Prevalence of Covid-19 Among Mothers and Infant and Their Factors of Infection Transmission: A Cross-Sectional Study

ABSTRACT

Aims: This study aims to determine the prevalence of newborns infected with COVID-19 and the factors associated with the transmission of COVID-19 infection in newborns. **Study design**: Research method, cross-sectional design, retrospective. The sample consisted of 145 infants, the inclusion criteria were 0-28 days, and the mother was infected with COVID-19.
Place and Duration of Study: The research location is one of the hospitals in DKI Jakarta Selatan. Implementation from March to May 2022.
Methodology: The instrument of observation used the medical records of mothers and babies. Chi-Square and Mann-Whitney data analysis.
Results: The results showed the characteristics of pregnant women infected with COVID-19: the average age of 29.87 years, gestational age of 37 weeks, and gestational age at delivery of 37 weeks. The prevalence of COVID-19 infection in infants born to mothers exposed to COVID-19 at the age of 0 days was 99.3%. 101 (69.7%) delivery by cesarean section, 44 (30.3%) spontaneous delivery. Transmission of COVID-19 to neonates based on transplacental factors was seen from the maternal D dimer value (p-value < 0.05). The relationship between confounding factors that affect the transmission of COVID-19 infection in neonates from pregnant women aged 26-35 years is the gestational age of the mother when infected. Likewise, the confounding factor of gestational age, namely maturity, has an effect on COVID-19 infection in neonates seen from gestational age at delivery.
Conclusion: The prevalence of infants infected with COVID-19 occurs at the age of 0 days, infection transmission is estimated from birth.

Keywords: COVID-19, pregnancy, transmission factors, newborn.

1. INTRODUCTION

There were 536 pregnant women exposed to COVID-19 in Indonesia in 2020 including 51.9% without symptoms (PWS), 72% with gestational age above 37 weeks, 3% died, and 4.5% were admitted to the ICU.[1] Exposure to COVID-19 infection in pregnant women can be transmitted to neonates. A study from China stated that of the 18 newborns treated, five were diagnosed with COVID-19 (two confirmed and three positive).[2] Other information stated that in a hospital in Surakarta in Indonesia, there were 62 babies born to mothers who were exposed to COVID-19 infection, and 20 (32%) babies were infected.[3] Examination through the SARS-CoV-2 PCR test revealed three newborns were positive for COVID-19.[4] The condition of babies born infected with COVID-19 has an APGAR score (AS) which varies, including AS (8-9) as much as 47 (75.8%), AS (9-10) as many as 15 (24.2%). In addition to the US, four infants had low birth weight, and one of them had the hypospadias.[3]

The potential risk of transmission of COVID-19 infection to newborns may be in three patterns, namely, through the transplacental, birth canal, and postpartum breastfeeding.[4] Transmission through the placenta can be through blood biochemical values and gestational age at infection. Previous studies suggested that the transmission of SARS-CoV-2 in neonates was caused by immunohistochemistry and very high viral loads, resulting in maternal viremia and placental

infection. Indications of transmission through the placenta are blood biochemical values, and RT PCR on placental tissue positive for SARS-CoV-2.[5] Indications for placental transmission are blood biochemical values, RT PCR on placental tissue positive for SARS-CoV-2.[5] Elevated CRP, NLR, and leukocytosis can help diagnose COVID-19.[6] Vertical transmission of COVID-19 by gestational age has been reported in the third trimester of the pregnancy. [7] The delay in fetal growth in utero by 10%, and in the last trimester, fetal tachycardia and fetal distress occurs.[8] Transcervical transmission factor describes the occurrence of transmission from feces during spontaneous delivery because SARS-CoV-2 has found in feces.[9] Transmission via environmental factors by thought to be via respiratory saliva splashing on mucous membranes.[10] A study of breast milk samples taken from 43 mothers who were positive for COVID-19 based on the PCR found breast milk samples positive for the virus in three mothers. Babies of three mothers whose breast milk tested positive for the COVID-19 virus, one child tested positive for COVID-19.[11]

Other information states that the transmission of COVID-19 to newborns may be through saliva splashes during the delivery process. This condition can occur through the mother or caregiver who was infected with SARS-CoV-2.[5] However, the vertical transmission of SARS-CoV-2 has not been evident until now.[5] Data regarding the transmission of COVID-19 infection from mother to fetus during pregnancy is still was limited.[4]

Based on the description of the information, it has known that there is a possibility of transmission of COVID-19 virus infection to newborns. Based on the description of the information, it is known that there is a possibility of transmission of COVID-19 virus infection to newborns. So it is necessary to explore the prevalence of newborns infected with SARS-CoV-2 and the transmission route of infection from mother to baby. All this information became the basis for research to explore the number of newborns infected with COVID-19 from mother to baby and the factors of transmission of COVID-19 infection from pregnant women to babies. The study of COVID-19 infection in newborns was carried out based on data on exposure to infection in pregnant women and exposure to infection after the baby was born. So this study aims to determine the prevalence of newborns infected with COVID-19 and the factors associated with the transmission of COVID-19 infection in newborns in Indonesia.

2. MATERIAL AND METHODS)

2.1 Design

A Cross-sectional research design with a retrospective approach was performed among 145 of infants with positive of COVID-19. The study population of newborns from mothers infected with COVID-19 based on PCR swab results in 2020-2021.

2.2 Population and Sample

Based on the population with a significance level of 5% using the Slovin formula, a sample of 145 people was obtained. The sample is selected based on the inclusion criteria, namely babies born to mothers infected with COVID-19, and infants aged 0-28 days. The exclusion criteria were babies born with defects. The sampling technique used was the purposive sampling technique. The research site is a hospital in DKI Jakarta, Indonesia.

2.3 Instrument

The research instrument was an observation sheet from Medical record. We were collected the data of maternal and the newborn data. Maternal data were included the mothers of demographics (age, gestational age at exposure to COVID-19 and delivery), blood biochemical values (leukocytes, D-dimer, C-Reactive Protein (CRP), neutrophil lymphocyte ratio (NLR), PCR value (CT Value, viral load), early contact (breastfeeding and formula feeding) and type of the delivery. Meanwhile, newborn data includes newborn demographics (PCR).

2.4 Data collection

Research data were obtained from medical records. Medical records of respondents were collected by hospital staff at the study site through a screening stage according to the inclusion criteria. Data collection techniques were carried out by observing the contents of medical records using research instruments. The data collected is from 2020-2021. Data collection was carried out from March to May 2022.

2.5 Ethical consideration

This study was approved by Ethical Clearance Committee of Indonesia with No. 010/KEPK/II/2022 on February 7, 2022).

2.6 Data analyses

Data analysis using SPSS 20 for windows with statistical tests for categorical data using frequency and percentage and numerical data using mean, median, and *SD*. Analysis of the relationship for category data using the Chi-Square test and for numerical data that is not normal using the Mann-Whitney test.

3. RESULTS AND DISCUSSION

3.1. Results

Table 1. Characteristics of pregnant women infected with COVID-19 (n=145)

Variable	Mean	Median	*SD*	Min	Max
Mother's Age					
Old Teen (17-25 Years)	29.87	30	5.78	17	42
Young Adults (26-35 Years)					
Old Adult (36-45 Years)					
Gestational Age					
First Trimester (0-13 Weeks)					
Second Trimester (14-27 Weeks)	37.45	38.00	2.11	28	41
Third Trimester (28-41 Weeks)					
Gestational age at delivery					
Premature (< 37 Weeks)	37.52	38.00	2.1	28	41
Mature (37-41weeks)					

Table describes the characteristics of pregnant women when infected with COVID-19, aged 29 years and an average gestational age of 37 weeks. At delivery, the average gestational age is 37 weeks.

Table 2. Prevalence of newborns infected with COVID-19 by time of infection (n=145)

Exposure time	n	%
< 0 day	144	99.3
> 0 day	1	.7
TOTAL	145	100

Table describes babies born to pregnant women infected with COVID-19, as many as 99.3% have been infected since birth

Table 3. Characteristics of transmission of COVID-19 infection in newborns based on Labour, Environmental factor dan Time factors:. (n=145)

Transmission Factor	n	%
Labour Factors		
Childbirth category		
Spontaneous	44	30.3
Sectio Cesaria	101	69.7
Environmental Factor		
Early contact category		
Pumped breast milk	19	13.1
Formula milk	126	86.9
Time Factor		
Category Infected time		
<0 days	144	99.3
>0 days	1	.7

The table describes the characteristics of transmission of COVID-19 infection in newborns, namely 69.7% in cesarean section deliveries, infants infected from birth at the age of fewer than 0 days 86.9%, and receiving formula milk

Results should be clearly described in a concise manner. Results for different parameters should be described under subheadings or in separate paragraph. Table or figure numbers should be mentioned in parentheses for better understanding.

Table 4. Relationship of transmission of COVID-19 infection in newborns based on transplacental factors: leukocytes, D-dimer, CRP, and NLR. (n=145)

Transmission Factor	Mean	Median	SD	Min	Max	*P-Value*
Transplacental factor						
Leukocyte Category	12.48	11.10	6.30	3.8	41.1	.211
Low (< 5.0 thousand/uL)						

Normal (5.0-10 thousand/uL) High (>10.0 thousand/uL) Category D-dimer						
Normal (<500ng/mL) Abnormal (>500 ng/mL)	3006.9	1838.0	3006.8	0	20000	.027
CRP Category Normal (<1,0mg/dL) Abnormal (>1.0mg /dL)	3.505	1.950	5.42	0.10	41.09	.837
NLR Category Normal (<6) Abnormal (>6)	7.65	5.50	7.46	1.30	52.30	.361

The transmission factor for COVID-19 infection in newborns is based on transplacental factors, namely the leukocyte, D-dimer, CRP, and NLR values are dominated by abnormal values. The value of D dimer has a significant (*p-value* < .027) relationship with newborn infection since in the womb.

Table 5. Relationship of confounding factors (mother's age and gestational age at delivery) to transmission of transplacental infection (blood biochemistry and gestational age at infection with COVID-19) in newborns.

Counfonding Factors Age (17-25 Years)	n	Median (Min-Max)	Rerata±SD	P-*value*
Leukocyte	33	13600 (5.9-33.9)	13.36±5.6	.355
D-dimer	33	3404 (668-12200)	3404,3±3035	.141
NLR	33	5.5 (1.30-52.3)	8.74±10.63	.58
CRP	33	2.6 (.20-41.09)	4.4±7.4	.48
Gestational age at infection COVID-19	33	38 (28-40)	37.36±2.5	.78
Counfonding Factor Age (26-35 Years)	n			
Leukocyte	89	10800(3.8-41.1)	12.08±6,6	.367
D-dimer	89	1730(0-14305)	2526±2342	.334
NLR	89	5.2(1.5-39.8)	6.9±5.8	.69
CRP	89	1.8 (.1-41.09)	3.38±5.0	.40
Gestational age at infection COVID-19	89	38(31-41)	37.4±2.1	**.04**
Counfonding Factor Age (36-45 Years)	n			
Leukocyte	23	9700 (3.9-24.2)	12.758±6.11	.67
D-dimer	23	2160 (531-20000)	4297±4573	.10
NLR	23	5.6 (2-29)	8.7±7.6	.3
CRP	23	1.72(.16-10.9)	2.6±2.7	.4
Gestational age at infection COVID-19	23	37 (34-40)	37.5±1.4	.9
*Counfonding Factor:*premature labor	n			
Leukocyte	55	12000 (3.8-41.1)	13.80±6.8	.08
D-dimer	55	2050 (531-9510)	30343±2440	.151
NLR	55	5.5 (1.70-39.80)	8.4±8.13	.11
CRP	55	19000 (.19-41)	4.75±7.96	.80
Gestational age at infection COVID-19	55	36 (28-40)	35.47±2.03	.18
Counfonding Factor: mature labor	n			
Leukocyte	90	10850 (3.8-41.1)	11.6±5.8	.367
D-dimer	90	1834(0-20000)	2990±3318	.334
NLR	90	5.4(1.3-52.3)	7.1±7.0	.69
CRP	90	2.02 (.10-19.12)	2.7±2.73	.40
Gestational age at infection COVID-19	90	39(36-41)	38.6± .90	**.04**

Table describes the transplacental factor namely, D-dimer is a significant relationship (p-value <.05) to newborns infected with COVID-19. This relationship had influenced by confounding factors, namely maternal age (26-35 years). Gestational age at the time of infection with COVID-19 had a significant relationship (p-value < .05) with newborns infected with COVID-19. This relationship had influenced by gestational age at delivery, namely term pregnancy

3.2 Discussion

In this study, it was found that of all pregnant women infected with COVID-19, almost all babies born were infected with COVID-19 and had been infected since the baby was born. The factor associated with the incidence of COVID-19 infection in newborns is the transplacental factor, namely the value of D dimer. Confounding factors related to the transmission of infection were maternal age (26-35 years) and gestational age at delivery.

Based on the characteristics of mothers in the current study, the highest percentage of pregnant women infected with COVID-19 is young adults (26-35 years). Based on previous research, it had also found that the average age of pregnant women infected with COVID-19 was the age of young adults. Likewise, the degree of aging affects the severity of illness and mortality of COVID-19 patients. Likewise, the degree of aging affects the severity of illness and mortality of COVID-19 patients.[12] The age with the highest level of difficulty occurs in the elderly, namely the age of 60 years and, over.[13] However, in this study, the age of pregnant women had not founded to be a very risky age according to the theory. Pregnant women are a population at risk not based on age but based on pregnant. [14]. The stated because pregnant women are in a state of immunosuppression, and physiological adaptive changes during pregnancy. [14].

The average gestational age of mothers with COVID-19 at delivery is the third trimester (28-41nweeks). This age includes vulnerability to complications. As stated by previous researchers, pregnant women infected with COVID-19 have a 1.33 times higher risk of giving birth prematurely than pregnant women who are not infected. The mean gestational age in this study was 37.5.[15] It is also reported that vertical transmission of COVID-19 from mother to fetus occurs in the third trimester of pregnancy.[7,16] The vertical transmission of COVID-19 infection from mother to baby based on the current study is transplacental factors, namely blood biochemical values (leukocytes, D-dimer, NLR, CRP), gestational age factor when infected with COVID-19, environmental factors, and childbirth factors. The result of transplacental factor analysis showed that the D-dimer of mothers infected with COVID-19 had a significant relationship with newborns infected with COVID-19. Where the infection has occurred in the uterus. The current finding of infants infected with COVID-19 less than zero days after delivery had based on PCR values. Likewise, acute progressive coagulopathy problematic with COVID-19 in term pregnant women showed a significant increase in D-dimer (12-17 times the value).[17] Pregnant women have a conventional value of 0.5 mg/L D-dimer as gestational age increases, D-dimer increases. This elevated D-dimer level is most likely due to continuous coagulation and fibrinolysis during placental the development. [18] So, the occurrence of transmission through the placenta can be caused by D-dimer. Other information states that the transplacental transmission of SARS-CoV-2 in newborns is caused by immunohistochemistry and very high viral loads, resulting in viremia in the mother and infecting the placenta. The results of a histological and immunohistochemical examination of the placenta showed inflammation. However, this study did not carry out an examination of the COVID-19 virus on the placenta and also a histological examination of the placenta.

Other transplacental factors such as leukocyte values, NLR, CRP, and gestational age when the mother was infected with COVID-19 were not associated with newborns infected with COVID-19 but had abnormal values. According to Koumoutsea et al.(2020), the average pregnant woman infected with COVID-19 has abnormal blood biochemical values such as leukocytes, D-dimer, CRP, and NLR. Laboratory parameters of elevated CRP, NLR, and leukocytosis can help predict the severity of COVID-19[6]. The results of a retrospective study stated that the SARS-CoV-2 virus was not found in newborns of mothers with confirmed COVID-19 after conducting blood, breast milk, amniotic fluid, and swab examinations.[19]

Based on the analysis of labor factors (section and spontaneous), there is no relationship between labor factors and newborns. The results of the research most types of delivery were Caesarean sections. This is supported by previous information that mothers give birth spontaneously, have a greater risk of infection and complications, and can endanger the condition of the mother and baby. The results of previous studies stated that babies born spontaneously tested positive for COVID-19 based on the results of a nasopharyngeal swab.[9] The results of the fecal and rectal swabs were declared infected with COVID-19, this condition can trigger the occurrence of COVID-19 infection in babies born spontaneously from zero days. However, in the current study, no cervical or fecal examination was carried out for the COVID-19 virus, so transcervical factors in newborns could not be identified

Based on analysis of environmental factors: presenting nutrition and time infected with COVID-19 to newborns. The results showed that was no relationship between environmental factors, namely the provision of nutrition to infants and the time of infection with COVID-19 in newborns. Another study also stated that there is no evidence that the COVID-19 virus can be transmitted through breast milk. In the current study, nutrition for newborns born to mothers infected with COVID-

19 is provided through expressed breast milk and formula. This condition can be a transmission factor through the environment. where there was an interaction between the baby and the mother who has been infected with COVID-19 or the helper who is the transmission of COVID-19 infection in newborns. However, this study did not examine the COVID-19 virus in breast milk. Babies who were fed formula milk are large enough to be infected with COVID-19, where the effect of transmitting the infection is not studied further. other studies have confirmed that the possibility of transmission through breast milk has not been established at this time.[20] There was no relationship between environmental factors and newborns infected with COVID-19 because since the baby had been born they have been treated in a separate room from the mother, and health workers have implemented the COVID-19 protocol properly so that transmission through the environment is minimal.[20]

The result of the analysis of the relationship of transmission factors (transplacental, transcervical/delivery, and the environment) to newborns was influenced by confounding factors: maternal age and gestational age at delivery. The results showed that the transplacental factor, namely gestational age when infected with COVID-19, was associated with newborns infected with COVID-19, influenced by maternal age (26-35 years). Age was very influential on the degree of illness and death of COVID-19 patients. For mothers infected with COVID-19 aged 18-29, mortality was four times higher for those aged 30-39, and 330 times higher for those aged 85 and over. The older you get, the more susceptible you are to eing infected with COVID-19. Maternal gestational age has a high risk for the welfare of the newborn.

Likewise, the effect of gestational age at delivery on the incidence of infection transmission in newborn. Mature delivery was found to influence the relationship between gestational age at the time of infection with COVID-19 and newborns infected with COVID-19. This illustrates that mothers, who were infected with COVID-19 at an early gestational age, have a long period for babies to be exposed to COVID-19 infection from their mothers if the baby is born until delivery is mature. Vertical transmission of COVID-19 from mother to fetus occurs in the third trimester of pregnancy. In addition, pregnant women with COVID-19 have a higher susceptibility to infection in the fetus. Elevated leukocyte levels in pregnant women with COVID-19 must be watched out for. [7]

4. CONCLUSION

Based on the results of the current study, it was found that babies born to mothers infected with COVID-19 were almost entirely infected. The characteristics of mothers exposed to COVID-19 infection are mostly young adults, all of them are in the third trimester, and most of them are at mature gestational age. Transplacental factor: Maternal D-dimer exposed to COVID-19 infection is associated with COVID-19-infected newborns. The relationship between labor/transcervical factors has not been identified in newborns infected with COVID-19. The factor of labor/transcervical from mother to newborn is spontaneous labor. The relationship between environmental factors, namely providing nutrition to newborns infected with COVID-19 has not been identified. Suggestions need further research to see the transmission factors that have not been identified that cause COVID-19 infection in newborns.

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AUTHORS' CONTRIBUTIONS

SM and AS both developed draft proposals and study designs, collecting data. SM revised the results and compiled the manuscript. All authors contributed to the manuscript and approved the version of the manuscript that was submitted.

CONSENT

This study takes data from hospital medical records, namely files containing notes and documents about patient identity, examination, treatment, actions, and other services that have been provided to patients. The data required for the study was approved by the hospital. A copy of the approval for data collection from the hospital's medical record was obtained by issuing a research permit by the head of the hospital's research department

ETHICAL APPROVAL

The research ethics test was issued by the Health Research Ethics Committee (KEPK) Health Polytechnic, Ministry of Health Jakarta 1. This study involved medical records from hospitals. Informed consent for the collection and publication of data taken from the hospital was reviewed by education and training officers and medical records officers. Data is taken without written identity, so confidentiality is maintained.

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

COVID-19 : corona virus disease 19
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
PCR: polymerase chain reaction;
RT: papid test;
APGAR: appearance, pulse, grimace, activity, respiration
ICU: intensive care unit
NLR: neutrophil lymphocyte ratio
CRP: C – reactive protein
CT Value: cycle threshold value.