

Access this article online

Quick Response Code:



Website:

www.pogsjournal.org

DOI:

10.4103/pjog.pjog_68_23

Comparison of maternal and fetal outcomes between COVID-19 and non-COVID-19 patients in a tertiary government hospital: A retrospective cohort study

Janine Carsola Pulido¹, Raissa Marie Tud²

Abstract:

INTRODUCTION: Although it is likely that outcomes in pregnancy differ between regions due to differences in health-care delivery, resources, and health protocols, the rampant increase in COVID-19 cases has proven its effects on the maternal and fetal outcomes. But to what extent does COVID-19 in pregnancy affect adverse maternal and neonatal outcomes compared to non-COVID-19 pregnant patients?

OBJECTIVES: This study aims to compare maternal outcomes (morbidity, mortality, intensive care unit [ICU] admissions, and cesarean section [CS] rate) and fetal outcomes (prematurity, APGAR score, neonatal ICU [NICU] admission, and mortality) between COVID-19 and non-COVID-19 cases.

METHODOLOGY: A retrospective cohort study was done through chart review of 240 patients, 120 for the COVID-19 group and 120 for the non-COVID-19 group. Demographic data, as well as maternal outcomes (i.e., morbidity, mortality, ICU admissions, and emergency CS), and adverse fetal outcomes (i.e., prematurity, low APGAR, NICU admission, and mortality) were gathered. These outcomes were also classified according to disease severity for the COVID-19 group. The effect of using investigational drugs to outcomes was also determined.

RESULTS: This study shows that adverse maternal outcomes were significantly increased with COVID-19 infection. Mortality was increased by 10% while morbidities (acute respiratory distress syndrome, disseminated intravascular coagulation, hemorrhage, and sepsis) were increased by 35%. ICU admission for COVID-19 patients was 10.8% higher, and the emergency CS rate was also increased by 10% in the COVID-19 group. Results also showed increased adverse fetal outcomes for the COVID-19 group, with a 10.8% increase in neonates being born prematurely, an 11.67% increase in low APGAR score, a 9.16% increase in mortality, and a 10% increase in NICU admission. The use of investigational drugs in cases of severe and critical COVID-19 did not have any significant benefits to the outcomes.

CONCLUSION: COVID-19 infection significantly increases both maternal and fetal outcomes, and these adverse effects correspond to the severity of the disease. The use of investigational drugs in severe and critical COVID-19 cases has no significant benefit to maternal and fetal outcomes.

Keywords:

COVID-19 in pregnancy, fetal outcomes, maternal outcomes

Introduction

Coronavirus had an initial outbreak and was first reported in Wuhan, China,

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

last December 2019 after an upsurge of a mysterious pneumonia characterized by fever, dry cough, fatigue, and occasional gastrointestinal symptoms.^[1] There was a rampant increase in the number of cases across different areas in mainland China

How to cite this article: Pulido JC, Tud RM. Comparison of maternal and fetal outcomes between COVID-19 and non-COVID-19 patients in a tertiary government hospital: A retrospective cohort study. *Philipp J Obstet Gynecol* 2023;47:294-301.

¹Quirino Memorial Medical Center, Antipolo, Rizal,

²Department of Obstetrics and Gynecology, Quirino Memorial Medical Center, JP Rizal Street, Project 4 Quezon City, Philippines

Address for correspondence:

Dr. Janine Carsola Pulido,
Blk 8 Lot 30, Kamagong Street Palmera Woodlands Brgy, Cupang, Antipolo, Philippines.
E-mail: pulido.janine@yahoo.com

Submitted: 18-Sep-2023

Revised: 10-Nov-2023

Accepted: 13-Nov-2023

Published: 28-Dec-2023

and subsequently worldwide, hence measures were initiated to contain the spread of this virus. Some of these preventive measures included social distancing, wearing of personal protective equipment, frequent hand washing, choosing open and well-ventilated spaces, as well as getting vaccinated. Furthermore, the development of novel variants has caused surges in COVID-19 cases, hence warranting further studies of this condition. The Philippines is one of the countries vastly affected by the pandemic. Its effect is evident, especially in the field of maternal and fetal health.^[2]

There is currently no clear evidence of *in utero* transmission.^[3] However, pregnant patients are at increased risk for developing the severe form of the disease, and this poses risks to both maternal and fetal well-being. Pregnant women also have a higher tendency of exacerbating their COVID-19-related diseases.^[3]

This study determined the maternal and fetal outcomes of patients with COVID-19 in comparison to non-COVID-19 patients, the relation of disease severity to the outcomes, and the effect of using investigational drugs among pregnant women with severe-to-critical COVID-19. The objectives of the study are as follows:

1. To determine the maternal outcomes of COVID-19-confirmed pregnant patients
 - a. In comparison to non-COVID-19 patients
 - b. In relation to disease severity
 - c. In relation to the use of investigational drugs
 - d. Specific outcome measures include rates of morbidity (i.e. surgical site infection, hemorrhages, and acute respiratory distress syndrome [ARDS]), mortality, and emergency cesarean section (CS).
2. To determine the fetal outcomes of babies delivered to COVID-19-confirmed pregnant patients.
 - a. In comparison to non-COVID-19 mothers
 - b. In relation to disease severity
 - c. Specific outcome measures include prematurity, low APGAR, neonatal intensive care unit [NICU] admission, morbidity, and mortality.

Further knowledge on COVID-19 would aid in proper counseling and management of pregnant patients and optimal timing of delivery of patients with the infection. The results of this study may also play a role in advocating vaccination and revising health policies.

Methodology

Study design

This is a retrospective cohort study where chart review was performed to determine the maternal and neonatal outcomes among pregnant patients with viable fetuses, who are confirmed to have COVID-19, in comparison

to pregnant patients without COVID-19, admitted from March 2020 to December 2021.

Subject selection

The study population consisted of 240 pregnant patients admitted during the inclusive dates. The first group comprised 120 patients confirmed to have COVID-19 while the other comprised 120 patients with uncomplicated pregnancies and without COVID-19.

Inclusion criteria

1. Pregnant patients aged 18 years and above with viable pregnancy (more than 24 weeks age of gestation (AOG))
2. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection confirmed using reverse transcription-polymerase chain reaction (RT-PCR) or antigen swab done prior to or at the time of their admission
3. Patients who delivered during their admission OR patients managed conservatively
4. Pregnant patients with no other comorbidities (such as thyroid disorder, hypertension, and diabetes)
5. Admitted from March 1, 2020, to December 31, 2021.

Exclusion criteria

1. Patients with nonviable fetuses (<24 weeks AOG)
2. Patients with comorbidities (such as thyroid disorder, hypertension, and diabetes) or who are considered high-risk pregnancies
3. Patients whose outcome measures cannot be determined or are incomplete.

Data collection, methods, and tool

The sample size was determined using the Cochran's formula for uniformity of the study. The sample size was computed to be 120 for each group. A list of eligible cases was generated from the census of hospital admissions from March 1, 2020, to December 31, 2021. The subjects were classified into two groups: the COVID-19 group and the non-COVID-19 group. All COVID-19-confirmed cases who met the inclusion criteria were included in the COVID-19 group. This group was further classified into asymptomatic, mild, moderate, severe, or critical. Sampling was done for the non-COVID-19 cases who met the inclusion criteria in order to generate the same size for the non-COVID-19 group. The charts of the included subjects were then retrieved.

The demographics, age of gestation, disease severity, RT-PCR result, maternal outcome measures (maternal morbidities, emergency CS, intensive care unit [ICU] admission, and mortality), and fetal outcomes (prematurity, APGAR scores, NICU admissions, and mortality) were collected from the

patients' charts. The data were grouped according to disease severity for the COVID-19 group.

Data analysis made use of percentage and frequency. Age and gestational age were both considered confounding variables in this study. As shown in Table 1, age and gestational age have computed odds ratio of 1.07 and 0.81, respectively, with 95% confidence interval. This means that these variables have a positive association with the maternal and fetal outcomes of both the COVID-19 and non-COVID-19 groups. Age and gestational age can influence both the dependent and independent variables. To nullify the effect of these confounding variables, linear regression and inverse propensity weight were used.

The demographics were analyzed by means of descriptive statistics. Analysis of variance was used to determine if there was a statistically significant difference in the maternal and fetal outcomes between the COVID-19 and non-COVID-19 groups, taking into consideration the confounding effects of age and gestational age. The margin of error in the study was set to 5% to have a 95% confidence level, respectively.

Results

Table 2 shows the comparison of maternal outcomes between the COVID-19 and non-COVID-19 groups. COVID-19-confirmed pregnant patients have a 35% higher risk of developing morbidity compared to non-COVID-19 pregnant patients. Figure 1 shows the morbidities associated with COVID-19 determined in this study. ARDS was seen in 76% of cases, followed by disseminated intravascular coagulation (10%) and hemorrhage and sepsis (7% respectively). The results also showed that COVID-19 increases maternal mortality by 10%. All mortality cases (12) were due to respiratory failure secondary to developing ARDS. In the COVID-19 group, ICU admission and emergency CS rate were increased by 10.8% and 10%, respectively. Shown in Figure 2 are the indications for emergency CS. Patients with mild-to-moderate COVID-19 underwent emergency CS for dystocia and deteriorating maternal status, while patients with critical COVID-19 underwent emergency CS for fetal indications (nonreassuring fetal status).

Table 3 shows the relationship between the disease severity and maternal outcomes. All adverse maternal outcomes (morbidity, mortality, ICU admission, and emergency CS) were significantly increased statistically as the disease severity increased. Maternal morbidity significantly increases for moderate-to-critical cases of COVID-19, having 91.6% and 100% rates, respectively. The maternal mortality rate for critical cases was 100%.

Table 1: Nullification of the effects of confounding variables such as age and gestational age

Groups	OR	SE	P (95% CI)
Age	1.07	0.02	1.02
Gestational age	0.81	0.05	0.71

OR: Odds ratio, SE: Standard error, CI: Confidence interval

Table 2: Comparison of maternal outcomes between COVID-19 and non-COVID-19 patients

Maternal outcomes (rate or %)	COVID-19, n (%)	Non-COVID-19, n (%)	P
Morbidity (SSI, ARDS, hemorrhages, etc.)	42 (35)	0	0.0085
Mortality	12 (10)	0	0.0054
ICU admission	13 (10.8)	0	0.0031
Emergency CS	12 (10)	2 (1.67)	0.0054

ARDS: Acute respiratory distress syndrome, ICU: Intensive care unit, CS: Cesarean section, SSI: Surgical site infection

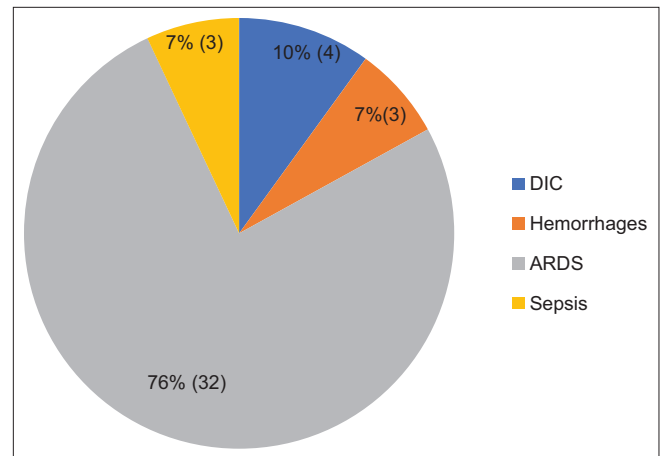


Figure 1: Morbidities in the COVID-19 group. DIC: Disseminated intravascular coagulation, ARDS: Acute respiratory distress syndrome

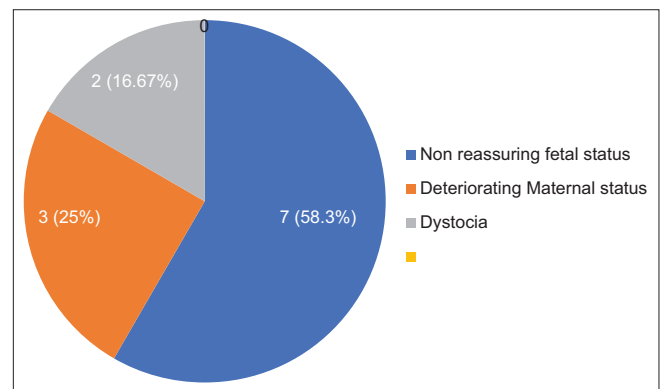


Figure 2: Reason for emergency cesarean section in the COVID-19 group. CS: Cesarean section

All patients in the critical COVID-19 group were also admitted to the ICU. Figure 3 shows a comparison of maternal outcomes according to disease severity.

Only one out of the 12 cases in the critical COVID-19 group was not given investigational drugs. However,

Table 3: Comparison of maternal outcomes in relation to disease severity

Maternal outcomes	Non-COVID-19, n (%)	Asymptomatic (n=36), n (%)	Mild (n=47), n (%)	Moderate (n=24), n (%)	Severe (n=1), n (%)	Critical (n=12), n (%)	P
Morbidity	0	3 (2.77)	4 (8.51)	22 (91.6)	1 (100)	12 (100)	0.0006
Mortality	0	0	0	0	0	12 (100)	0.0003
ICU admission	0	0	0	1 (4.16)	0	12 (100)	0.0002
Emergency CS	0	0	3 (6.38)	2 (8.33)	0	7 (58.3)	0.0016

ICU: Intensive care unit, CS: Cesarean section

Table 4: Comparison of maternal outcomes in relation to use of investigational drugs

Maternal outcomes	Use of investigational drugs		P
	With, n (%)	Without, n (%)	
Morbidity (SSI, ARDS, etc.)	11 (91.67)	1 (0.83)	0.478949
Mortality	11 (91.67)	1 (0.83)	0.478949
ICU admission	11 (91.67)	1 (0.83)	0.478949
Emergency CS	10 (83.33)	2 (1.67)	0.412678

ARDS: Acute respiratory distress syndrome, ICU: Intensive care unit, CS: Cesarean section, SSI: Surgical site infection

Table 5: Comparison of fetal outcomes between COVID-19 and non-COVID-19 patients

Fetal outcomes	COVID-19 confirmed (%)	Non-COVID-19 (%)	P
Prematurity	13 (10.8)	0	0.0026
Low Apgar	14 (11.67)	0	0.0147
NICU admission	12 (10)	0	0.0059
Mortality	11 (9.16)	2 (1.67)	0.0087

NICU: Neonatal intensive care unit

the use of remdesivir and tocilizumab in severe and critical cases did not result in significant improvement in any adverse maternal outcome, as shown in Table 4. The rates of adverse maternal outcomes were statistically the same for critically ill patients regardless of the use of investigational drugs.

Table 5 shows the comparison of fetal outcomes, in terms of prematurity, APGAR score, NICU admission, and mortality, between the COVID-19 and non-COVID-19 groups. All adverse fetal outcomes were significantly increased in the COVID-19 group. There is a note of a 10.8% increase in prematurity and a 6.67% increased chance of APGAR scores below 7 in the COVID-19 group. The chance of NICU admission is 10% higher, while mortality is increased by 9.16% in the COVID-19 group compared to the non-COVID-19 group. Similar to maternal outcomes, fetal outcomes were also affected by the severity of the disease, as shown in Table 6. Figure 4 is a graphic presentation of fetal outcomes according to disease severity.

The use of remdesivir and tocilizumab in severe and critical cases did not result in significant improvement in any fetal outcome, as shown in Table 7. Adverse fetal outcomes were statistically the same for critically

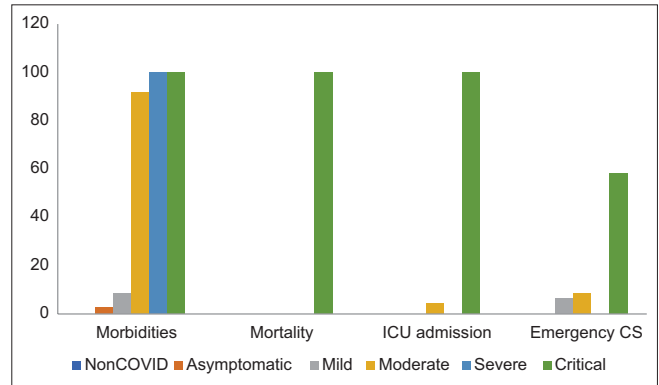


Figure 3: Comparison of maternal outcomes according to disease severity.
ICU: Intensive care unit, CS: Cesarean section

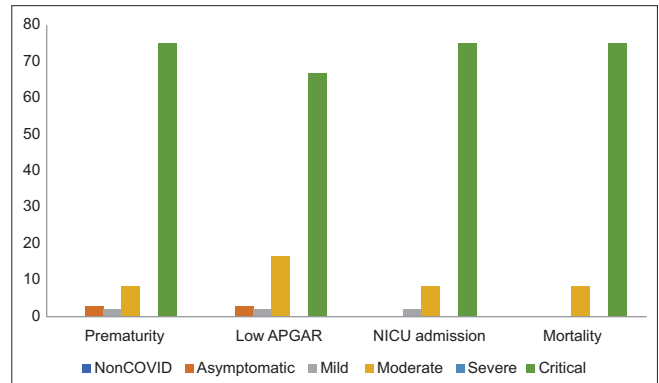


Figure 4: Comparison of fetal outcomes according to disease severity.
NICU: Neonatal intensive care unit

ill mothers regardless of the use of investigational drugs.

Discussion

Maternal outcomes

COVID-19 in pregnancy is found to be associated with a significant increase in severe maternal morbidity, mortality, and neonatal complications compared to pregnant women without the infection, as seen in a multinational cohort study by Villar *et al.* According to their study, women with COVID-19 were at higher risk for preeclampsia/eclampsia, severe infections, ICU admissions, maternal mortality, preterm birth, and severe neonatal morbidity.^[4] Their findings were consistent with the results of this study, where maternal morbidity and mortality were significantly increased

Table 6: Comparison of fetal outcomes in relation to disease severity

Fetal outcomes (rate or %)	Non-COVID-19	Asymptomatic (n=36), n (%)	Mild (n=47), n (%)	Moderate (n=24), n (%)	Severe (n=1), n (%)	Critical (n=12), n (%)	P
Prematurity	0	1 (2.77)	1 (2.12)	2 (8.33)	0	9 (75)	0.0002
Low Apgar	0	1 (2.77)	1 (2.12)	4 (16.67)	0	8 (66.7)	0.0002
NICU admission	0	0	1 (2.12)	2 (8.33)	0	9 (75)	0.0003
Mortality	2 (1.67)	0	0	2 (8.33)	0	9 (75)	0.0006

NICU: Neonatal intensive care unit

Table 7: Comparison of fetal outcomes in relation to use of investigational drugs

Fetal outcomes	Use of investigational drugs		P
	With, n (%)	Without, n (%)	
Prematurity	11 (91.7)	1 (0.83)	0.348720
Low Apgar	8 (66.7)	4 (0.33)	0.432353
NICU admission	9 (75)	3 (2.5)	0.348720
Mortality	10 (83.3)	2 (1.67)	0.435628

NICU: Neonatal intensive care unit

in pregnant patients diagnosed to have COVID-19. In this study, the most common morbidity associated with COVID-19 infection in pregnancy was ARDS, followed by disseminated intravascular coagulopathy, hemorrhage, and sepsis. ARDS was also the primary cause of death for majority of the maternal mortality, as well as the indication for ICU admission.

A study by Sadeghi *et al.* showed a positive correlation between maternal mortality and ICU admission. In their study, they found that desaturation was the only independent predictor for ICU admission due to the subsequent development of ARDS, necessitating the need for intubation.^[5] Incidentally, the rates of ICU admission and mortality among pregnant COVID-19 patients in our results were found to be similar, suggestive of a positive correlation between mortality and ICU admission.

Aside from increased morbidity and mortality, women with COVID-19 have lower rates of initiation of labor resulting in higher cesarean delivery rates, as well as increased rates of complications.^[6] This is consistent with the relatively high CS rates in regions in China severely affected by the COVID-19 outbreak.^[7] A systematic review also showed a strong correlation between premature birth and the presence of COVID-19 symptoms, exhibited as the highest Cesarean section rate performed in COVID-19 for preterm deliveries.^[8] Two of the most frequent indications for CS were the symptoms of exacerbation, such as severe acute respiratory distress (33.5%) and fetal distress (24.6%).^[8]

In this study, there is a 10% increase in emergency CS rate in the COVID-19 group, primarily due to deteriorating maternal condition (i.e. disseminated intravascular

coagulation, ARDS, sepsis, and hemorrhage) and fetal distress. Recurrent variable and late decelerations were prevalent despite resuscitations. Most of the patients who underwent abdominal delivery were between 26 and 32 weeks of gestation, as reflected by the 10.8% increase in prematurity in the COVID-19 group. The indications for emergency CS are shown in Figure 2. Majority of the indications for Emergency Cesarean section are due to Non reassuring fetal status then followed by Deteriorating maternal status and dystocia, respectively. These results are comparable to a study by Di Mascio *et al.* which showed that one of the leading indications for preterm delivery was fetal distress, and that women with COVID-19-diagnosis delivered earlier than those without COVID-19 diagnosis, after approximately 30-week gestation.^[9]

Fetal outcomes

Deterioration of maternal status translates to fetal distress. Hence, patients with COVID-19 infection who develop ARDS and other complications are predisposed to higher chances of having low APGAR score of the neonates upon delivery. This is evident in the 6.67% increase in APGAR scores <7 in the COVID-19 group as compared to the non-COVID-19 group. The study of Chao *et al.* showed that the risk of having an APGAR score <7 in COVID-19-positive mothers was 25.4 times higher than those who did not have COVID-19, suggesting that maternal COVID-19 status impacts neonatal APGAR scores.^[10] The main determinants of adverse prenatal outcomes in fetus from COVID-19-confirmed mothers are maternal ventilatory support, early gestational age, and low birth weight. There is also a strong correlation between severe maternal symptoms and newborn’s outcome.^[9]

Pregnant women with COVID-19 are highly likely to have preterm births as adverse pregnancy outcomes.^[11] The increase in cesarean delivery due to clinical indications and fetal distress results in increased preterm births and subsequent NICU admissions, as the age of gestation at the time of delivery can have complications which would necessitate NICU admission. Premature delivery was correlated with a lower value of oxygen saturation leading to increase in development of ARDS in fetuses whose mother tested positive for COVID-19.^[12] These are consistent with our results demonstrating that majority

Downloaded from http://journals.lww.com/pjog by BhDMf5ePHkav1zEum11CqMNa+KJLHEZgbsIho4XMI0hCwC1AW nYOp/IIQH3d3D00ORy7T7vSF14C13VC1y0abggQZXdG6j2MwIZLeI= on 12/29/2023

of NICU admissions in the COVID-19 group were due to prematurity, followed by respiratory distress syndrome secondary to extreme prematurity.

In this study, the primary reason for neonatal mortality was respiratory distress secondary to extreme prematurity. The study by Di Mascio *et al.* showed that the rate of perinatal death increases due to prematurity.^[9] The study by Chao *et al.* showed that maternal COVID-19 increases the chances of neonatal mortality by up to 9%.^[10]

Interestingly, in contrast to this study, a research conducted in the Philippine General Hospital showed that the majority of pregnant women with clinically confirmed COVID-19 have generally good maternal and neonatal outcomes. Moreover, it showed that infected pregnant mothers and their neonates born to COVID-19-infected mothers are discharged stable.^[12]

Disease severity

Pregnant women carry potential risks for severe illness from COVID-19 infection, resulting in admission to ICUs, extracorporeal membrane oxygenation, or mechanical ventilation, and death as compared to nonpregnant women in reproductive age.^[13] Thus, increasing severity of a disease, particularly of COVID-19 in pregnancy, is proportional to the chances of having morbidity, mortality, ICU admission, and emergency CS due to its associated complications.^[9] The same is evident in our results which shows a significant increase in all adverse maternal outcomes as disease severity progresses. The risk of undergoing an emergency CS was increased even in mild cases of COVID-19. Patients who develop moderate COVID-19 were found to have significantly higher chances of morbidity and even ICU admission, while the risk of morbidity, emergency CS delivery, ICU admission, and mortality increases exponentially for patients having severe and critical COVID-19. These findings are logical given the profound effect of the disease on the patient's respiratory function.

Vertical transmission

A study by Wang *et al.* showed that the most conclusive evidence of intrauterine transmission of COVID-19 would be to confirm the replication of SARS-CoV-2 in fetal pulmonary tissues, but it is mostly not feasible. Currently, the practical way to test whether there has been intrauterine viral infection is to look for the presence of the virus in placental, amniotic fluid, cord blood and neonatal pharyngeal swab samples.^[14] Based on existing data on this study, there is currently no evidence of intrauterine infection caused by vertical transmission in women with COVID 19 in the third trimester.^[14] However, the sample population of this study utilized

COVID-19 pregnant mothers with mild-to-moderate infection during the third trimester alone. Hence, the time interval from clinical manifestation to delivery was short and also the severity of the infection might be insufficient to cause vertical transmission.^[14]

In a local study done by Clemente *et al.* conducted in Philippine General Hospital, majority of pregnant women with COVID-19 infection and their neonates had good outcomes. All 14 dyads with collected specimens that included amniotic fluid, placental tissue, umbilical cord, and neonate nasopharyngeal swab tested negative for SARS-CoV-2 RT-PCR swab. Almost all the neonates born to COVID-19-infected mothers are stable-term infants, and there was no evidence of vertical transmission.^[12]

In contrast, in a study by Kotlyar *et al.*, it was found that in 936 neonates from mothers with COVID-19, 27 neonates tested positive for COVID-19 using nasopharyngeal swab, indicating a pooled proportion of 3.2%.^[15] Severe ARDS viral RNA testing in neonatal cord blood was positive in 2.9% of samples, 7.7% in placental samples, 0% in both urine and amniotic fluid samples, and 9.7% in rectal swabs. Therefore, vertical transmission is still possible and seems to occur in minority of cases.^[15]

Our results also showed that maternal COVID-19 is associated with higher rates of adverse fetal outcomes. The study of Chao *et al.* showed that the risk of having an APGAR score < 7 in COVID-19-positive mothers was 25.4 times higher than those without, suggesting that maternal COVID-19 status impacts neonatal APGAR scores.^[10] Premature delivery was also correlated with a lower value of oxygen saturation leading to an increase in development of ARDS in fetuses whose mother tested positive for COVID-19.^[10] Increasing severity of the disease leads to deterioration of maternal condition, further leading to fetal distress. This increase in fetal distress results in increased cesarean delivery of preterm fetuses. Since most of these preterm deliveries were between 26 and 32 weeks of gestation, NICU admissions also increased.

Use of investigational drugs

Remdesivir, an inhibitor of the viral RNA-dependent RNA polymerase, was identified early as a promising therapeutic candidate for COVID-19 because of its ability to inhibit SARS-CoV-2 *in vitro*. In a study by Beigel *et al.*, COVID-19 patients given remdesivir had a shorter time to recovery than patients in the placebo group. They found in their study that the benefit of remdesivir was larger when given earlier in the illness.^[16] In addition to remdesivir, the World Health Organization added tocilizumab, a monoclonal antibody, to its list of prequalified treatments for COVID-19. Tocilizumab has been shown to reduce death in patients who are severely

ill, rapidly deteriorating and have increasing oxygen needs.^[17] At the time of our study, both these drugs were given only to pregnant patients with severe or critical COVID-19 as compassionate use because of the lack of safety profile to the fetus.

Results of this study showed that the use of remdesivir and tocilizumab in severe and critical COVID-19 cases did not cause a significant improvement in any of the maternal and fetal outcomes studied. All 12 patients from the severe and critical COVID-19 groups received the said investigational drugs, but all of them expired. Given the advanced stage and rapid progression of the disease of these patients, there could have been insufficient time for the medications to have any effect. In addition, the added stress of the emergency surgery that the patients underwent could have negated or dampened the effect of the investigational drugs. Finally, since gestational age is a major determinant of fetal outcome, the use of remdesivir and tocilizumab will have no apparent effect to the fetal outcomes of babies delivered prematurely.

Conclusion

In contrast to pregnant women without COVID-19 infection who have uneventful labor and delivery, as well as good neonatal outcomes, this study shows that having COVID-19 increases the chances of undergoing emergency CS by 8.3% and developing morbidities such as ARDS, DIC, hemorrhage, and sepsis by as much as 35%. ICU admission and mortality are likewise increased by 10.8% and 10%, respectively. As the rate of preterm delivery is increased due to clinical indications and fetal distress, low APGAR score, NICU admission, and neonatal mortality were subsequently increased in neonates of mothers with COVID-19 at the time of delivery. These maternal and neonatal adverse outcomes were found to increase in proportion to disease severity. The use of investigational drugs in severe and critical COVID-19 cases has no significant benefit to maternal and fetal outcomes.

The results of this study are limited by the small sample size, especially the group given investigational drugs (remdesivir and tocilizumab), as well as by the lack of comorbidities of the COVID-19 group. The limited sample sizes may not be representative of the whole population, while the presence of comorbidities may influence COVID-19 infection.

Recommendation

As such, it is our recommendation that future researchers consider a multi-institutional study to allow for larger sample sizes for the COVID-19 and non-COVID-19 groups and to include those with comorbidities. The effect of COVID-19 vaccination on maternal and fetal outcomes is also of substantial interest for future studies.

Acknowledgment

This is to acknowledge the people who made this research paper possible:

Almighty Creator for being the center of my faith and who strengthens me holistically to accomplish and finish this paper.

Authorship contributions

Pulido, Janine C - Involved in the conceptualization, methodology, data curation, writing of the original draft, review and editing.

Pulido, Janine C - Involved in conceptualization, methodology, review and editing of the draft.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Wu YC, Chen CS, Chan YJ. The outbreak of COVID-19: An overview. *J Chin Med Assoc* 2020;83:217-20.
2. Kotlar B, Gerson EM, Petrillo S, Langer A, Tiemeier H. The impact of the COVID-19 pandemic on maternal and perinatal health: A scoping review. *Reprod Health* 2021;18:10.
3. Wang LM, Lai SP, Liang SJ, Yang ST, Liu CH, Wang PH. Maternal and fetal outcomes of the pregnant woman with COVID-19: The first case report in Taiwan. *Taiwan J Obstet Gynecol* 2021;60:942-4.
4. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, *et al.* Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: The INTERCOVID multinational cohort study. *JAMA Pediatr* 2021;175:817-26.
5. Sadeghi A, Eslami P, Dooghaie Moghadam A, Pirsalehi A, Shojaee S, Vahidi M, *et al.* COVID-19 and ICU admission associated predictive factors in Iranian patients. *Caspian J Intern Med* 2020;11:512-9.
6. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, *et al.* Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020;9:51-60.
7. Zhang J, Zhang Y, Ma Y, Ke Y, Huo S, He L, *et al.* The associated factors of cesarean section during COVID-19 pandemic: A cross-sectional study in nine cities of China. *Environ Health Prev Med* 2020;25:60.
8. Smith V, Seo D, Warty R, Payne O, Salih M, Chin KL, *et al.* Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *PLoS One* 2020;15:e0234187.
9. Di Mascio D, Sen C, Saccone G, Galindo A, Grünebaum A, Yoshimatsu J, *et al.* Risk factors associated with adverse fetal outcomes in pregnancies affected by Coronavirus disease 2019 (COVID-19): A secondary analysis of the WAPM study on COVID-19. *J Perinat Med* 2020;48:950-8.
10. Chao M, Menon C, Elgendi M. Validity of Apgar score as an indicator of neonatal SARS-CoV-2 Infection: A scoping review. *Front Med (Lausanne)* 2021;8:782376.
11. Adhikari EH, Spong CY. COVID-19 vaccination in pregnant and lactating women. *JAMA* 2021;325:1039-40.
12. Clemente MJ, Amosco M, Octavio B, Bravo SL, Villanueva-Uy E, *et al.* Maternal and neonatal outcomes of pregnant women with clinically confirmed COVID-19 admitted at the Philippine general

- hospital. *Acta Med Philipp* 2021;55:183-90. Available from: <https://actamedicaphilippina.upm.edu.ph/index.php/acta/article/view/2863/2323>. [Last accessed on 2023 Dec 03].
13. Saccone G, Sen C, Di Mascio D, Galindo A, Grunebaum A, Yoshimatsu J, *et al.* Maternal and perinatal outcomes of pregnant women with SARS COV2 infection. *Ultrasound Obstet Gynecol* 2020;67:232-41. Available from: <https://obgyn.onlinelibrary.wiley.com/doi/10.1002/uog.23107>. [Last accessed on 2023 Dec 03].
 14. Wang C, Zhou YH, Yang HX, Poon LC. Intrauterine vertical transmission of SARS-CoV-2: What we know so far. *Ultrasound Obstet Gynecol* 2020;55:724-5. Available from: <https://obgyn.onlinelibrary.wiley.com/doi/full/10.1002/uog.22045>. [Last accessed on 2023 Dec 03].
 15. Kotlyar AM, Grechukhina O, Chen A, Popkhadze S, Grimshaw A, Tal O, *et al.* Vertical transmission of coronavirus disease 2019: A systematic review and meta-analysis. *Am J Obstet Gynecol* 2021;224:35-53.e3.
 16. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, *et al.* Remdesivir for the treatment of COVID-19 – Final report. *N Engl J Med* 2020;383:1813-26.
 17. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, *et al.* Compassionate use of remdesivir for patients with severe COVID-19. *N Engl J Med* 2020;382:2327-36.