Original Article

COVID-19 Infection in Parturients: Comparative Neonatal and Maternal Outcomes in a Single-Institute Regional Hospital in Thailand

Apichaya Swangjang MD[1], Totsapon Jiamton MD[1]

[1] Department of Obstetrics and Gynecology, Chonburi Hospital, Chonburi, Thailand

Objective: Chonburi province is ranked fourth in Thailand in terms of COVID-19 cases. The objective was to compare neonatal and maternal outcomes among pregnant women with and without COVID-19 infection delivered in Chonburi hospital.

Materials and Methods: The present study was a retrospective matched cohort study that included all pregnant women who delivered between January 1 and August 31, 2021, at Chonburi Hospital, Thailand. The exposure group comprised women with a current or previous positive COVID-19 PCR test, while the comparators were the PCR negative group. The matching ratio was 1:4, based on gestational and maternal age, parity, and the closest delivery date. Clinical data were obtained from medical records.

Results: Forty-six pregnant women had a positive COVID-19 PCR, 24 (52.17%) were Thai and 22 (47.83%) were of other ethnicities. Most (60.87%) were asymptomatic or required no medical assistance. Three (6.52%) had severe pneumonia and required respiratory support. Neither maternal death nor vertical transmission was detected. Compared with 184 COVID-19-negative pregnant women, no significant differences in low APGAR score of less than 7, and preeclampsia in the 46 COVID-19-positive pregnant women were observed. However, COVID-19-positive pregnant women showed an increased rate of neonatal respiratory distress (RD) (relative risk [RR] 2.55; 95% confidence interval [CI] 1.04 to 6.21] and clinical early-onset neonatal sepsis (RR 3.60; 1.55 to 8.36). Additionally, a higher cesarean section rate was observed in the COVID-19 positive group (RR 1.45, 1.11 to 1.85).

Conclusion: There were no significant differences in neonates with APGAR of less than 7 between the cohort of 46 pregnant women who tested positive for COVID-19 and those who tested negative. However, a higher rate of cesarean delivery, presumed early-onset neonatal septicemia, and RD in the COVID-19 positive group were noted and should be monitored.

Keywords: COVID-19; Pregnancy; Neonatal outcome; Birth asphyxia

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Following the emergence of COVID-19 infection in late 2019, Thailand was the first country outside China to publicly report the detection and successful identification of the viral genome[1]. Shortly afterward, the virus became widespread and represented one of the most important issues in the national public health. During the epidemic first wave, the implementation of non-pharmaceutical interventions, such as government regulations to restrict people's movements, was the key factor in the efficient control of the spread of the disease[2,3]. However, due to the shortage of effective vaccination administration, the public health policies, legislative measures, and the emergence of more virulent variants, the epidemic has increased uncontrollably in the early 2021[4,5]. According to the Thai Ministry of Public Health (MoPH), as of August 31, 2021, there have been 1,204,729 COVID-19 cases reported, with 11,495 COVID-19 related deaths[6]. During the third wave of the epidemic, the COVID-19 infection rate in pregnant women also rapidly increased[7]. The first case report of COVID-19 in a pregnant woman in Thailand was published in August 2020[8], but no additional information has been reported since then.

The literature on the effect of COVID-19 infection on pregnant women has been continually updated since the pandemic begun. For example, the

Correspondence to:

Jiamton T.

Department of Obstetrics and Gynecology, Chonburi Hospital, Chonburi, 69 Sukhumvit Road, Bansuan Subdistrict, Mueang Chonburi District, Chonburi 20000, Thailand.

Phone: +66-89-8159565

Email: totsapon@nmu.ac.th

ORCID: 0000-0002-3290-7140

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PregCOV-19 Living Systematic Review Consortium Analysis in the United Kingdom has shown a higher rate in admissions to intensive care units (ICUs) that required invasive ventilation in pregnant women with COVID-19 infection compared with the non-infected patient[9]. In addition, a study from the UK Obstetric Surveillance System (UKOSS) showed a higher mortality rate among pregnant women with COVID-19 infection than women without COVID-19 disease[10].

Neonatal outcomes related to COVID-19 infection remain controversial. Although prior studies have shown a higher rate of intrapartum fetal distress, birth asphyxia, or preterm delivery in COVID-19-positive pregnancies[11-14], recent comparative studies showed no difference in lower APGAR score or worse composite neonatal outcomes between the women with and without COVID-19 infection[15-20]. Studies demonstrated a higher rate of cesarean sections in COVID-19-positive pregnancies due to maternal indications, maternal demands, and hospital policies[16,17,21-23].

Chonburi province is recognized as the economic center of Thailand's eastern seaboard. The area is crowded with industries, commercial companies, and tourist destinations. According to the Thai MoPH, Chonburi province is ranked the fourth in Thailand in terms of COVID-19 cases[6]. Chonburi Hospital is a tertiary, non-profit governmental hospital. As a result, it has seen the number of admissions of pregnant women infected with COVID-19 increase since May 2021. The present study aimed to compare maternal and neonatal outcomes among pregnant women with and without COVID-19 infection seen at Chonburi Hospital during the first eight months of 2021.

Materials and Methods

Data collection

The present study was a single-center, retrospective cohort study conducted at Chonburi regional hospital, Thailand. The Institutional Review Board of the Chonburi Hospital Medical Education Center granted ethics approval under a waiver of informed consent (ref. 6364RH3). All women who delivered between January 1 and August 31, 2021, were included in the study. The authors implemented Universal COVID-19 testing for all patients at the time of hospital admission, regardless of symptoms or exposure history. The reason for a nasopharyngeal (NP) swab for a reverse transcription-polymerase chain reaction (RT-PCR) test was classified as a "pre-admission test" for all women with labor pain or specified as "Contact patient under investigation (PUI)"/"symptomatic"/"active case finding" if no labor pain was present. The exposure group comprised all patients who delivered and were currently or had a previously positive COVID-19 RT-PCR results. For each case, the matching was performed to minimize the difference in baseline maternal characteristics and to avoid the over rate of extremely preterm gestation in the nature of the tertiary referral setting. The present study data were selected from the hospital electronic database, searching for non-exposure cohort matched for the gestational age at birth within one-week, maternal age within five years, the parity status, and the closest delivery date to the case. Patients in the control group must have received negative RT-PCR test results throughout the course of their pregnancy and never experienced any symptoms of COVID-19, never been quarantined, or previously came into direct contact with a PUI. Because the number of limited available cases, the sample size, and the intention to include all COVID-19 cases in the present study period, therefore, a priority power calculation was not performed. Instead, post hoc power calculations were assessed for the birth asphyxia rate and the respiratory distress (RD). According to the previous studies, the matching ratio was varied[12,15,19,24-26]. The authors selected the matching ratio of 1:4, and the sample size had a power of 85.46% in post hoc calculations using the protocol of Exact: Proportion between two groups, two-tailed test, α of 0.05 (G*Power, version 3.1.9.7, 2020; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, German).

Clinical data were collected and reviewed from both patients' electronic medical records and their hospital files. Demographic data included ethnicity, which was self-reported during admission and double-checked against the patient's passport, work permit, and the government healthcare database. In addition, maternal and neonatal outcomes were recorded, including the APGAR scores, birth weight, RD, neonatal infection, complications, and death. The authors did not routinely collect umbilical cord arterial blood gas or fetal scalp blood pH sampling; therefore, the birth asphyxia was solely defined based on the 1-minute and 5-minute APGAR score less than 7 as specified by Thai MoPH[27]. Newborn RD is defined as neonates that exhibited tachypnea with a respiratory rate of more than 60 respirations per minute, grunting, subcostal retractions, nasal flaring, and cyanosis within 24 hours of life[28] with documented RD by a neonatologist. Neonatal sepsis was defined according to the WHO criteria[29] as a

positive hemoculture in the presence of clinical signs and symptoms of infection or the presence of clinical infection and at least two abnormal laboratory results when blood culture was negative. They are also divided into early-onset sepsis (EOS) if symptoms started before 72 hours of life, and late-onset (LOS) if symptoms start afterward and must be documented by pediatricians. According to the authors' institutional policy, all babies born to COVID-19-positive mothers during the study period were considered PUI. These babies were admitted to the sick newborn department until they received two negative COVID-19 test results at birth and after 24 hours of life. The hospital course of COVID-19 disease, complications, ICU admission, and laboratory results in the exposure group prior to or during delivery were also recorded. Imaging was reviewed with a radiologist and an internal medicine physician. According to the previously published criteria[30], the outcome of COVID-19 was categorized as asymptomatic, symptomatic-independent, moderate, severe, or death. The authors also categorized moderate disease into 1) asymptomatic pneumonia, 2) pneumonia with mild symptoms with score of 4 or, 3) pneumonia requiring oxygen support by mask or nasal prongs with a score of 5 to further elucidate the characteristics of the disease in the present study cohort.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous data were described as means (standard deviations) or medians (interquartile range, IQR), depending on the normality of each distribution. Categorical data were described using counts and percentages. Where data were missing such as blood test not done, proportions were presented from known cases. Maternal and neonatal outcomes between the two groups were compared using chi-square test, independent t-test, and Mann-Whitney U test. Risk estimates were expressed as relative risks (RRs) and 95% confidence intervals (CIs). All statistical tests were considered to be significant at a p-value less than 0.05.

Results

Between January 1 and August 31, 2021, 2,918 women delivered at Chonburi Hospital. During the pandemic period, all women (100%) admitted to the labor room or cohort ward received a NP swab sent for an RT-PCR test for SARS-CoV-2. Of the 2,918 women, 46 were diagnosed with COVID-19 infection.

Baseline characteristics between the two groups

Baseline characteristics of pregnant women with COVID-19 are shown in Table 1. The mean age of women who tested positive for COVID-19 was 29.4 years (SD 4.6). All women with COVID-19 infection who delivered were in the third trimester, with a mean gestational age of $38^{1/7}$±2 weeks. Their ethnicity varied and 24 (52.2%) were Thai and 22 (47.8%) were Burmese, Cambodian, or Laotian. In the control group, the proportion of other SEA ethnicities delivered in the present study institute was 15.2%. During the first eight months of 2021, the mean proportion of non-Thai delivery was 16.5%, with a range of 13.0 to 20.1.

The two groups showed no differences in maternal age, parity, gestational age, body mass index (BMI), antenatal care, and associated antenatal comorbidities. The median age was 29.4 years (IQR 25.6 to 32.9) in COVID-19-positive patients, and 28.8 years (IQR 25.5 to 34.7) in COVID-19-negative patients. At delivery, the median gestational age was $38^{3/7}$ weeks (range 33 to $40^{6/7}$) in COVID-19-positive patients and $38^{1/7}$ (IQR $33^{1/7}$ to $41^{6/7}$) in COVID-19-negative patients. Among patients of other South-East Asian ethnicities, there was a higher proportion who tested positive for COVID-19 (22, 47.8%) than of tested negative for COVID-19 (28, 15.2%). This difference was statistically significant ($p<0.001$).

For other comorbidities, a higher rate of chronic hepatitis B virus (HBV) infection was found among patients positive for COVID-19 (3, 6.5%) than among COVID-19-negative patients (1, 0.5%), which was statistically significant different ($p=0.006$). All COVID-19-positive patients with chronic HBV infection were asymptomatic, had normal alanine aminotransferase levels, and did not require medication. Other comorbidities, such as hypertension, diabetes mellitus, and sexually transmitted diseases, were comparable between the two groups. These and other comparisons of baseline characteristics are summarized in Table 1.

Clinical data of pregnant women with COVID-19

Clinical COVID-19 data are shown in Table 2. These women had a history of contact with COVID-19-infected family members (56.5%) or individuals in the workplace (15.2%). Among the infected women, 54.3% had at least one symptom of COVID-19. The four most common symptoms were cough and nasal congestion (37.0%), fever (32.6%), and anosmia (30.4%). Twenty-one women were asymptomatic before admission (45.7%), one-fifth (21.7%)

Table 1. Baseline characteristics between COVID-19 positive and negative pregnant women

	COVID-19 positive pregnant women (n=46)	COVID-19 negative pregnant women (n=184)	p-value
Age at delivery; median (IQR)	29.4 (25.6 to 32.9)	28.8 (25.5 to 34.7)	0.753[a]
Parity; n (%)			
Nulliparous	20 (43.5)	75 (40.8)	0.738[b]
Gestational age at delivery; median (range)	$38^{3/7}$ (33 to $40^{6/7}$)	$38^{1/7}$ ($33^{1/7}$ to $41^{6/7}$)	0.563[a]
BMI; median (range)	23.4 (21.6 to 26.4)	23.7 (21.6 to 26.0)	0.867[a]
>30 kg/m^2; n (%)	1 (2.2)	13 (7.1)	0.215[b]
Ethnicity; n (%)			<0.001[b]*
Thai	24 (52.2)	156 (84.8)	
South-east Asian	22 (47.8)	28 (15.2)	
Associated medical comorbidities; n (%)			
Hypertension	0 (0.0)	2 (1.1)	0.478[b]
Diabetes	2 (4.4)	8 (4.4)	1.000[b]
Hepatitis	3 (6.5)	1 (0.5)	0.006[b]*
Thyroid disease	0 (0.0)	0 (0.0)	
Venereal diseases	0 (0.0)	2 (1.1)	0.478[b]
Antenatal clinic visits; median (range)	9 (5 to 10)	9 (7 to 10)	0.352[a]
Antenatal visit <5 times; n (%)	6 (13.0)	19 (10.3)	0.596[b]
No antenatal care until delivery; n (%)	0 (0.0)	9 (4.9)	0.126[b]
Associated antenatal comorbidities; n (%)			
Gestational diabetes	1 (2.2)	12/175 (6.9)	0.230[b]
Hemoglobin level at 2nd trimester; median (range)	12 (11 to 12)	12 (11 to 12)	0.105[a]
Anemia at 2nd trimester (Hb <10.5 g/dL)	5 (10.9)	26/175 (14.9)	0.488[b]
Smoking habit	1 (2.2)	6 (3.3)	0.701[b]
Vaccination; n (%)			
Seasonal influenza vaccination	43 (93.5)	174 (94.6)	0.775[b]
COVID-19 vaccination	4 (4.4)	17 (9.2)	0.909[b]

IQR=interquartile range; BMI=body mass index; Hb=hemoglobin

[a] Mann-Whitney-U test, [b] Chi-square, * p≤0.05, statistical significance

remained symptomless throughout their hospital stay.

Laboratory tests were also evaluated for any abnormalities in all symptomatic patients but not done in asymptomatic women. Among those who had blood tests, four patients (10.5%) had leukocytosis, six (15.7%) had leukopenia, eight (21.1%) had lymphopenia, and three (7.9%) had thrombocytopenia. In addition, more than half had elevated levels of C-reactive protein (CRP) (60.5%), D-dimer (52.9%), and procalcitonin (57.1%).

Chest radiographs were taken from 43 patients, seven symptomatic patients (28.0%) had normal chest X-ray patterns, and 11 asymptomatic patients (52.4%) had abnormal chest X-ray patterns. Of the 29 patients with abnormal chest X-ray patterns, 27 (93.1%) had peripheral ground-glass or reticulo-nodular patterns, and two (6.9%) had diffuse alveolar distribution. The chest X-ray findings were bilateral and involved the middle to lower lung zone (51.7%), other findings were unilateral, more commonly on the right side (37.9%) than the left side (10.3%). Twenty-nine patients had pneumonia (63.0%). Only one woman (2.2%) had pneumonia with hypoxemia that required correction with high-flow nasal cannula oxygen (HFNC) and was transferred to the ICU for seven days. No death was reported.

Overall, favipiravir, corticosteroids, anti-coagulants, and antibiotics were administered in 45 (97.8%), 28 (60.9%), 13 (28.3%), and eight (17.4%) patients, respectively. There were complications reported in four patients as one had superimposed bacterial pneumonia, one had group B streptococcus septicemia, and one had a urinary tract infection. In addition, one patient suffered a ruptured ovarian cyst during cesarean delivery and had to be reexplored for surgical correction due to bleeding. This case also had other underlying conditions, including overt diabetes mellitus, morbid obesity, and a history of previous cesarean section.

Table 2. Characteristics, symptoms, and outcomes of pregnant women delivered in Chonburi hospital who had laboratory-confirmed SARS-CoV-2 infection

Characteristics	n (%)
Gestational age at diagnosis of COVID-19 (weeks); mean±SD	$37^{4/7}\pm2^{2/7}$
Status of possible sick contact (n=46)	
Family members	26 (56.5)
Workplace	7 (15.2)
Unknown	13 (28.3)
Reason for nasopharyngeal swab (n=46)	
Pre-operation or pre-admission test	33 (71.7)
Symptomatic	7 (15.2)
High-risk contact of PUI	6 (13.0)
Interval from positive RT-PCR to delivery (days) (n=46); median (range)	0 (0 to 31)
RT-PCR positive on delivery date	27 (57.4)
RT-PCR positive >7 days prior to delivery	7 (15.2)
Neonatal COVID-19 RT-PCR (n=47)	0 (0.0)
Signs and symptoms (n=46)	
Asymptomatic	21 (45.7)
Fever	15 (32.6)
Cough	17 (37.0)
Myalgia	10 (21.7)
Dyspnea	5 (10.9)
Nasal congestion	17 (37.0)
Anosmia	14 (30.4)
Headache	5 (10.9)
Loss of appetize	4 (8.7)
Diarrhea	1 (2.2)
Desaturation	3 (6.5)
Laboratory tests	
RT-PCR cycle threshold (CT) value (n=46); mean±SD	
• Target 1 (ORF1)	24.1±7.4
• Target 2 (Egene)	23.8±6.8
Complete blood count (n=38)	
• Leukocyte count (/mm^3); mean±SD	9,901.9±3,761.1
• Lymphocyte count (/mm^3); mean±SD	1,453.4±550.2
• Platelet count (/mm^3); mean±SD	214,285.7±61,335.3
• Leukocytosis	4 (10.5)
• Leukopenia	6 (15.7)
• Lymphopenia	8 (21.1)
• Thrombocytopenia	3 (7.9)

Characteristics	n (%)
Laboratory tests	
C-reactive protein (mg/L) (n=38); median (IQR)	6.3 (3.3 to 24.5)
• Elevated C-reactive protein	23 (60.5)
D-dimer (mg/L FEU); median (IQR)	2.2 (1.4 to 11.9)
• Elevated D-dimer (n=34)	18 (52.9)
Procalcitonin (ng/mL); median (IQR)	0.06 (0.03 to 0.14)
• Elevated procalcitonin (n=28)	16 (57.1)
Chest radiograph (n=43)	
Abnormal chest radiograph	29 (67.4)
Pattern (n=29)	
• Ground-glass opacities	15 (51.7)
• Reticulo-nodular pattern	11 (37.9)
• Consolidation	3 (10.3)
Distribution	
• Peripheral	27 (93.1)
• Diffuse	2 (6.9)
Location	
• Bilateral, mid to lower lung	15 (51.7)
• Unilateral, right, mid to lower lung	11 (37.9)
• Unilateral, left, mid to lower lung	3 (10.3)
Outcome in COVID-19 (n=46)	
Asymptomatic	10 (21.7)
Mild symptoms, independent	7 (15.2)
Pneumonia, asymptomatic	11 (23.9)
Pneumonia with mild symptoms	15 (32.6)
Pneumonia with oxygen mask or nasal prongs	2 (4.3)
Pneumonia with high flow nasal canular	1 (2.2)
Intubation, mechanical ventilation	0 (0.0)
Death	0 (0.0)
Lengths of hospital stay (days); median (IQR)	9 (4 to 14)
ICU admission	1 (2.2)
Need for oxygen support without intubation	3 (6.5)
Treatment with	
Favipiravir	45 (97.8)
Remdesivir	0 (0.0)
Corticosteroid	28 (60.9)
Anticoagulant	13 (28.3)
Antibiotic	8 (17.4)

SD=standard deviation; BMI=body mass index; IQR=interquartile range; PUI=patient under investigation; RT-PCR=reverse transcription polymerase chain reaction; FEU=fibrinogen equivalent unit; ICU=intensive care unit

More than half of COVID-19 patients (30/46 cases, 65.2%) were delivered by cesarean section. Nineteen of 30 cases (63.3%) had solid obstetric indications with nine for prior cesarean delivery, three of each for fetal distress and cephalopelvic disproportion, two for placenta previa with hemorrhage, and one of each for breech presentation and termination of severe preeclampsia. Eleven patients were performed due to concerns related to COVID-19, time, and resource management.

According to the hospital's policy during the study period, all newborns from COVID-19-infected patients were immediately separated from their mother and had no delayed cord clamp. All newborns were admitted to the intermediate ward for observation and NP swabs for RT-PCR were taken from all cases

Table 3. Comparison of neonatal and obstetric outcomes among pregnant women who tested positive and negative for COVID-19

	COVID-19 positive pregnant women	COVID-19 negative pregnant women	p-value	Relative risk (95% CI)
Neonatal outcome; n (%)	(n=47)	(n=188)		
APGAR score at 1 minute; median (IQR)	9 (8, 9)	9 (8, 9)	-	-
Neonates with 1-minute APGAR <7	2 (4.3)	6 (3.2)	0.719	-
APGAR score at 5 minutes; median (IQR)	10 (9, 10)	10 (10, 10)	-	-
Neonates with 5-minute APGAR <7	1 (2.1)	2 (1.1)	0.561	-
Birthweights; mean±SD	3,071.1±520.2	2952.93±513.3	0.160[1]	-
Infant with low birth weight	5 (10.6)	29 (15.4)	0.404	-
Birthweight small of gestational age	0 (0.0)	10 (5.3)	0.106	-
Respiratory distress	7 (14.9)	11 (5.9)	0.037*	2.55 (1.04 to 6.21)
Presence of endotracheal intubation, HFNC, CPAP	7 (14.9)	10 (5.3)	0.023*	2.80 (1.13 to 6.97)
Presence of NICU admission	2 (4.3)	3 (1.6)	0.258	-
Apnea	0 (0.0)	0 (0.0)	-	-
Neonatal jaundice	3 (6.4)	23 (12.2)	0.253	-
Early-onset septicemia	9 (19.2)	10 (5.3)	0.002*	3.60 (1.55 to 8.36)
Late-onset septicemia	1 (2.1)	1 (0.5)	0.287	-
Overall neonatal septicemia	10 (21.3)	11 (5.9)	0.001*	3.64 (1.64 to 8.05)
Neonatal death	0 (0.0)	0 (0.0)	-	-
Obstetric outcome; n (%)	(n=46)	(n=184)		
Preterm delivery	11 (23.9)	53 (28.8)	0.508	-
Prolong PROM	1 (2.2)	4 (2.2)	1.000	-
Meconium-stained amniotic fluid	2 (4.4)	9 (4.9)	0.877	-
Presence of abnormal tracing during labor	3 (6.5)	3 (1.6)	0.63	-
Preeclampsia	3 (6.5)	3 (1.6)	0.63	-
Postpartum hemorrhage	1 (2.2)	3 (1.6)	0.801	-
Route of delivery			0.05*	1.45 (1.11 to 1.88)
• Cesarean delivery	30 (65.2)	83 (45.1)		
• Operative vaginal delivery	1 (2.2)	5 (2.7)		
• Spontaneous vaginal delivery	15 (32.6)	96 (52.2)		
Indication for cesarean delivery			<0.001	-
• Previous cesarean section	9 (19.6)	33 (17.9)		
• Fetal distress	3 (6.5)	3 (1.6)		
• Cephalopelvic disproportion	3 (6.5)	24 (13.0)		
• Placenta previa with hemorrhage	2 (4.3)	7 (3.8)		
• Breech presentation	1 (2.2)	7 (3.8)		
• Severe preeclampsia termination	1 (2.2)	1 (0.5)		
• Due to concerns related to COVID-19	11 (23.9)	0 (0.0)		
• Others	0 (0.0)	8 (4.3)		

IQR=interquartile range; SD=standard deviation; HFNC=high flow nasal cannular; CPAP=continuous positive airway pressure; NICU=neonatal intensive care unit; PROM=prolonged rupture or membrane

[1] t-test; others: chi-square; * p≤0.05, statistical significance

twice, 24 hours apart. All newborns were negative for COVID-19 by RT-PCR, thus, in the present study, no vertical transmission was reported.

Neonatal outcomes

Of the 46 and 184 mothers in each group, some gave birth to twins, hence the number of newborns being 47 and 188 in the COVID-19-positive and the -negative groups, respectively. There were two (4.3%) newborns with an APGAR score of less than 7 at one minute in the COVID-19-positive group compared with six newborns (3.2%) with an APGAR score of less than 7 in the negative group, although this was not a statistically significant different. Similarly, there was no statistically significant difference in scores of less than 7 with the APGAR score at 5-minute.

RD was seen in 7/47 cases (14.9%) in the COVID-19-positive group, which was significantly

higher than the 11/188 cases (5.9%) seen in the negative group (p=0.037). In addition, the rate of EOS in newborns born to COVID-19-positive mothers was 9/47 (19.2%), significantly higher (p=0.002) than the rate in newborns of the negative group at 10/188 (5.3%). Overall, the neonatal septicemia rate was also significantly higher (p=0.001) in newborns of the positive group compared with the negative group.

There were no statistically significant differences in infants born with low birth weight, neonatal jaundice, neonatal ICU admission, and LOS. In addition, no newborn deaths, being small for gestation age, or apnea were found in any newborns of either group (Table 3).

Obstetric outcomes

The rate of cesarean sections in the COVID-19-positive group was 30/46 cases (65.2%), which was higher than the 83/184 cases (45.1%) in the negative group. This difference was significant (p=0.05). However, there were no statistically significant differences between the two groups in preterm delivery, prolonged preterm premature rupture of the membranes (PPROM), meconium-stained amniotic fluid, presence of abnormal tracing, preeclampsia, and postpartum hemorrhage (Table 3).

After estimating the RRs and 95% CIs in the neonatal and the obstetric outcomes, statistically significant differences remained in overall neonatal septicemia, EOS, the presence of neonatal airway support, RD, and the cesarean delivery rates, with the RR of 3.64, 3.60, 2.80, 2.55 and 1.45, respectively.

Discussion

From the baseline characteristics, the authors noticed a higher proportion of the other South-East Asian ethnicities in the COVID-19 positive compared with the negative group. Public health data from Chonburi province also showed that industrial workers and people living in a cluster of immigrant workers were at higher risk of COVID-19 infection than the rest of the population in this area[7]. Comparative studies in 2021 also observed the ethnic disparity between exposure and the control group[11,16-18,21,22,31]. However, there is evidence that no racial inequality was associated with obstetric outcomes during the pandemic, especially preterm birth[32]. Therefore, the authors suggest gathering and monitoring national data about ethnic disparities in adverse birth outcomes as the COVID-19 pandemic continues in Thailand. There was also a higher chronic, inactive HBV infection rate in the COVID-19-positive group. Nevertheless, in a retrospective cohort study of the outcome of COVID-19 infection in patients with HBV infection, HBV infection had no significant effect on COVID-19 results[33].

The present study primary outcome, the neonatal APGAR score at one minute, showed no difference between the two groups, supporting the findings of the previous cohort studies[13-20]. This result may reflect the present study asymptomatic and mild COVID-19 case, unlike the studies with a high proportion of symptomatic pneumonia or maternal comorbidities, resulting in a higher fetal distress rate or birth asphyxia[11,12]. The present study also showed a higher proportion (65.2%) of cesarean sections in pregnancies with COVID-19 infection than those without. Global data showed the rate of COVID-19-related cesarean indication and overall pregnancy indication at 49.8% (95% CI 31.8 to 67.8) and 66.7% (43.3 to 86.8)[23]. The majority of the present study cesarean sections were performed in response to obstetric indications (41.3%). However, in a minority of cases (23.9%), cesarean sections were performed due to concerns related to COVID-19. This was due to a lack of understanding about COVID-19 during the early stages of the pandemic, problems around maternal status or fetal infection, and time and resource management. Lately, comparative studies reveal no increase in cesarean birth between the two groups[11,18,25,31,34]. Hence, the authors were concerned about the high cesarean section rates and the recent attempt to decrease the rates of surgical interventions.

Unlike the previous cohort studies[13,14], the present study showed a higher rate of RD in neonates born to COVID-19-positive mothers. One study with a high incidence of hypertensive disorder in pregnancy reported a significantly higher neonatal intubation rate in the COVID-19 group but an insignificant RD rate[18]. In detail, four out of the present study seven infants had respiratory distress syndrome (RDS), and three out of seven patients were transient tachypnea of the newborn (TTN). All cases with RD were delivered by cesarean section. The authors are concerned that the increased rate of cesarean section in COVID-19 patients might increase the risk of RD among newborns in this group[35]. There was also a statistically significant higher rate of diagnosis of EOS and overall neonatal sepsis in COVID-19-positive patients compared with the COVID-19-negative patients. After reviewing the course of those newborns with diagnosed EOS, it was found that most cases had leukocytosis, leukopenia, high immature neutrophils, or increased inflammatory markers, but negative

hemoculture. The majority of infants were presumed EOS based on clinical symptoms, hemodynamic variables, laboratory factors, and concerns about maternal fever. The authors found one study from the U.S. that reported a non-significant difference in the rate of neonatal sepsis[31]. Therefore, this inconsistent finding needs review and monitoring.

The present study showed no differences between the two groups in obstetric complications, such as preeclampsia and preterm delivery, which differed from the reports from other cohort studies[13,14]. Studies have introduced the concept of a "preeclampsia-like syndrome", a specific vascular pathology induced by COVID-19 similar to the changes seen in preeclampsia[26,36,37]. A recent largest prospective multinational comparative "INTERCOVID" study reveals a strong independent association between preeclampsia and COVID-19, especially among nulliparous women. The risk was highest when COVID-19 was diagnosed in the last seven days of pregnancy[24]. It results in preterm birth, severe perinatal morbidity and mortality, and adverse maternal outcomes. However, the present study did not reach a significant higher preeclampsia rate between the COVID-19 positive and negative groups at 6.52% versus 1.63% (p=0.63), despite higher nulliparous proportion compared to the reference study[24] at 43.5% versus 28.7%, and most of the cohort delivered within seven days after positive RT-PCR, compared to the reference study at 84.8% versus 64.7%. This concordance may reflect the present study lower maternal cardiovascular comorbidity compared to the reference study[24] at 0% versus 30.5%, lower mean BMI at 24.2±3.5 versus 28.5±8.5, and the different ethnicity where SEA ethnicity contributed 2.6% to the total study population in the reference study. A former systematic review that had a 1.9% pooled population from Asia, also suggested that COVID-19 during pregnancy was associated with higher odds of preeclampsia[38]. Therefore, the authors recommend collecting more data to confirm this association in SEA ethnicity. Additionally, findings from a recent study suggested there may be the maternal-fetal transmission of COVID-19[39]. Still, the authors found no vertical transmission in the present study by two negative neonatal NP RT-PCR test results 24 hours apart.

A strength of the present study is by using a matched cohort between the two groups to minimize confounding factors. In addition, the outcomes were presented in three aspects, characteristics of COVID-19 infections, comparative pregnancy outcomes, and neonatal outcomes. A limitation of the present study includes the limited number of severe cases of COVID-19. There is also little practical use of antibody tests in Thailand, so the present study may have missed prior asymptomatic infections in individuals despite the pre-admission universal RT-PCR test.

Conclusion

There was no statistical difference in birth asphyxia rates between the cohort of mothers with and without COVID-19 infection delivered in Chonburi regional hospital. However, a higher rate of cesarean delivery, neonatal septicemia, and RD were noted in mothers with COVID-19 than in those without COVID-19, which should be monitored in this group.

What is already known on this topic?

Neonatal and pregnancy outcomes related to COVID-19 remain controversial. Recent comparative studies showed no difference in lower APGAR scores or worse composite neonatal outcomes between women with and without COVID-19, but higher preeclampsia and cesarean birth rate.

What this study adds?

This study represents the cohort of COVID-19 in pregnancy in a regional part of Thailand during the first eight months of 2021. The finding reveals a similar rate of birth asphyxia, based on APGAR score, and preeclampsia between mothers with and without COVID-19. However, a higher rate of cesarean delivery, clinical early-onset neonatal septicemia, and RD were noted in mothers with COVID-19.

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Conflicts of interest

The authors declare that they have no competing interests.

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