ORIGINAL ARTICLE

Outcomes of Infants Born to Mothers with SARS-CoV-2 Infection in a Tertiary Hospital

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The authors declare that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and all authors have met the requirements for authorship.

ABSTRACT

Introduction: Pregnant women are a susceptible population to emerging infections. Recent published data have shown evidence of possible transplacental transmission of SARS-CoV-2. However, at present there are not enough data to determine its effect on the fetus. This study aims to determine the outcomes of infants born to mothers with SARS-CoV-2 infection.

Methods: A retrospective descriptive institution-based study using data collected from medical records of infants born to confirmed COVID-19 mothers delivered from April to June 2020.

Results: Of the 47 neonates, none of them were positive for SARS-CoV-2 RT-PCR. Majority were born full-term, mean gestational age of 37 weeks, weight of 2867 grams, appropriate for gestational age, good APGAR score, and delivered through cesarean section. Symptomatic neonates (27.7%) had tachypnea and vomiting as the most common manifestation, 13.3% had lymphopenia while pneumonia was the predominant radiologic finding. There was a significant association between the presence or absence of symptoms among mothers and neonates (p=0.037).

Conclusion: The neonatal outcome in this study was good with 98% survival at 2 weeks of life. There was note of 2.1% morbidity and mortality. Given that the clinical data in newborns are very limited and the possibility of a vertical transmission is still uncertain, it is crucial to closely monitor neonates with increased risk of COVID-19 infection.

KEYWORDS: *COVID-19, Neonates, Vertical transmission*

INTRODUCTION

Emerging infections have been shown to have an important impact on pregnant women and their fetuses, with increased risk of complications.[1] Human coronaviruses (CoV) are among the most common pathogens that cause respiratory infection. Among these are the Severe Acute Respiratory Syndrome (SARS) caused by SARS-CoV and Middle East Respiratory Syndrome (MERS) caused by MERS-CoV that appeared in 2003 and 2012, respectively. There are sparse data on the effects of SARS and MERS on pregnancy. For SARS, among 7 first-trimester infections, 4 ended in spontaneous abortion. Four of 5 women with SARS after 24 weeks' gestation delivered preterm. For MERS, there were 13 case reports in pregnant women, 2 pregnancies ended in fetal demise and 2 were born preterm. There was no evidence of in utero transmission seen in both coronaviruses.[1]

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first recognized in Wuhan, China in December 2019.[2,3] While most people with COVID-19 develop mild or uncomplicated illness, approximately 14% develop severe disease requiring hospitalization and oxygen support and 5% require admission to an intensive care unit.[3,4] Pregnant women are a susceptible population of SARS-CoV-2 and are more likely to have complications and even progress to severe illness.[5] In the accumulating data, it is already clear that COVID-19 is less severe in pregnancy than the 2 previous coronavirus infections.[5]
SARS-CoV-2 is mainly transmitted through respiratory droplets, but other transmission routes have been hypothesized.[6] Recent published data have shown evidence of possible transplacental transmission of SARS-CoV-2 from mother to infant,[6,7,8,9] despite prior claims that vertical transmission does not occur. In Paris and Italy, SARS-CoV-2 RNA was found on the fetal side of the placenta in a few mothers who received a diagnosis of COVID-19, with the neonates also testing positive for COVID-19 on nasopharyngeal[6,9] and rectal swab RT-PCR,[6] suggesting that vertical transmission is possible.

At present, there aren't enough data to determine the effect of COVID-19 infection on the fetus. Whether COVID-19 has mother-to-child vertical transmission, and its short and long-term harm to the offspring is still unclear.[2] In the Philippines, outcomes of newborns born to COVID-19 positive mothers have not yet been evaluated. Thus, this study aims to determine the clinicodemographic profile, laboratory, radiologic findings and treatment of infants born to mothers with confirmed COVID-19 and to associate maternal features with neonatal outcomes.

METHODOLOGY

Study Design

A retrospective, descriptive institution-based study design was used to describe the outcome of all neonates born to confirmed COVID-19 mothers at the Philippine General Hospital (PGH).

Study Population and Setting

All neonates born to confirmed COVID-19 mothers from April 1, 2020 to June 31, 2020 delivered at the Philippine General Hospital were included in this study. Mothers with inconclusive RT-PCR results had swab tests repeated and if positive, infants were included in this study. Those with negative results on repeat swab test were considered non-COVID thus infants were not included in this study.

Definition of terms[10,11]

1. Close contact – person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms:
   a. Face-to-face contact with a probable or confirmed case within 1 meter and for at least 15 minutes;
   b. Direct physical contact with a probable or confirmed case;
   c. Direct care for a patient with probable or confirmed COVID-19 disease without using recommended personal protective equipment; OR
   d. Other situations as indicated by local risk assessments
2. Cluster – is an unusual aggregation, real or perceived, of health events that are grouped together as to time and space and that is reported to a public health department.
3. Exposure – if the child has been in close contact with sick individuals or suspect, probable or positive COVID-19 patients, whether from home or during travel to areas with localized

transmission or local communities under quarantine.

4. COVID-19 Confirmed – any individual, with or without symptoms, who has laboratory-confirmed COVID-19 reverse transcription polymerase chain reaction (RT-PCR) test result from an accredited laboratory.
5. Survived – patient who is alive and well during the first 14 days of life.
6. Expired – patient who for any reason, died within 14 days from delivery.
7. Morbidity – patients who were sent home but had a new onset infection or illness within 14 days of life.
8. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) – is the method used for the nucleic acid amplification testing, which is the preferred diagnostic tool for diagnosing SARS-CoV-2 infection.
9. Feeding intolerance – inability to digest enteral feedings presenting as residual volume of more than 50%, abdominal distention or emesis or both and the disruption of the patient's feeding plan.[12]

Data Collection and Procedure

All infants born to confirmed COVID-19 mothers who were delivered at PGH from April 1, 2020 to June 30, 2020 and subsequently referred to the INTROP (Infectious and Tropical Diseases in Pediatrics) service were identified. All corresponding neonatal and maternal charts were retrieved, reviewed and had all the necessary data needed for the study.

The following maternal data were recorded: (1) age, (2) gravida (parity), (3) pregnancy-related complications, (4) co-morbidities, (5) mode of delivery, (6) presenting signs and symptoms, (7) close contact with individuals proven or highly suspected of COVID-19, (8) history of travel to areas with localized transmission within the last 14 days, and (9) resides in an area or neighborhood with clustering of influenza-like illnesses.

The following neonatal data were recorded: (1) gender, (2) age of gestation in weeks, (3) birthweight, (4) size for gestational age, (5) APGAR score, (6) signs and symptoms, (7) underlying disease and complications, (8) laboratory results, (9) treatment, and (10) outcome.

Upon review, all infants of mothers with COVID-19 infection were delivered under contact, droplet and airborne transmission precautions. Neonates were immediately dried, transferred and isolated in the COVID NICU. As a precaution, NO early skin to skin contact, delayed cord clamping and non-separation from the mother were done and the mother wore a surgical mask during delivery. Nasopharyngeal swab (NPS) or Oropharyngeal (OPS) specimens and/or Endotracheal aspirate (ETA) specimens if the patient is intubated, were obtained from all neonates at 24 to 48 hours of life. The samples were placed in a viral transport medium and were sent to the Medical Research Laboratory (MRL) of PGH for processing via RT-PCR for COVID.

Study Outcome

The demographics, clinical features, laboratory, radiologic findings and treatment of infants born to confirmed COVID-19 mothers were described. The neonates were classified as survived, expired or morbidity depending on their outcome within the first 14 days of life.

Data Processing and Analysis

Descriptive statistics was employed. Univariate analysis was done by generating the frequency and percentage distribution for all categorical variables. Bivariate analysis was performed using Fisher's exact test or Chi square test, whichever is available, to determine the association between maternal and neonatal variables.

Ethical Considerations

This study was submitted and approved by the Philippine General Hospital Expanded Hospital Research Office (EHRO) Technical Review Panel and the University of the Philippines Manila Research Ethics Board (UPMREB) prior to data collection. This was conducted in accordance with the principles that have their origin in the Declaration of Helsinki and is consistent with the International Conference on Harmonization Tripartite Guidelines and the Good Clinical Practice Guidelines (ICH-GCP).

A waiver of informed consent was requested from the Ethical Panel since the research presents no more than minimal risk, the waiver or alteration will not severely affect the rights and welfare of the participants. In accordance with the National Ethical Guidelines of Health and Health-related Research 2017, the research cannot be carried out without the waiver and the review

of medical records and its anonymity will be maintained. Data was solely collected by the primary investigator. All patient information were anonymized via identification codes and kept confidential. Soft copy of the files utilized password encryption saved in a USB storage device. This and the data collection forms will be kept in filing cabinets under lock and key, accessed only by the investigators. The data will be securely stored for at least ten years from the date of final publication and will be destroyed thereafter. The risk to privacy is minimal in this study, however in case of a breach, matter will be forwarded immediately to the PGH data privacy officer.

The investigators declare that there was no conflict of interest in the conduct of this study. There was no funding received from any individual nor institution.

RESULTS

Of the 109 deliveries at PGH from April to June 2020, forty-five pregnant women had confirmed COVID-19. Forty-three mothers had singleton delivery, while 2 had twin pregnancy. Twenty-seven (60%) out of the forty-five were multi-gravid with a mean age of 29 years old (15 to 39 years). Sixty four percent (64.4%) were asymptomatic, while 35.6% had symptoms of the disease which most commonly presented with cough (62.5%). Only seven (15.6%) had an identified significant exposure. Twenty-two mothers (48.9%) had co-morbidities, majority of which was gestational diabetes mellitus (40.9%), while 6 (13.3%) had pregnancy-related complications such as intrauterine fetal distress (66.7%) and premature rupture of membranes (33.3%). The summary of the maternal clinical features is presented in Table 1.

Table 1: Clinical Demographic Profile of Mothers with SARS-CoV2 Infection

Variables	N (45)	%
Age		
<21 years old	2	4.4%
21-30 years old	21	46.7%
>30 years old	22	48.9%
Mean age	29.7 year old (15 to 39 year old)	
Obstetric score		
Primigravid	18	40%
Multigravid	27	60%
No co-morbidities	23	51.1%
With Co-morbidities	22	48.9%
Gestational diabetes mellitus	9	40.9%
Gestational hypertension	5	22.7%
Pre-eclampsia	4	18.2%
Chronic hypertension	4	18.2%
Bronchial asthma	3	13.6%
Diabetes mellitus type II	2	9.1%
Hypothyroidism	2	9.1%
Multiple myoma	2	9.1%
Multinodular toxic goiter	1	4.5%
Hepatitis B	1	4.5%
ADHD	1	4.5%
Pregnancy-related Complications	6	13.3%
Intrauterine fetal distress	4	66.7%
Premature rupture of membranes (PROM)	2	33.3%
Mode of delivery		
Cesarean Section	32	71.1%
Spontaneous Vaginal Delivery	13	28.9%
Asymptomatic	29	64.4%
Symptomatic	16	35.6%
Cough	10	62.5%
Fever	5	31.2%
Dyspnea	3	18.7%
Coryza	3	18.7%
Sore throat	1	6.2%
Diarrhea	1	6.2%
Body malaise	1	6.2%
Anosmia	1	6.2%
With Exposure	7	15.6%
Close contacts	6	85.7%
Travel history	1	14.3%
Clustering	0	0%

There was a total of 47 neonates born to confirmed COVID-19 mothers. As shown in Table 2, 53.2% were males, while 46.8% were females. Majority was born full-term (91.5%), with a mean age of gestation of 37 weeks (29 to 40 weeks) and average weight of 2867 grams (615-3860 grams), appropriate for gestational age (95.7%), with good APGAR score (95.7%). The predominant mode of delivery was cesarean section (71.1%), primarily due to a previously scarred uterus.

Table 2: Demographics of Infants born to Mothers with SARS-CoV 2 Infection

Variables	N (47)	%
Gender		
Male	25	53.2%
Female	22	46.8%
Age of gestation (AOG)		
Full term	43	91.5%
Preterm	4	8.5%
Mean AOG	37 weeks (29 to 40 weeks)	
Birth weight		
≥2500 grams	40	85.1%
1500-2499 grams	5	10.7%
1000-1499 grams	1	2.1%
<1000 grams	1	2.1%
Mean Birthweight	2867 grams (615-3860 grams)	
Size for gestational age		
AGA	45	95.7%
SGA	2	4.3%
LGA	0	0%
APGAR score		
≥7	45	95.7%
<7	2	4.3%

All live births were swabbed at 24 to 48 hours of life and showed a negative SARS-CoV-2 PCR result. Thirty-four neonates (72.3%) had no symptoms and were sent home immediately with a reliable caregiver. Of the 27.7% who were symptomatic, the predominant underlying cause were feeding intolerance (30.8%), neonatal pneumonia (23.1%) and transient tachypnea of the newborn (23.1%) with clinical manifestations as presented in table 3. Vomiting (38.5%), tachypnea (38.5%) and apnea (23.1%) were the most common presentation.

Table 3: Clinical Manifestations of Infants born to Mothers with SARS-CoV2

Signs and Symptoms	N=47	%
Asymptomatic	34	72.3%
Symptomatic	13	27.7%
Tachypnea	5	38.5%
Vomiting	5	38.5%
Apnea	3	23.1%
Poor activity	2	15.4%
Cyanosis	2	15.4%
Abdominal distention	1	7.7%
Regurgitation	1	7.7%
Hypotension	1	7.7%
Underlying Disease		
Feeding intolerance	4	30.8%
Pneumonia	3	23.1%
Transient tachypnea of the newborn	3	23.1%
Respiratory distress syndrome	2	15.4%
Pneumothorax	2	15.4%
Early onset sepsis	1	7.7%
Pulmonary insufficiency of prematurity	1	7.7%
Necrotizing enterocolitis	1	7.7%
Septic ileus	1	7.7%

The neonates in this study who were symptomatic or had risk factors for sepsis were worked up and none had with leukopenia nor thrombocytopenia. Two or 13.3% had a lymphocyte count of less than 20%, and 55.6% had elevated procalcitonin levels. The most common radiologic finding was pneumonia (55.6%). Details of the laboratory and radiologic findings are seen in tables 4, 5 and 6. A second RT-PCR was sent in one neonate who was intubated on the second day of life due to pneumothorax, that still turned out negative.

Table 4: Laboratory findings of Symptomatic Infants born to Mothers with SARS-CoV2

Test	N	%
CBC	(N = 15)	
WBC		
<4 x10^9 cells/L	0	0%
Normal	14	93.3%
>30 x10^9 cells/L	1	6.7%
Lymphocytes		
<20%	2	13.3%
Normal	10	66.7%
>40%	3	20%
PLT <100,000 x10^9 cells/L		
Yes	0	0%
No	15	100%
CRP	(N = 9)	
≤6	9	100%
>6	0	0%
Procalcitonin	(N = 9)	
≤0.5	5	55.6%
>0.5	4	44.4%
Blood Culture	(N = 11)	
No growth	11	100%
With growth	0	0%

**WBC-white blood cell; CRP-C-reactive protein*

Table 5: Radiologic findings of Symptomatic Infants born to Mothers with SARS-CoV2

Findings	N=9	%
Pneumonia	5	55.6%
Ileus	3	33.3%
Reticulogranular ground glass appearance w/ air bronchogram	2	22.2%
Pneumothorax	2	22.2%
Normal	2	22.2%

Table 6: SARS-CoV-2 RT-PCR results of Infants born to Mothers with SARS-CoV2

SARS CoV-2 RT-PCT	N=48	%
Result		
Negative	48	100%
Positive	0	0%
Specimen		
NPS	41	85.4%
OPS	5	10.4%
ETA	2	4.2%

Six (12.8%) out of the 47 newborns needed respiratory support (Table 7) upon delivery. One (16.7%) was placed on non-invasive positive pressure ventilation (NIPPV), while the other 5 (83.3%) were intubated and hooked to a mechanical ventilator for an average of 9.4 days (2 to 21 days).

Table 7: Treatment instituted to Infants born to Mothers with SARS-CoV2

Treatment	N=47	%
Respiratory Support		12.8%
Intubated	5	83.3%
Average days intubated	9.4 days (2 to 21 days)	
NIPPV	1	16.7%
None	41	87.2%
Antibiotics		
No	36	76.6%
Yes	11	23.4%
IVIG		
No	47	100%
Yes	0	0%

As shown in table 7, antibiotic therapy was given to 11 patients (23.4%). None were given investigational drugs for management of COVID-19 such as intravenous immunoglobulin. The average length of hospital stay for all infants was 7 days, where 95.8% were discharged with good outcome (Table 8). There was noted one mortality, preterm, 33 weeks, low birthweight, who expired due to severe respiratory distress syndrome and pneumothorax. The said neonate was intubated due to tachypnea associated with progressing respiratory distress, desaturation and hemodynamic instability. Patient was given surfactant therapy and was started on empiric antibiotics. However, patient expired on the 30th hour of life. One morbidity was also noted, full term, 39 weeks, who was discharged on the 2nd day of life. However, on the 3rd day, patient developed jaundice and fever, was readmitted and managed as a case of neonatal pneumonia, started on Ceftazidime and Amikacin with noted clinical improvement. Other than the radiologic finding and elevated C-reactive protein and procalcitonin, the rest of the laboratory work-ups were unremarkable. A repeat NP swab was also done upon readmission, which was still negative for SARS-CoV-2. Patient was eventually sent home after 10 days.

Table 8: Outcome Infants born to Mothers with SARS-CoV2

Outcome	N=47	%
Survived	45	95.8%
Expired	1	2.1%
Morbidity	1	2.1%

Further statistical analyses using the Fisher's exact test was done to check for association between the maternal features and neonatal outcomes, infant's weight, gestational age and APGAR score. It revealed that there were no significant associations observed except for mother having symptoms. The presence or absence of symptoms among mothers was noted to be significantly associated with the presence or absence of symptoms among neonates (p=0.037).

Table 9: Test of Association of Maternal Features to Infant's Signs and Symptoms

Variables	Signs and Symptoms N (%)		*p*-value
MATERNAL	**Asymptomatic**	**Symptomatic**	
Comorbidities	17 (50%)	5 (38.5%)	0.140
No Co-morbidities	17 (50%)	8 (61.5%)	
Pregnancy-related Complications	4 (11.8%)	2 (15.4%)	0.131
No complications	30 (88.2%)	11 (84.6%)	
Mode of delivery			0.749
Cesarean Section	24 (70.6%)	10 (76.9%)	
Spontaneous Vaginal Delivery	10 (29.4%)	3 (23.1%)	
Symptomatic	10 (29.4%)	8 (61.5%)	**0.037**
Asymptomatic	24 (70.6%)	5 (38.5%)	

DISCUSSION

When pregnant women become infected with viral pneumonia, they are more likely to have obstetrical complications and may progress to severe disease.[2,13,14,15,16] The severity of viral pneumonia in pregnancy is evidently related to physiological and immunological changes that result in a shift from cell-mediated to humoral-mediated immunity.[2,11]

Several systematic reviews on pregnant women with SARS-CoV-2 infection have been done, mostly from China, and showed that majority of the infected mothers were noted to be in their third trimester of pregnancy,[17] underwent cesarean section where several authors cited fetal distress as the reason behind the decision[18] and preterm birth, PROM and pre-eclampsia were the identified sequela.[19]

Like in literatures, majority or 71.1% of the mothers in our study delivered via cesarean section. However, it was primarily due to a previously scarred uterus. Only 6 (13.3%) out of the 45 mothers had pregnancy-related complications with intrauterine fetal distress as the most common. Twenty-two mothers (48.9%) had co-morbidities. In contrast to what was observed in the above studies in China, majority of mothers in our study had gestational diabetes mellitus (40.9%), with lower rates of pre-eclampsia (18.2%).

The Philippine Society of Newborn Medicine (PSNBM) reviewed five journals on the clinicodemographic profile of infants born to COVID-19 suspect or confirmed mothers and found that despite being born to a mother with SARS-CoV-2 infection, most neonates were born term, with a birthweight of more than 2500 grams, appropriate for gestational age and an APGAR score of more than 7.[20] Similar to our study, 91.5% of the infants were born full term with normal birthweight (85.1%), appropriate for gestational age (95.7%) and a good APGAR score (95.7%).

One of the difficult questions about COVID-19 in neonates is whether perinatal transmission of SARS-CoV-2 exists. Vertical transmission of many microorganisms from an infected mother to her fetus can lead to devastating results.[21] Transmission usually occurs during intrauterine life through the placenta, or during delivery by ingestion or aspiration of cervicovaginal secretions, and in the postpartum period by breastfeeding. To prove the possibility of an intrauterine viral infection, RT-PCR assay on multiple tissue samples deriving from placenta, amniotic fluid, cord blood, and neonatal nasopharyngeal swab has been recommended.[22] However in this study only NP swab was done due to the limited availability of test kits and constraints on finances.

In February 2020, Wang et al. reported the first case of neonatal SARS-CoV-2 infection admitted at the Tongji Hospital in Wuhan, China where the mother was confirmed with COVID-19. The clinical manifestations of

the mother and the baby were both mild and the baby's prognosis was good. The male infant in the case reported was delivered via emergency cesarean under contact, droplet, and airborne transmission precautions. Early cord clamping was done and patient was transferred to an isolation room in the neonatal nursery shortly after delivery. The newborn's pharyngeal swab was done at 36 hours of life and showed a positive result. However, the nucleic acid detection tests done on the cord blood and placenta in this case turned out to be negative, which do not support the diagnosis of intrauterine transmission.[2] This was followed by a cohort study on 33 neonates born to mothers with COVID-19 from Wuhan Children's Hospital. Three of the 33 infants (9%) presented with early onset SARS-CoV-2 infection. The most common symptom was shortness of breath with findings of pneumonia. Consistent with previous studies, these infants also had a favorable outcome. Strict infection control was implemented during delivery increasing the likelihood that the SARS-CoV-2 in these neonates were maternal in origin.[23]

Another case from Peru was reported on a neonate born to a mother with severe presentation of COVID-19 in pregnancy. A major finding in this case is the positive testing on RT-PCR of the neonatal nasopharyngeal swab as soon as 16 hours after delivery, repeated at 48 hours of life for confirmation which also turned out to be positive. Ventilatory support was required for 12 hours only with favorable outcome and not requiring antibiotic treatment. In utero transmission was strongly suspected due to sterility of the procedure and isolation measures implemented immediately after birth.[24] However for both studies,[23,24] testing of other tissues samples were not done.

In our study, none of the infants had positive result for SARS-CoV-2 PCR. Furthermore, majority were sent home after 24-48 hours and those with symptoms improved after they were managed accordingly.

The timing of sampling and contact with the infected mother may be pivotal to ascertaining when transmission occurs.[25] On the latest guidelines released by the Center for Disease Control and Prevention (CDC) on the Care for Newborns (3 August 2020), neonates born to mothers with suspected or confirmed COVID-19, regardless of mother's symptoms, should have testing performed at approximately 24 hours of age. If initial test results are negative, CDC recommends repeating the test at 48 hours. But for asymptomatic neonates expected to be discharged early, a single test can be performed between 24-48 hours of age.[26] This was similar to what was done to our study population where the swab was performed on day 1 to day 2 of life. However, for those who stayed at the hospital beyond 48 hours, the swab was repeated only on one neonate who had pneumothorax, result still turned out to be negative.

Despite recent reports on a few neonates turning out to be positive for SARS-CoV-2, there have also been studies on newborns of COVID confirmed mothers who had negative PCR results but were symptomatic upon birth. In the clinical analysis report by Zhu et al., nine of ten neonates born to COVID-19 infected mothers were symptomatic (respiratory distress in 6, gastrointestinal symptoms in 4, fever in 2, thrombocytopenia in 2 accompanied by abnormal liver function and 1 baby died of multiple organ failure and DIC).[27] Fan et al reported two neonates with mild lymphocytopenia and radiological findings of pneumonia, although both appeared clinically well and eventually made a full recovery.[28] Similarly, Peng and colleagues also reported on a newborn whose mother was positive for SARS-CoV-2, who presented with tachypnea, moaning, and periodic breath immediately after birth and was hooked to a nasal continuous positive airway pressure.[29] Notably, none of these neonates tested positive for SARS-CoV-2. Evidence of intrauterine transmission was also assessed by testing the amniotic fluid, cord blood, neonatal throat swab and breastmilk samples [28,30] even including vaginal secretions, placenta, venous blood from mother, and anal swab, sputum, venous blood, urine samples from the newborn,[28] which all tested negative for SARS-CoV-2.

Clinical features of COVID-19 in infected newborns, especially preterm infants, might be non-specific and include acute respiratory distress syndrome, temperature instability, gastrointestinal, cardiovascular dysfunction and lethargy.[31,32] Laboratory findings were not distinct and may show a normal or decreased leukocyte count, lymphopenia and mild thrombocytopenia. Radiologic findings were commonly pneumonia and ileus.[20]

In our study, while a greater number of the delivered neonates were asymptomatic (72.3%), 27.7% had symptoms commonly presenting as tachypnea (38.5%), vomiting (38.5%) and apnea (23.1%). None had

leukopenia and thrombocytopenia, only 2 (13.3%) had a lymphocyte count of less than 20%, which subsequently improved in the succeeding complete blood counts. Similar in the literatures mentioned earlier, although non-specific, the most common radiologic findings were pneumonia (55.6%) and ileus (33.3%). Six (12.8%) out of the 47 newborns needed respiratory support upon delivery, majority of which were preterms with respiratory distress syndrome and pulmonary insufficiency. Eleven (23.4%) of the neonates were given antibiotics with good clinical response. Comparably, the neonates in our study also showed a favorable outcome (95.8%).

Further statistical analyses showed that there was a significant association between the presence or absence of symptoms among mothers and neonates (p=0.037). From this, clinicians can anticipate that symptomatic mothers during delivery will most likely have symptomatic infants thus making a clinician more prepared in the management of these newborns.

At present, there have been recent published data showing evidence of possible transplacental transmission.[6,7,8,9] Although these findings may serve as a confirmation of placental infection, definitive evidence of congenital infection has not yet been proven and needs further studies. These suggest that infections in the placenta may not always equate with vertical transmission, although its possibility cannot be fully excluded at this time.[7]

CONCLUSION AND RECOMMENDATIONS

This is the first study in the Philippines to assess the outcomes of infants born to mothers with SARS-CoV-2 infection. Although the results of this study did not support the possibility of an intrauterine vertical transmission, there was a noted significant association between the presence or absence of symptoms among mothers and neonates. The fetal and neonatal outcomes appear very good, with 2.1% morbidity and mortality. These outcomes were achieved with intensive, active management which might be the best practice in absence of more robust data. Standard, droplet, contact and airborne precautions should be maintained with immediate separation of the newborn from the mother upon delivery until further evidence. Given that the clinical data on COVID-19 in pregnant women and their newborns are still very limited, with its ill-defined short and long-term harm to the offspring due to the uncertainty of a possible vertical transmission, it is therefore crucial to screen pregnant women and implement strict infection control measures, and closely monitor neonates with increased risk of COVID-19 infection.

Since this is a retrospective review, this study was dependent on medical records/charts. Hence, we recommend prospective studies with a larger sample size and longer study period. To help assess evidence of vertical transmission, testing for the SARS-CoV-2 virus should be done on multiple sites (placenta, amniotic fluid, cord blood, breastmilk, etc.) which may improve the detection rate and reduce false negative diagnoses. Repeating the swab at 48 hours of life for neonates who required a longer stay at the hospital as recommended by CDC should also be considered.

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