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Prenatal Covid-19 on Toddler Development

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Abstract
Along with the spread of the COVID-19 pandemic, there has been an increase in reports of confirmed cases of pregnant women with COVID-19. Exposure to the virus in pregnancy can affect the fetus and result in long-term vulnerability to abnormalities in the child's brain development. This study aimed to determine the impact of prenatal Covid-19 on the development of toddlers. The research method uses observational cross-sectional analysis. Secondary data on confirmed Covid-19 mothers were obtained from Prof. RD Kandou General Hospital, Wolter Monginsidi Hospital, and Manado Adventist Hospital. Primary data on toddler development using the KPSP Development Questionnaire instrument were obtained from 10 Community Health Centers in Manado City with a total of 92 respondents for two, 46 respondents were born to mothers with Covid-19 during the prenatal period and 46 toddlers were born to mothers who were not confirmed to have Covid-19 during the prenatal period. The results showed that there was no significant effect with a p-value of 0.562 for toddlers born to Covid-19 mothers on impaired gross motor, fine motor, socialization, independence, speech, and language development. Based on the results of the study it can be concluded that both toddlers born to Covid-19 mothers and toddlers who were not born to Covid-19 mothers are at risk of experiencing growth disturbances, especially toddlers born during the Covid-19 pandemic because there could be long-term effects that could occur in infants who are exposed to the virus during the prenatal/intrauterine period.

Keywords: Covid-19, SARS-CoV-2, Prenatal, Toddler Development.

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1. INTRODUCTION

Novel Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome 2 (SARS-CoV-2) has caused a major pandemic that started in Wuhan worldwide and is still a global problem. Till September 2022 infected more than 614 million confirmed cases and caused more than 6.5 million deaths globally (Kementerian Kesehatan Republik Indonesia, 2022). The world's first case occurred in China in December 2019, COVID-19 was detected in Indonesia on March 2, 2020, and on April 9, 2020, it spread to 34 provinces in Indonesia (Direktorat Jenderal Pencegahan dan Penanggulangan Penyakit, 2021). The COVID-19 pandemic has caused quite high morbidity and mortality, September 2022 in Indonesia a total of 6.42 million cases and 158 thousand deaths (University of Oxford, 2022) (Kementerian Kesehatan Republik Indonesia, 2022).

Along with the spread of the COVID-19 pandemic, reports of COVID-19 cases in pregnant women have also increased. SARS-COV-2 infection is associated with an increased risk of maternal morbidity and mortality (Ahmad et al., 2022), (Metz et al., 2022). It has been reported that pregnant women are more susceptible to severe COVID-19 than non-pregnant women, especially in the second and third trimesters of pregnancy (Badr et al., 2021), (Zambrano et al., 2020)

Meta-analysis studies suggest that vertical transmission is from mother to infant low (Goh et al., 2021). However, some literature states that SARS-CoV-2 infection in pregnant women in the second and third trimesters increases obstetric and neonatal risks and improves baby care in the NICU (Neonatal Intensive Care Unit) (Badr et al., 2021) (Wei et al., 2021). This is in line with a retrospective cohort study of infants born to mothers with severe COVID-19 associated with NICU care and growth retardation (Hamidi et al., 2022)

Toddlers born during the COVID-19 pandemic show a significant or low overall verbal, non-verbal, motor, and cognitive decline compared to toddlers born before the COVID-19 pandemic (Deoni et al., 2021) (Dyer, 2021). According to (Naidu et al., 2022) the cytokine storm induced during COVID-19 in Pregnancy can cause severe inflammatory damage to the fetus, and if not controlled, can later lead to disorders such as autism spectrum and brain development abnormalities in the neonate. And activation of the mother's immune response, increased inflammation, and changes in cytokine expression has been suggested as some of the mechanisms that cause long-term effects in infants (Shook et al., 2022)

Studies that further discuss the consequences of the impact of COVID-19 on mothers' prenatal care for babies who are born while developing, require careful monitoring of the baby born to mothers diagnosed with COVID-19 so that they can be detected earlier if there are developmental disorders. Toddlerhood is a golden period where rapid brain development occurs, so early detection is needed for the development of toddlers, especially those born during the COVID-19 pandemic because some literature states that toddlers exposed to the intrauterine virus can experience developmental delays. This study aimed to determine the impact of prenatal Covid-19 on the development of toddlers.

2. RESEARCH METHOD

This type of research is observational research with a quantitative approach. In terms of data collection, this research is classified as cross-sectional research. A cross-sectional design, inclusion criteria for toddlers born during the pandemic to mothers with positive prenatal PCR COVID-19, toddlers born to mothers not confirmed for COVID-19, and exclusion criteria for toddlers with congenital abnormalities. The research was conducted from December 2022 to February 2023. Data on toddlers born during the COVID-19 pandemic from July 2020 to

November 2023 were obtained retrospectively through medical record data at Prof RD Kandou Regional General Hospital, Wolter Monginsidi Hospital, and Manado Adventist Hospital which are Hospitals for Pregnant Women Care, Delivery, and postpartum confirmed COVID-19.

Primary data for toddler development was carried out at 10 Puskesmas in the city of Manado, measuring the development of toddlers using the Developmental Pre Screening Questionnaire instrument, this questionnaire is the standard set by the Ministry of Health. The questionnaire consists of 10 questions for each age, if the answer is yes 9-10 the development is appropriate, the answer is yes 7-8 the development is doubtful, and if the answer is yes < 6 the development is a deviation. Toddler development is measured during toddler visits to the Health Center and direct visits to toddler homes. The purposive sampling technique consisted of 92 respondents who were divided into two groups 46 toddlers born to Covid-19 mothers and 46 toddlers born to mothers who were not confirmed to have Covid-19. Toddler development data was tested using SPSS 25 and analyzed using the *chi Square* statistical test with a p-value *<0.05* to determine the relationship between Covid-19 and toddler development. This research has received research ethics from the ethics committee of the Faculty of Public Health, Hasanuddin University number 14737/UN4.14.1/TP.01.02/2022, and ethics from Prof. RD Kandou Hospital 005/EC/KEPK-KANDOU/I/2023.

3. RESULTS AND DISCUSSION

Table 1. Prevalence of Under-fives born during the Covid-19 pandemic.

Toddlers born during a pandemic	**n**	**%**
Toddlers born to Covid-19 mothers	46	50
Toddlers born to mothers not confirmed for Covid-19	46	50
Total	92	100

Table 1 illustrates that 46 (50%) toddlers were born to prenatal Covid-19 mothers and the control group of toddlers who were not born to mothers who were confirmed to have Covid-19 prenatal period were 46 (46%) toddlers.

Table 2. Characteristics of mothers with confirmed Covid-19 and mothers of toddlers who are not confirmed with Covid-19.

Characteristics of mothers	**Mother Covid-19**		**Mother is not confirmed Covid-19**	
	n=46	**%**	**n=46**	**%**
Age				
20 – 35 years	41	89.1	43	93.5
> 35 years	5	10.9	3	6.5
Work				
Work	41	89.1	40	87
Doesn't work	5	10.9	6	13
Parity				
Primipara	17	37.0	18	39.1
Multipara	26	56.5	26	56.5
Grande Multipara	3	6.5	2	4.3
Labor Method				
Spontaneous	14	30.4	15	32.6
Sectio Caesarea	32	69.6	31	67.4

Table 2 describes the characteristics of mothers under five born to mothers with Covid-19 aged 20-35 years 41 (89.1 %), as well as mothers born to mothers not confirmed to have

Covid-19 aged 20-35 years (93.5%). Mother's occupation, both mothers with confirmed Covid-19 41 (89.1%) and mothers not confirmed with Covid- 19 40 (87%), the majority did not work. The parity of mothers under five with confirmed Covid-19 was 26 (56.5%) and not confirmed with Covid-19, the majority of whom were multipara, namely 26 (56.5%). Delivery Method The majority of deliveries were by Sectio Caesarea, the group of mothers with confirmed Covid-19 sectio caesarea was 32 (69.6%) and mothers under five who were not confirmed with Covid-19 were 31 (67.4%).

Table 3 Characteristics of Respondents Toddlers born to mothers with Covid-19 and Toddlers born to mothers who were not confirmed to have Covid-19 during the prenatal period.

Characteristics of Toddlers	Toddler Mother Covid-19 prenatal period		Toddler Mothers were not confirmed for Covid-19 during the prenatal period	
	n=46	%	n=46	%
Age				
0-12 months	21	45.7	21	45.7
>12 months–36 months	25	44.3	25	44.3
Gender				
Boy	28	60.9	22	47.8
Girl	18	39.1	24	52.2
Age When the toddler was born				
Preterm	3	65	3	6.5
Term	43	93.5	43	93.5
Nursing Room at Birth				
Rooming-in	6	13.0	44	95.7
Neonate	27	58.7	2	4.3
Nicu	13	28.3	0	0

Table 3. The age characteristics of the respondents, both those born to Covid-19 mothers and toddlers born to mothers who were not confirmed to have Covid-19, both of whom were the majority aged > 12 months-36 months, namely 25 (44.3%). Based on gender, the majority of respondents born to mothers with prenatal Covid-19 were male, 28 (60.9%) respondents and the majority of respondents born to mothers who were not confirmed to have Covid-19 were female, namely 24 (52.2%) respondents. Based on age at birth, the majority of respondents who were born to mothers with Covid-19 and from mothers who were not confirmed to have Covid-19 were both born at term, namely 43 (93.5%) as well as the majority of toddlers who were not confirmed to have Covid-19, the majority were born at term, namely 43 (93.5 %) of respondents. Based on the treatment room for toddlers born to mothers with Covid-19, the majority were treated in the neonate/observation room, namely 27 (58.7 %) respondents and toddlers born to mothers who were not confirmed to have Covid-19, the majority were rooming in, 44 (95.7%) respondents.

Table 4. Distribution of the Frequency of Toddlers born during the Covid-19 pandemic based on toddler development.

Toddlers born during the Covid-19 pandemic	Development					
	A Deviation Occurred		Doubtful		Appropriate	
	n	%	n	%	n	%
Toddler mother Covid -19 prenatal period	1	2.2	7	15.2	38	82.6
The mother's toddler was not confirmed for Covid-19 during the prenatal period	0	0	7	15.2	39	84.4

Table 4 shows that there were 7 (15.2%) respondents born to Covid-19 mothers who had doubtful developments, and 1(2.2%) respondent had the possibility of deviation. and respondents who were born to mothers who were not confirmed to have Covid-19, there were 7 (15.2%) respondents who experienced doubtful developments.

Table 5. Association of toddlers born to Covid-19 mothers during the prenatal period on toddler development.

Toddlers born during the Covid-19 pandemic	Development				p=values
	Doubtful + Deviations Occur		Appropriate		
	n	%	n	%	
Toddler mother Covid -19 prenatal period	8	17.4	38	82.6	0.562
The mother's toddler was not confirmed for Covid-19 during the prenatal period	7	15.2	39	84.4	

Table 5 shows the results of the statistical test using chi-square, the result is p 0.562, which means that there is no association between toddlers born to Covid-19 mothers on toddler development. The results of a study conducted in Kuwait, the majority (90%) of infants aged 10-12 months born to mothers with SARS-CoV-2 infection during pregnancy had good outcomes and only 10% showed developmental delays, and toddlers who experienced a risk of delays development is that toddlers born to mothers infected with SARS-CoV-2 during the first and second trimesters are compared to the third trimester (Ayed et al., 2022).

Infections experienced by pregnant women in the first trimester are important because these are the stages of brain development such as primary neuralation (3-4 weeks), prosencephalic development (2-3 months), and neuronal proliferation (3-4 months), occur in early stage. stage (Rashighi & Harris, 2014). Infection with several common pathogens, such as cytomegalovirus (CMV), Zika virus, Rubella virus, *Mycobacterium tuberculosis* (TB), and *Toxoplasm*, during the first and early second trimesters, increases the risk of symptomatic infants, up to 32% having neurologic manifestations (Curcio et al., 2020). In the third trimester, viral infections can cause premature birth, and pre-eclampsia with hypertension, regardless of the severity of Covid-19 (Wang et al., 2020), (Wang, et al., 2022).

Likewise, with research conducted in China (Wu et al., 2021) SARS-CoV-2 during late pregnancy does not increase the risk of developmental delays in the child 3 months after delivery. Results of a recent meta-analysis by (Pinheiro et al., 2023) stated that there is no evidence to confirm the relationship between prenatal/gestational exposure to SARS-CoV-2 and delays in child neurodevelopment that can affect child development. This is also in line with a study conducted in Spain (Vázquez et al., 2021) showing normal psychomotor

development at 6 months follow-up. This is supported by a study conducted in New York by (Shuffrey et al., 2022) There were no significant group differences between exposed and unexposed infants on any of the 5 ASQ-3 subdomain scores (communication, gross motor, fine motor, problem-solving, or social-personal skills) at 6 months of age.

The study states that children born in 2019 before the COVID-19 pandemic did not experience a decrease in developmental scores, compared to children born in 2020 at the start of the COVID-19 pandemic and in 2021 measurements of gross motor, fine motor, visual and language development were carried out. children have developmental deficiencies (Dyer, 2021). Likewise toddlers born to mothers confirmed to have COVID-19 at the age of experiencing developmental disorders in communication, gross motor, fine motor, problem-solving, and social (Shah et al., 2023) (Cheng et al., 2021).

Gestational exposure negatively impacts gross motor skills, fine motor communication, and problem-solving (Huang et al., 2021) (Pinheiro et al., 2023) . In addition, a child's developmental disorder can involve various factors such as environmental, emotional, cognitive, nerve function, and psychological emotions experienced by a mother both prenatally and postnatally which can affect parenting (Papadopoulos et al., 2022) (Soetjiningsih, & Gde Ranuh, 2022) . It can be concluded that Covid-19 can indirectly affect the development of toddlers, namely through parenting from parents, babies born with low weight, and early delivery.

According to researchers, both toddlers born to Covid-19 mothers and not both have a risk of developmental disorders, although not significantly. A child's development is inherently shaped by the environment in which they learn, grow and play. genetic factors, nutrition, and stimulation, the stress experienced by the mother during the perinatal period is a factor that supports the growth and development of the fetus and especially the brain (Soetjiningsih, & Gde Ranuh, 2022), (Provenzi et al., 2021).

Researchers assume that even though a child's development begins in the womb and the problems experienced with or without SARS-Cov-2 infection, environmental exposures related to the COVID-19 pandemic can affect developing babies and children through various factors such as the environment, stimulation, parenting style, in this study most of the mothers of toddlers did not work so they had more time with their children so that they could provide more stimulation with the children so that the researchers assumed that this was one of the good factors for the group of toddlers born to mothers with Covid-19 and the control group did not experience significant developmental delays. And according to (Miguel et al., 2019) Prenatal, peripartum, and postnatal difficulties affect child behavior and neurodevelopment. Exposure to environmental enrichment and positive influences can reverse this effect.

The development of children under five must be monitored according to their age development, especially toddlers born during a pandemic because some literature states that toddlers who are exposed to COVID-19 since in the womb are more at risk of developmental disorders, as well as toddlers who have not been exposed since birth. pregnant women with COVID-19 because they are also at risk of developing developmental disorders as studies conducted in New York, toddlers born during the COVID-19 pandemic, both exposed and not exposed to COVID-19 in the womb when compared to toddlers born before the COVID-19 pandemic, namely those born in 2018 – June 2020, toddlers born during the COVID-19 pandemic had significantly lower gross, fine motoric, and personal social development scores (Shuffrey et al., 2022)

The limitation of this study is that most of the infants born to COVID-19 mothers during the third prenatal period because they represent 95.6% of the sample, therefore our observations

cannot be translated to those born to infected mothers in the early period of pregnancy, who are theoretically more at risk.

4. CONCLUSION

Based on the results of the study, there was no significant difference between toddlers born during the COVID-19 pandemic, both those who were exposed to COVID-19 during the prenatal period and toddlers who were not exposed to COVID-19 during the prenatal period, both of whom were at risk for developmental disorders but not significantly. Toddlers who are at risk for a decrease in developmental disorders are toddlers born to COVID-19 mothers in the prenatal period, there is 1 toddler who experiences developmental deviations. studies on the effects of intrauterine exposure to SARS-CoV-2 are still developing so it is necessary to carry out prospective studies with larger samples to determine the long-term effects caused by exposure to COVID-19 in the prenatal period. It is recommended for health practitioners to monitor the development of children under five so that if health complications occur, they can be handled earlier.

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