

# Incidence and Associated Factors of COVID-19 Infection among Newborns: A Cross-Sectional Study in Thailand

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## Abstract

**Background and Rationale:** COVID-19 is the pandemic that has significantly impacted disease control measures, daily life, and healthcare services. Pregnant women and newborns are vulnerable populations at increased risk of severe illness and adverse outcomes. This study aimed to identify the incidence and associated factors of newborn COVID-19 infection. Understanding these would benefit in developing effective strategies to mitigate the risks associated with COVID-19 infection during pregnancy and infancy.

**Methodology:** This cross-sectional quantitative study utilized data from a country-wide reporting system of pregnant and postpartum women infected with COVID-19 and their newborns in Thailand. The study included 6,048 newborns born to infected mothers from December 2020 to May 2022. The outcome was the incidence of newborns infected with COVID-19. The exposure factors were mothers'

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Received 27 July 2023; Revised 17 October 2023; Accepted 12 December 2023

**Suggested citation:** Tangwiwat P, Tuangrattananon T, Limchumroon W, Ingthom B, Topothai C, Topothai T. Incidence and associated factors of COVID-19 infection among newborns: a cross-sectional study in Thailand. *Journal of Health Systems Research* 2023;17(4):748-64.

พิมลพรรณ ต่างวิวัฒน์, ฐิติกรณ ตวงรัตนานนท์, วรณชนก ลิ้มจรรย์, เบญจวรรณ อังทม, ชมพูนุท โตโพธิ์ไทย, ฐิติกร โตโพธิ์ไทย. อุบัติการณ์และปัจจัยเสี่ยงของการติดเชื้อโควิด-19 ในกลุ่มทารกแรกเกิด: การศึกษาแบบภาคตัดขวางในประเทศไทย. *วารสารวิจัยระบบสาธารณสุข* 2566;17(4):748-64.

characteristics including age, nationality, vaccination status, gestational age at infection detection and at delivery, the severity of COVID-19 infection, delivery mode, and newborns' characteristics including birth weight, mother-newborn separation after birth, and infant feeding. Multivariable logistic regression was used to examine associations between characteristics and newborn COVID-19 infection.

**Results:** The proportion of newborns infected with COVID-19 was relatively low (6.4%). Maternal age was associated with infection risk, with newborns of mothers aged 20-34 years (adjusted odds ratio: AOR = 0.60, 95%CI: 0.43-0.81) and  $\geq 35$  years (AOR = 0.64, 95%CI: 0.44-0.93) having a lower likelihood of infection compared to the youngest age group. Newborns of mothers known of infection during postpartum had a higher likelihood of infection (AOR = 3.75, 95% CI: 2.16-6.51). The severity of COVID-19 infection in mothers was inversely associated with newborn infection risk (AOR = 0.67, 95% CI: 0.47-0.96). Term newborns had a lower likelihood of being infected with COVID-19 (AOR = 0.49, 95% CI: 0.29-0.84) compared to preterm newborns. Complete separation of mother and newborn after birth was associated with the lowest likelihood of infection (AOR = 0.18, 95% CI: 0.11-0.30). Newborns who were fed breast milk substitutes, or a combination of substitutes and maternal milk had a higher likelihood of infection (AOR = 4.16, 95% CI: 2.32-7.45) compared to those directly breastfed or fed with expressed breastmilk.

**Conclusion:** This study contributes to the understanding of newborn COVID-19 infection and its risk factors in Thailand. The relatively low proportion of infected newborns and the identified factors provide guidance for preventive measures and optimizing care during the pandemic. Continued research is needed to further explore these factors and address knowledge gaps for effective prevention and management strategies.

**Keywords:** COVID-19, newborn, incidence, mother to child transmission, Thailand

## อุบัติการณ์และปัจจัยเสี่ยงของการติดเชื้อโควิด-19 ในกลุ่มทารกแรกเกิด: การศึกษาแบบภาคตัดขวางในประเทศไทย

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### บทคัดย่อ

**ที่มาและความสำคัญ:** การแพร่ระบาดของโรคโควิด-19 ส่งผลกระทบอย่างมากต่อมาตรการควบคุมโรค การใช้ชีวิตประจำวัน และการจัดการบริการด้านสุขภาพ หญิงตั้งครรภ์และทารกเป็นประชากรกลุ่มเสี่ยงต่อการเจ็บป่วยที่รุนแรงจากการติดเชื้อ การศึกษานี้ มีวัตถุประสงค์เพื่อหาอุบัติการณ์การติดเชื้อโควิด-19 ในกลุ่มทารกแรกเกิด รวมถึงปัจจัยที่ส่งผลต่อการติดเชื้อในทารกแรกเกิด ซึ่งน่าจะเป็นประโยชน์ในการพัฒนากลยุทธ์ที่มีประสิทธิภาพในการป้องกันการติดเชื้อโควิด-19 จากมารดาสู่ทารก

**วิธีการศึกษา:** การศึกษานี้ เป็นการศึกษาแบบภาคตัดขวาง โดยใช้ข้อมูลจากระบบรายงานทั่วประเทศของหญิงตั้งครรภ์และหญิงหลังคลอดที่ติดเชื้อโควิด-19 และทารกในประเทศไทย ข้อมูลที่ใช้ในการศึกษาประกอบด้วย ทารกจำนวน 6,048 คนที่เกิดจากการติดเชื้อโควิด-19 ตั้งแต่ ธันวาคม พ.ศ. 2563 ถึงพฤษภาคม พ.ศ. 2565 ตัวแปรตามคืออุบัติการณ์ของการติดเชื้อโควิด-19 ของทารกแรกเกิด ตัวแปรต้น ได้แก่ อายุมารดา สัญชาติมารดา สถานะการฉีดวัคซีนของมารดา อายุครรภ์ที่ตรวจพบการติดเชื้อ อายุครรภ์ขณะคลอด ความรุนแรงของโควิด-19 ในมารดา วิธีการคลอด น้ำหนักแรกเกิดของทารก การแยกมารดาและทารก และการให้อาหารทารก วิเคราะห์ความสัมพันธ์ระหว่างตัวแปรต้นและตัวแปรตาม ด้วยวิธีวิเคราะห์การถดถอยโลจิสติกแบบพหุ (multivariable logistic regression)

**ผลการศึกษา:** พบอุบัติการณ์ของทารกแรกเกิดที่ติดเชื้อโควิด-19 ค่อนข้างต่ำ (ร้อยละ 6.4) ทารกที่เกิดจากการตั้งครรภ์ที่มีอายุระหว่าง 20-34 ปี (adjusted odds ratio: AOR = 0.60, 95%CI: 0.43-0.81) และอายุ  $\geq 35$  ปี (AOR = 0.64, 95%CI: 0.44-0.93) มีโอกาสติดเชื้อโควิด-19 ต่ำกว่ามารดาที่มีอายุน้อยกว่า ทารกที่มารดาได้รับการตรวจพบเชื้อในช่วงหลังคลอด มีโอกาสติดเชื้อสูงกว่า (AOR = 3.75, 95% CI: 2.16-6.51) เมื่อเทียบกับมารดาที่ได้รับการตรวจพบเชื้อในช่วงก่อนคลอด ทารกที่มารดามีความรุนแรงของการติดเชื้อมาก มีโอกาสติดเชื้อต่ำกว่า (AOR = 0.67, 95% CI: 0.47-0.96) เมื่อเทียบกับมารดาที่มีความรุนแรงของการติดเชื้อน้อย ทารกที่คลอดครบกำหนดมีโอกาสติดเชื้อต่ำกว่า (AOR = 0.49, 95% CI: 0.29-0.84) เมื่อเทียบกับทารกที่คลอดก่อนกำหนด ส่วนทารกที่ถูกแยกจากมารดาในช่วงหลังคลอด มีโอกาสติดเชื้อต่ำกว่า (AOR = 0.22, 95% CI: 0.09-0.51) เมื่อเทียบกับทารกที่ไม่ถูกแยกจากมารดาในช่วงหลังคลอด ส่วนทารกที่กินนมผงอย่างเดียว หรือกินผสมนมผงและนมแม่ มีโอกาสติดเชื้อสูงกว่า (AOR = 4.16, 95% CI: 2.32-7.45) เมื่อเทียบทารกที่ได้ดื่มนมแม่จากเต้า หรือได้รับการป้อนนมแม่ที่ปั๊บบจากเต้า

**สรุปผลการศึกษา:** การศึกษานี้ช่วยสร้างความเข้าใจเกี่ยวกับการติดเชื้อโควิด-19 ในกลุ่มประชากรทารกแรกเกิดในประเทศไทยและปัจจัยเสี่ยงที่เกี่ยวข้อง โดยผลการศึกษาพบอุบัติการณ์ของการติดเชื้อในระดับต่ำ การเข้าใจปัจจัยที่มีความสัมพันธ์ต่อการติดเชื้อโควิด-19 นี้จะมีประโยชน์ในการพัฒนาแนวทางการป้องกันและการดูแลมารดาและทารกระหว่างการระบาดของโควิด-19 ทั้งนี้ ควรมีการศึกษาเพิ่มเติมในประเด็นปัจจัยอื่นๆ ที่อาจเกี่ยวข้อง รวมถึงมาตรการป้องกันการติดเชื้อโควิด-19 จากมารดาสู่ทารกต่อไป

**คำสำคัญ:** โควิด-19, ทารก, อุบัติการณ์, การติดเชื้อจากมารดาสู่ทารก, ประเทศไทย

## Background and Rationale

COVID-19, caused by the SARS-CoV-2 virus, is a highly infectious disease affecting humans and animals, primarily targeting the respiratory and digestive systems.<sup>(1)</sup> The virus spreads through respiratory droplets and contact with contaminated surfaces.<sup>(1)</sup> Pregnant women and newborns were one of the most vulnerable populations with heightened susceptibility to severe illness and mortality from COVID-19.<sup>(2)</sup> While pregnancy can compromise the mother's immune system, leading to changes in lymphocyte count and in-

creased inflammation-related cytokines, COVID-19 may additionally affect multiple organ systems of women during pregnancy, including the respiratory and cardiovascular systems, blood coagulation, immune response, and placental function.<sup>(3,4)</sup>

Although maternal deaths have been relatively rare,<sup>(4)</sup> COVID-19 infection causes several symptoms in pregnant women. Common symptoms include fever, cough, fatigue, diarrhea, shortness of breath, sore throat, and muscle pain.<sup>(2)</sup> Advanced maternal age has been associated with an increased risk of severe illness in pregnant

women with COVID-19.<sup>(4,5)</sup> Vaccination during pregnancy has been shown to provide protection against severe COVID-19 illness in pregnant individuals and existing evidence also supports the safety and efficacy of COVID-19 vaccines in pregnant women.<sup>(6)</sup>

In newborns, COVID-19 infection can present with a range of symptoms. Common symptoms include fever, respiratory distress, cough, nasal congestion, and gastrointestinal symptoms such as diarrhea and vomiting.<sup>(7)</sup> Since neonatal symptoms can sometimes be nonspecific and may overlap with other neonatal conditions, it is challenging to solely rely on a clinical presentation for diagnosing COVID-19 in this population. Timely and accurate laboratory testing, such as reverse transcription-polymerase chain reaction (RT-PCR), is crucial for the diagnosis of COVID-19 in newborns.

Literature showed that COVID-19 infection is linked to several maternal and fetal complications, such as miscarriage, stillbirth, preterm birth, and intrauterine growth restriction.<sup>(3,4,8,9)</sup> A significant proportion of infants born to COVID-19-positive mothers have required treatment in the Neonatal Intensive Care Unit.<sup>(3,4)</sup> Vertical transmission of COVID-19 from mothers to neonates is documented, especially in the third trimester, but rare from available limited data.<sup>(8,10)</sup> Evidence suggested that mothers with severe symptoms, including pneumonia and respiratory distress, have been associated with a higher likelihood of mother-newborn transmission,<sup>(4)</sup> the late third-trimester

infection has been associated with an increased risk of vertical transmission and the gestational age at COVID-19 infection and delivery mode may influence the risk of mother-newborn transmission.<sup>(8)</sup>

However, the mode of delivery, whether vaginal or caesarean delivery and breastfeeding have been topics of investigation and concerns regarding the risk of mother-newborn transmission.<sup>(9)</sup> Although existing evidence suggests that the risk of viral transmission through breastfeeding is low,<sup>(9)</sup> precautions such as mask-wearing, hand hygiene, and avoiding coughing or sneezing near the infant have been recommended and applied.<sup>(2)</sup>

In Thailand, the COVID-19 outbreak has significant impact on the whole country, in terms of, disease control measures, daily lifestyle change, and access to healthcare services, with a considerable number of 4,752,422 confirmed cases and 34,371 deaths from COVID-19 as of July 17, 2023.<sup>(11,12)</sup> Pregnant women and infants in Thailand were endangered by the risk of infection, the control measures, and barriers to utilizing maternity services during the pandemic.<sup>(13)</sup> To the best of our knowledge, no study reported on the COVID-19 situation in neonates in Thailand.

Therefore, this study aimed to investigate the incidence of mother-newborn COVID-19 transmission in Thailand and its association with maternal and newborn characteristics. Understanding these is essential for developing effective strategies to mitigate the risks associated with COVID-19 infection during pregnancy and infancy in Thailand.

## Methodology

### Sample, tool, and procedure

This study utilized data from the country-wide reporting system of pregnant women and postpartum women within 6 weeks infected with COVID-19 and their newborns from all public and private hospitals from December 1, 2020, to May 31, 2022.

The report form of pregnant and postpartum women's 6-week COVID-19 infection consists of six sections. Section 1: Personal information, including (1) province, (2) hospital, (3) age, and (4) nationality. Section 2: Infection data, including (1) gestational age or postpartum week at diagnosis, and (2) severity of symptoms. Section 3: Vaccination history, including (1) vaccination status and (2) number of vaccine doses received. Section 4: Pregnancy outcomes, including (1) delivery information, (2) delivery mode, and (3) gestational age at delivery. Section 5: Newborn information, including (1) birth status, (2) birth weight, (3) Apgar score, (4) neonatal infection status, and (5) severity of neonatal symptoms. Section 6: Breastfeeding status, including (1) separation of mother and infant and (2) infant feeding. Section 7: Maternal mortality causes and identified risk factors. The researchers developed the pregnant women and postpartum women 6-week COVID-19 infection report form and conducted meetings with the maternal and childcare team for COVID-19-infected women to collect data in the form. The reporting channel was developed using Google Forms and

tested in a general hospital in Samut Sakhon province. It was then refined by national experts before being used for data collection.

The researchers prepared a letter of collaboration and distributed it to hospitals under the Ministry of Public Health, including the Bangkok Metropolitan Administration's Medical Service Department, Armed Forces hospitals, Police hospitals, University Hospital Network (UHosnet), and Private Hospital Associations, for data reporting. The researchers explained the data reporting process to the hospitals through remote meeting systems. The researchers obtained permission to use data from the Pregnant Women and Postpartum Women 6-Week Infection Report System, which is managed by the Health Promotion Bureau of the Department of Health. The researchers collected data from pregnant women and postpartum women's 6-week COVID-19 infection report system, focusing on the variables defined and covered by the research objectives. For this study, we included data from newborns born to mothers who were infected with COVID-19 within 14 days and received treatment in hospitals with complete information on postpartum care and newborn characteristics.

### Measures

#### Participants' characteristics

Participants' characteristics in the study include their mothers' age (in years), maternal nationality, maternal COVID-19 vaccination, maternal COVID-19 severity, maternal gestational age

when COVID-19 infection was detected, delivery mode, gestational age at delivery, birth weight, mother-newborn separation after birth, and infant feeding.

For maternal and newborn characteristics, age was classified into three categories (less than 20, 20–34, and over 35 years old, according to the definition of teenage and elderly pregnancy, nationality was categorized into two categories (Thai and non-Thai), maternal COVID-19 vaccination was divided into two categories (no vaccination, and at least one dose), maternal gestational age when COVID-19 infection detected was divided into three groups (less than 37, from 37 weeks, according to the definition of preterm/term labor, and postpartum), maternal COVID-19 severity was classified into two categories (no or mild symptom, and moderate to severe (pneumonia with/without endotracheal intubation)), gestational age at delivery was classified into two categories (preterm: less than 37, and term: from 37 weeks), delivery mode was categorized into two categories (vaginal delivery and caesarean delivery), birth weight was classified into two categories (less than 2,500 grams and at least 2,500 grams) according to the definition of low/normal birth weight, respectively. For postpartum care, mother-newborn separation after birth was classified into three types (no separation, partial separation (same room with a 2-meter distance, or different rooms but staying together sometimes), and complete separation), infant feeding was categorized into two categories (breastfeeding (directly from breast or by expressing)

and breastmilk substitute or a combination (of breastmilk substitute and maternal breastmilk)).

### **Newborn COVID-19 infection**

Newborn COVID-19 infection refers to the detection of COVID-19 infection using the RT-PCR (real-time polymerase chain reaction) method. The newborn COVID-19 infection was reported as yes (RT-PCR positive) and no (RT-PCR negative).

### **Data management and statistical analysis**

A descriptive analysis was conducted to assess the frequency and percentages of newborn COVID-19 infection. The association between participants' characteristics and their COVID-19 infection were examined using the chi-square test and Fisher's exact test, and the statistical significance was reported as a *p*-value. Multivariable logistic regression was used to examine relationships between participants' characteristics and their COVID-19 infection. The association was reported as adjusted odds ratio (AOR), 95% confidence interval (95% CI), and *p*-value.

Analyses were conducted in Stata Statistical Software version 17 (StataCorp LP, College Station, TX, USA).

### **Ethics approval and consent**

The Department of Health, Ministry of Public Health, Thailand did not seek ethical clearance from the start of the project, as the Department of Health has authority in conducting the country-wide reporting system of pregnant women and



postpartum women within 6 weeks infected with COVID-19 and their newborns from all public and private hospitals. Another reason for not applying for ethical clearance during that period was the emergent nature of the situation of COVID-19, necessitating swift data collection for timely decision-making in the care of pregnant women and newborns, such as breastfeeding practices, postpartum separation of mother and child, and the consideration of COVID-19 vaccination for pregnant women. During this time, data collection proceeded without formal ethical clearance. At a later stage in the project, an application for ethical approval was submitted to the Institutional Review Board of the Department of Health, Ministry of Public Health, Thailand, and research ethics approval (No. 564/2565) was granted in October 2022. The Health Promotion Bureau of the Department of Health authorized the research team with access to the survey data for research purposes in this study.

## Results

### Study participants

The study initially enrolled a total of 14,109 mothers who were infected with COVID-19 across the country. Of these, 7,026 (50% of total) were excluded as 6,935 mothers had not delivered and 91 got aborted. Of 7,083 newborns delivered (3,436 by vaginal delivery, 3,548 by caesarean delivery, and 99 by either vaginal delivery or caesarean delivery but the mothers were dead),

219 were excluded due to missing information on postpartum care, specifically pertaining to mother-newborn separation and infant feeding. Moreover, 842 participants were excluded due to missing data on newborn and maternal characteristics, particularly birth weight, gestational age at delivery, maternal vaccination, and maternal age. Consequently, the final sample size for analysis comprised 6,022 newborns, as depicted in Figure 1. Of these, 329 COVID-19 infected newborns (5.5%) were identified as infection in utero.

### Participant characteristics

The characteristics of all participants are presented in Table 1. Most newborns had mothers aged between 20 and 34 years (72.3%), and their mothers were Thai (70.8%). Most of them had mothers who did not receive the COVID-19 vaccine (76.6%). The gestational age at the time of COVID-19 infection of their mothers was at least 37 weeks (78.4%). A substantial portion of newborns had mothers who exhibited either no symptoms or mild symptoms of COVID-19 (86.4%). Based on the gestational age of delivery, most of the newborns were term (86.8%). The proportion of vaginal delivery and caesarean delivery was approximately equal. Furthermore, most newborns had a birth weight of at least 2,500 grams (87.1%). Regarding postpartum care, most newborns were completely separated from their mothers (90.6%). Most of them were also fed with a breastmilk substitute or a combination of breastmilk substitute and maternal breastmilk (91.4%).

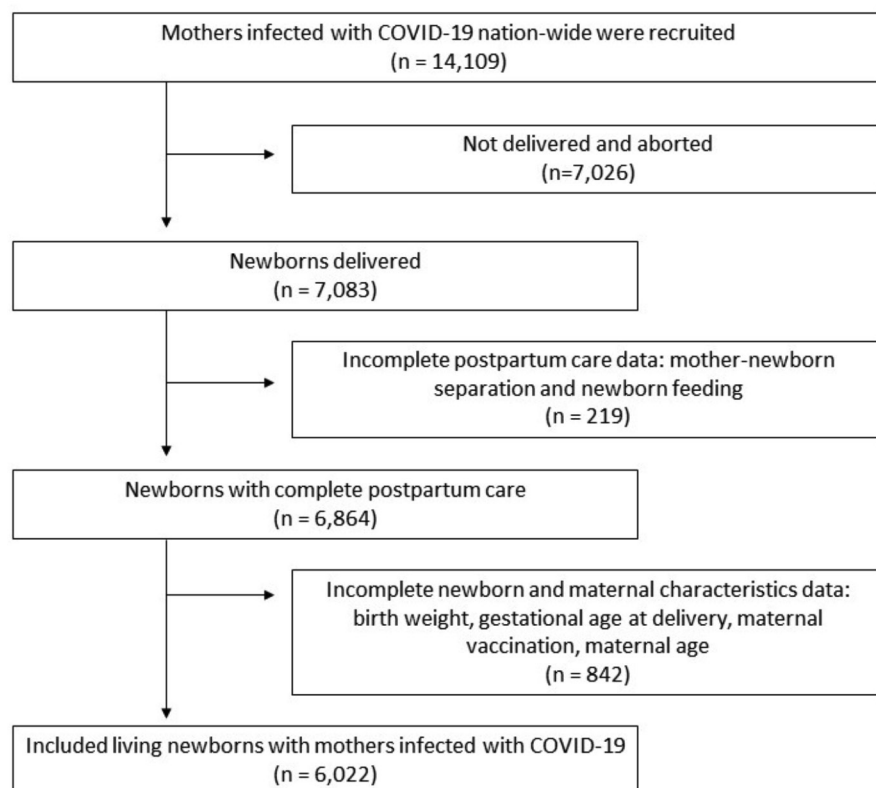


Figure 1 Study participant flow chart

Table 1 Characteristics of the overall sample and according to the newborn COVID-19 infection

Participants' characteristics	Overall		Non-COVID-19 infected newborn		COVID-19 infected newborn		p-value <sup>a</sup>
	n	% (column)	n	% (row)	n	% (row)	
Overall sample	6,022	100.0	5,637	93.6	385	6.4	
Maternal age (year)							0.006
< 20	570	9.5	516	90.5	54	9.5	
20-34	4,355	72.3	4,094	94.0	261	6.0	
≥ 35	1,097	18.2	1,027	93.6	70	6.4	
Maternal nationality							0.60
Thai	4,262	70.8	3,994	93.7	268	6.3	
Non-Thai	1,760	29.2	1,643	93.3	117	6.7	
Maternal COVID-19 vaccination (≥ 1 dose)							0.39
No	4,612	76.6	4,324	93.8	288	6.2	
Yes	1,410	23.4	1,313	93.1	97	6.9	



**Table 1** Characteristics of the overall sample and according to the newborn COVID-19 infection (cont.)

Participants' characteristics	Overall		Non-COVID-19 infected newborn		COVID-19 infected newborn		p-value <sup>a</sup>
	n	% (column)	n	% (row)	n	% (row)	
Maternal gestational age when COVID-19 infection detected (week)							< 0.001
< 37	1,105	18.3	1,035	93.7	70	6.3	
≥ 37	4,719	78.4	4,438	94.0	281	6.0	
Postpartum	198	3.3	164	82.8	34	17.2	
Maternal COVID-19 severity							0.02
No or mild symptoms	5,200	86.4	4,852	93.3	348	6.7	
Moderate to severe symptoms (pneumonia with/without endotracheal intubation)	822	13.6	785	95.5	37	4.5	
Gestational age of delivery (week)							0.15
Preterm	780	13.2	721	92.4	59	7.6	
Term	5,242	86.8	4,916	93.8	326	6.2	
Delivery mode							0.59
Vaginal delivery	3,001	49.8	2,804	93.4	197	6.6	
Caesarean delivery	3,021	50.2	2,833	93.8	188	6.2	
Birth weight (gram)							0.78
< 2,500	779	12.9	731	93.8	48	6.2	
≥ 2,500	5,243	87.1	4,906	93.6	337	6.4	
Mother-newborn separation							< 0.001
No separation	453	7.5	403	89.0	50	11.0	
Partial separation	114	1.9	106	93.0	8	7.0	
Complete separation	5,455	90.6	5,128	94.0	327	6.0	
Infant feeding							0.69
Breastfeeding (direct/expressed)	518	8.6	487	94.0	31	6.0	
Breastmilk substitute or a combination (of breastmilk substitute and maternal breastmilk)	5,504	91.4	5,150	93.6	354	6.4	

<sup>a</sup> Bivariate association between categorical variables and infant COVID-19 infection were examined via chi-square analyses (maternal gestational age when COVID-19 infection was detected using Fisher's exact test)

### The proportion of COVID-19 infection among newborns

Most newborns in the study were negative for COVID-19 (93.6%). Newborns with mothers in the youngest group had the significantly highest proportion of COVID-19 infection (9.5%) among all maternal age groups (see Table 1). Newborns whose mothers were infected with COVID-19 during the postpartum period had the significantly highest proportion of COVID-19 infection (17.2%). Newborns whose mothers had no or mild COVID-19 symptoms had a significantly higher proportion of COVID-19 infection (6.7%). Newborns who were completely separated from their mothers had the significantly lowest proportion of COVID-19 infection (6.0%) compared to other separation types, followed by newborns in the partial separation group (7.0%).

### Association between COVID-19 infection in newborns and their characteristics: multivariable logistic regression

Table 2 presents the results from the multivariable logistic regression examining the association between COVID-19 infection in newborns and their characteristics. Compared to newborns with mothers in the youngest age group, those with mothers aged 20–34 years had the significantly lowest likelihood of being infected with COVID-19 (AOR = 0.60, 95%CI: 0.43–0.81), followed by those with mothers aged  $\geq 35$  years (AOR = 0.63, 95%CI:

0.43–0.92).

Regarding the timing of maternal infection, newborns with mothers infected with COVID-19 during the postpartum period had a significantly higher likelihood of being infected with COVID-19 (AOR = 3.75, 95% CI: 2.16–6.51), in comparison to those with mothers who were infected during gestational age less than 37 weeks. Furthermore, in comparison to newborns with mothers who had no or mild symptoms of COVID-19, those with mothers who experienced moderate to severe symptoms were significantly less likely to be infected with COVID-19 (AOR = 0.67, 95% CI: 0.47–0.96). Moreover, term newborns had a lower likelihood of being infected with COVID-19 (AOR = 0.49, 95% CI: 0.29–0.84) compared to preterm newborns.

In addition, considering the separation after birth between mother and newborn, newborns in the complete separation group had the significantly lowest likelihood of COVID-19 infection (AOR = 0.18, 95% CI: 0.11–0.30) compared to those in the non-separation group, followed by newborns in the partial separation group (AOR = 0.21, 95% CI: 0.09–0.51). For newborn feeding, those who were fed by breast milk substitute or a combination of breastmilk substitute and maternal breastmilk had a significantly higher likelihood of COVID-19 infection (AOR = 4.16, 95% CI: 2.32–7.45) compared to those breastfed either directly from the breast or indirectly through milk expressing.

**Table 2** Multivariable logistic regression analyses of the association between the newborn COVID-19 infection and participants' characteristics (shown only  $p$ -value < 0.05)

Characteristics	Newborn COVID-19 infection			
	AOR	95% CI		$p$ -value
		Lower	Upper	
<b>Maternal age (year)</b>				
• 20-34	0.60	0.43	0.81	0.001
• $\geq 35$	0.63	0.43	0.92	0.02
• reference = < 20				
<b>Maternal gestational age when COVID-19 infection detected (week)</b>				
• $\geq 37$	1.46	0.91	2.35	0.12
• Postpartum	3.75	2.16	6.51	<0.001
• reference $\leq 37$				
<b>Maternal COVID-19 severity</b>				
• Moderate to severe symptoms (pneumonia with/without endotracheal intubation)	0.67	0.47	0.96	0.03
• reference = no or mild symptoms				
<b>Gestational age of delivery (week)</b>				
• Term	0.49	0.29	0.84	0.009
• reference = preterm				
<b>Mother-newborn separation</b>				
• Partial separation	0.21	0.09	0.51	<0.001
• Complete separation	0.18	0.11	0.30	<0.001
• reference = no separation				
<b>Infant feeding</b>				
• Breastmilk substitute or mixed	4.16	2.32	7.45	<0.001
• reference = breastfeeding (direct/expressed)				

AOR = adjusted odds ratio, 95% CI = 95% confidence interval, multivariable logistic regression model adjusted for maternal nationality, maternal COVID-19 vaccination, delivery mode, birth weight, and the correlates above.

## Discussion

This is the first study in Thailand that provides novel insights into the epidemiology of, and factor associated with COVID-19 infection among newborns born to infected mothers in Thailand. The study found a relatively low proportion (6.4%)

of COVID-19 positive among newborns born to infected mothers in Thailand. The likelihood of infection was lower for newborns whose mothers were at normal age for 20-34 years and more than 35 years, compared to those with mothers who were younger. Newborns with mothers

experiencing moderate to severe symptoms had a lower likelihood of infection than those with mild or no symptoms. Newborns whose mothers were infected during the postpartum period had a higher proportion of COVID-19 infection compared to those infected during pregnancy. Complete separation of newborns from their mothers was associated with the lowest likelihood of COVID-19 infection.

The low proportion of newborns infected with COVID-19 in our study aligns with results from previous research and appeared to support the argument that vertical transmission of COVID-19 from mother to newborn is low.<sup>(8)</sup> Although this finding could reassure pregnant women regarding the low risk of COVID-19 transmission from mothers to newborns, it is still important to apply preventive measures of viral transmission at any stage of pregnancy, delivery, or postpartum to minimize the risk of transmission.<sup>(2)</sup>

The association between maternal age and COVID-19 infection in newborns is an intriguing finding from this study. Younger mothers had a higher rate of transmission, a plausible explanation could be from lower health literacy levels, differences in health behaviors, and varieties of social and economic circumstances.<sup>(14)</sup> Older mothers, assumably to be mature mothers, may hold higher levels of health awareness, adherence to preventive measures, and health management. Younger mothers might encounter difficulties associated with social and economic factors, thereby increasing their vulnerability to viral exposure.<sup>(15)</sup> Further research exploring the interplay of socio-

demographic factors, health behaviors, and health literacy is needed to understand the underlying mechanisms driving the association between maternal age and COVID-19 infection in newborns. Additionally, investigating the influence of social and economic factors on the risk of viral exposure among younger mothers can yield valuable insights and provide suggested target interventions and support strategies.

The timing of maternal infection was identified as a critical factor influencing COVID-19 infection among newborns. Newborns whose mothers were infected during the postpartum period had a higher likelihood of infection compared to those with mothers who were infected during pregnancy. This may be attributed to droplet contamination, as a common mode of horizontal transmission.<sup>(9)</sup> This finding emphasizes the need for robust infectious control measures and comprehensive postpartum care to mitigate the risk of COVID-19 transmission to newborns.<sup>(2)</sup> However, the possibility of vertical transmission could not be excluded by this result, as the survey solely recorded the date of confirmed infection, we could not know whether mothers got infected before delivery if their RT-PCR tests show positive results after birth. Thus, the possibility of both horizontal transmission through droplet contamination and potential vertical transmission highlights the importance of vigilance and adherence to preventive measures to protect the vulnerable newborn population during this critical period.

The impact of maternal COVID-19 symptoms on newborn infection yielded a surprising result.

Newborns born to mothers experiencing moderate to severe symptoms had a notably reduced likelihood of infection compared to those born to mothers with either no or mild symptoms. This unexpected finding may be attributed to the stringent infection control measures implemented in specialized healthcare settings, such as intensive care units or isolation wards, where these mothers may receive treatment and could not make much contact with the newborns.<sup>(2,10)</sup> The implementation of strict protocols in these settings may reduce the risk of viral transmission within the healthcare environment.

The term newborns had a lower likelihood of being infected with COVID-19 may be influenced by several factors. Term newborns may benefit from passive immunity through the transfer of maternal antibodies. These antibodies, which the mother produces after exposure to the virus or vaccination, can provide some level of protection to the newborn in the early weeks of life.<sup>(6)</sup> Moreover, term newborns typically spend less time in healthcare settings than premature infants who may require longer hospital stays. Since healthcare facilities have been identified as potential sources of COVID-19 transmission, less time spent in such settings may result in reduced exposure to the virus. Additionally, term newborns generally have more developed respiratory systems and have fewer underlying health conditions compared to preterm infants. This may contribute to a lower risk of severe respiratory complications if they contract COVID-19, as their lungs are better equipped to handle respiratory challenges.

The separation between mother and newborn after birth emerged as a noteworthy factor associated with COVID-19 infection. Newborns who were completely separated from their mothers had the lowest likelihood of infection, followed by those in the partial separation group. While this finding emphasizes the importance of decreased contact and potential exposure between infected mothers and their newborns, it is essential to acknowledge the potential negative consequences of separation on bonding and breastfeeding.<sup>(16,17)</sup> Complete separation can disrupt the critical early bonding period between mother and baby and impede the establishment of successful breastfeeding practices, which offer numerous benefits for both maternal and infant health.<sup>(7)</sup> Therefore, the implementation strategies such as partial isolation, which combines appropriate infection control measures with limited contact and support for breastfeeding, could be a valuable consideration in optimizing outcomes for both mother and baby.<sup>(18)</sup>

The study further examined infant feeding practices concerning COVID-19 infection. Newborns who received breast milk substitutes exclusively or a combination of breast milk substitutes and maternal breast milk had a significantly higher likelihood of COVID-19 infection in comparison to those who were directly breastfed or fed with expressed breast milk through pumping. This finding could be explained by the benefits of breastfeeding as breastmilk transfers specific antibodies against COVID-19 and offers optimal nutrition for newborns.<sup>(7,19)</sup> This finding underscores

that breastfeeding should be promoted and supported during the COVID-19 pandemic. Applying direct breastfeeding or breastmilk pumping could be considered based on maternal and baby conditions while adherence to appropriate infectious control measures should be established.

In terms of the healthcare system for delivery, the Department of Medical Services, Ministry of Public Health, in collaboration with expert professors from various medical faculties, has developed guidelines for the diagnosis, management, and prevention of hospital-acquired COVID-19 infections for medical personnel in Thailand.<sup>(20)</sup> These guidelines have been continuously adapted to suit the evolving situation. The current management approach for pregnant women with COVID-19 has been revised based on the supportive data from this study. It is recommended that their care be similar to non-pregnant individuals, except for cases with risk factors for severe illness such as age  $\geq 35$ , obesity (body mass index  $\geq 30$ ), hypertension, pregestational diabetes, and pre-eclampsia, which should be considered for hospitalization. There are limitations to the administration of antiviral drugs due to safety concerns for the fetus. For cases with pneumonia, Remdesivir is recommended throughout every trimester of pregnancy, while Favipiravir can be administered in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters if deemed more beneficial than the risks, with decision-making involving the patient and their relatives due to its potential teratogenic effects. Regarding the mode of delivery, it should be considered based on obstetric indications.

Afterbirth, the infant should stay with the mother, with a minimum distance of 2 meters maintained, and breastfeeding allowed, with the mother always wearing a mask, washing hands, and cleaning the breasts before and after every contact with the infant.

For COVID-19 vaccination in Thailand, it is recommended that pregnant women after 12 weeks and breastfeeding women receive vaccines similar to the general population, using the available vaccines during that time with a preference for messenger ribonucleic acid (mRNA) vaccines.<sup>(21)</sup> Currently, the COVID-19 pandemic is not severe, and the majority of the population has developed immunity to COVID-19 through vaccination and previous infections. Therefore, the Department of Disease Control recommends annual vaccinations, especially for at-risk groups, including pregnant women after 12 weeks of gestation. The vaccination is administered once a year, with a gap from the last injection or history of infection of at least 3 months. All types and batches of vaccines certified by the Thai Food and Drug Administration can be used.

This research possesses several strengths that enhance its scientific value. Foremost, this pioneering aspect fills a crucial gap in the current literature and offers unique insights into the COVID-19 infection and its risk factors among newborns in Thailand. Second, the study boasts a large sample size of newborns born to mothers infected with COVID-19 collected systematically from various provinces throughout the country.

This extensive coverage enhances the generalizability of the findings to the wider population of pregnant women and newborns in Thailand. Third, the study collected comprehensive information on various factors related to COVID-19 infection, encompassing maternal age, vaccination status, symptom severity, timing of infection, postpartum care, and newborn feeding practices. Additionally, the utilization of multivariable logistic regression analysis, which adjusted for potential confounding variables, strengthens the validity of the results by controlling for potential confounders and providing adjusted estimates of the associations.

However, several limitations should be acknowledged. Firstly, the study relied on self-reported data, which may be subject to reporting biases and missing information. Secondly, the exclusion of 50% of the enrolled mothers introduced a potential selection bias, primarily due to incomplete information on the prevalence of newborn infection among unborn newborns. It is worth noting that further research, including the entire population of newborns, would be valuable for a more thorough investigation. Thirdly, the study focused on specific characteristics and factors; other potentially relevant variables were not included in the analysis. Future research could explore additional factors that may contribute to COVID-19 infection and transmission among mothers and newborns. Finally, this study utilized a cross-sectional design, which restricts the ability to establish causal relationships between

the identified factors and COVID-19 infection in newborns. Longitudinal studies would be valuable for further investigating causal associations and understanding the temporal dynamics of COVID-19 transmission among this population.

## Conclusion

This study sheds light on the characteristics and factors associated with COVID-19 infection among newborns born to infected mothers. The findings indicated a relatively low proportion of COVID-19 positive among newborns. Maternal age, timing of COVID-19 infection, gestational age at delivery, maternal and newborn separation after birth, and infant feeding practices emerged as important factors influencing the likelihood of infection. These results provide valuable insights for guiding preventive measures and optimizing the care of pregnant women and newborns for the COVID-19 pandemic. Further research is necessary to explore these factors more comprehensively and address knowledge gaps, ultimately enhancing our understanding of mother-newborns COVID-19 vertical transmission and supporting evidence-based strategies for effective prevention and management.

## Abbreviations

ACE-2: angiotensin-converting enzyme 2, RT-PCR: reverse transcription polymerase chain reaction, AOR: adjusted odds ratio; CI: confidence interval



## Acknowledgement

The authors would like to express their gratitude to all health care facilities throughout Thailand for providing the valuable database and to all participants and staff involved in the study. We would like to thank Dr. Suwannachai Wattana-yingcharoenchai, Director-General, Department of Health, for his support on this study. We also would like to thank Associate Professor Chanane Wana-pirak from the Department of Obstetrics and Gynecology, Chiang Mai University, for his support and advice throughout the study course. We reserve special thanks to Dr. Viroj Tangcharoensathien, Dr. Rapeepong Suphanchaimat, and Ms. Jintana Jankhotkaew from the International Health Policy Program (IHPP) for their unrelenting academic and statistical support and advice for the study.

## Authors' contributions

Conceptualization, PT, TT1, WL, BI; formal analysis, PT, BI, CT, TT2; resources, PT, TT1, WL, BI; writing—original draft preparation, PT, TT1, WL, BI, CT, TT2; writing—review and editing, PT, TT1, WL, BI, CT, TT2; visualization, PT, BI, TT2; project administration, PT, TT1, WL, BI; funding acquisition, PT, TT1, WL, BI. All authors have read and agreed to the published version of the manuscript.

## Funding

This research was funded by the Department of Health.

## Consent for publication

N.A.

## Competing interests

The authors declare no conflict of interest.

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