admission or referral to a higher level of care.[15] Those who had severe cases were linked with increasing age, high body mass index, chronic hypertension, and preexisting diabetes.[1] The risk of maternal mortality was 1.6% which is 22 times higher in the group of women with COVID-19 infection, which occurred in institutions from less developed regions, implying that COVID-19 in pregnancy can be lethal in the absence of a comprehensive ICU services.[15] The higher susceptibility of pregnant women to respiratory pathogens was linked to the immunosuppressive state of pregnancy as mentioned in a study by Liu *et al.*[14] and Wastnedge *et al.*[16] Progesterone-induced changes such as increased oxygen consumption, respiratory tract edema may lead to a lower threshold for hypoxia which can vilify already toxic symptoms of airborne diseases such as COVID-19.[14,16] Hence, pregnancy may be a magnifier for the disease entity and careful clinical management is warranted. The study failed to demonstrate the association of COVID-19 in pregnancy with worsening of the maternal outcome as well as its relation to the presence of maternal comorbidities. This may be attributed to the role of universal screening of pregnant women upon admission. It allows detection of the presence of the virus at an earlier stage, permitting obstetricians to facilitate early intervention and infection control. This may also explain why the majority of the COVID-19 positive group were asymptomatic.

In the studies of Hassan *et al.*, Wastnedge *et al.*, and Villar *et al.*, they found an increased risk for neonatal complications such as low birth weight, fetal distress, fetal growth restriction, and perinatal mortality.[5,15,16] The increased rate of admission to neonatal care unit was secondary to a higher incidence of preterm delivery among those with COVID-19 infection. Although vertical transmission of COVID-19 is still poorly understood there have been reports of neonates who have tested positive for the virus.[2,19] It is interesting to note that these neonates rarely exhibited respiratory symptoms. Further research could be done to illuminate whether infection of COVID occurs in utero, during labor or birth, or from handling by allied healthcare professionals immediately in the postpartum period.

One of the most intriguing and adaptive mechanisms of COVID-19 is its propensity to be a great mimicker. It initially presents with nonspecific symptoms which could be again construed as part of the physiologic changes of pregnancy. Its symptoms may even be completely ignored by the general population until progression. This sort of thinking may explain why comparative studies have concluded that COVID-19 positive pregnant patients are considered higher risk candidates for intensive care admission and invasive mechanical ventilation. The risk is further compounded if preexisting comorbidities are present such as hypertension, diabetes, obesity, advanced maternal age, and asthma. A careful and comprehensive multidisciplinary approach is warranted to shield both expecting mother and unborn child from virus exposure such as limiting trips to hospitals, regular teleconsult follow-up and an open communication channel.

Limitation of the study and recommendations

Retrospectively, improvements in the study conducted could be done so that succeeding studies may contribute more information on the virus and its effects on the parturient patient. Further evaluation on the interaction of gestational diabetes and preeclampsia with the COVID-19 virus may yield better understanding and management since, for example, severe preeclampsia may mirror severe COVID-19. The timeframe of the study may focus on the first and second trimester as well if COVID-19 has any long-standing or permanent sequelae in these stages of the trimester.

Future researches may also benefit from a different study design. The concluded study opted to use a retrospective cohort as compared to a prospective cohort due to limitations in data collection, number of deliveries, and willingness of patients to be tested before the third trimester. Continuing with a retrospective study carries a small but even present risk of selection bias due to the availability of records. The detection of COVID-19 as well relied heavily on the presence of testing kits, willingness to be tested and the requirement of universal swabbing for all patients seeking admission despite the absence of symptoms. The study may further be strengthened with the reduction of reporting bias found in the neonatal outcomes which may be supplemented with further testing comparison of a COVID-19 group. However, with all biases accounted, the study holds it validity and strength in showing the adverse effects that the virus has on this stage and process of labor.

Conclusion

In this study, there was no evidence to associate that the presence of COVID-19 infection in pregnancy causes an increase risk of morbidity and mortality in mothers and their neonates, especially for those individuals who were asymptomatic and has no comorbidities. Close surveillance should be done on those pregnant with the infection, especially if it is detected before term, as these patients are predisposed to having preterm labor. Further research is needed to understand the true extent of the risks and to improve the management of these special population.

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Conflicts of interest

There are no conflicts of interest.

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