

ORIGINAL ARTICLE

The Impact of COVID-19 on Birth Weight during Pregnancy

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ABSTRACT

Introduction: Coronavirus is a viral pathogen that can be transmitted through respiratory droplets, leading to severe infectious diseases. This study aimed to ascertain the influence of the COVID-19 pandemic on birth weight during pregnancy.

Methods: This study used secondary data and a retrospective case-control approach for observational analysis. The case and control groups each had 153 samples. The case group was further separated into symptomatic and asymptomatic categories. Statistical analyses were performed to determine how COVID-19 infection in pregnant women affected birth weight. Fisher's exact test was used to evaluate data for the subgroups of asymptomatic and symptomatic individuals, while the Mann-Whitney test was used to compare the infection's impact.

Results: Most participants were 21–35 years old (78.2%). The findings showed that 85% of pregnant COVID-19 patients were in their third trimester. Mothers diagnosed with COVID-19 had infants with birth weights of >4,000 grams (3.3%), 2,500–4,000 grams (43.1%), and <2,500 grams (53.6%). Birth weight distribution in women unaffected by COVID-19 was >4,000 grams (14.4%), 2,500–4,000 grams (67.3%), and <2,500 grams (18.3%). The Mann-Whitney statistical test was performed using SPSS. It yielded a p-value of 0.001, less than the significance level of 0.05, indicating a correlation between confirmed COVID-19 infection in pregnant women and birth weight.

Conclusion: This study found that the presence of COVID-19 infection during pregnancy significantly affects infants' birth weight.

INTRODUCTION

Coronavirus is a virus transmitted through respiratory droplets and causes serious diseases for those infected. Decades ago, this virus mutated as Middle East Respiratory Syndrome Corona Virus (MERS-Cov) and Severe Acute Respiratory Syndrome Corona Virus

(SARS-Cov), the newly discovered mutation is SARS-CoV-2. It gave rise to the emerging coronavirus disease 2019 (COVID-19).¹ The first outbreak of COVID-19 occurred in December 2019 in Hubei Province, Wuhan, China.² The infection spread across the

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globe rapidly, and the World Health Organization (WHO) announced it was a pandemic.³ WHO reported that on 18 October 2021, globally, there were 240,260,449 confirmed cases, and at the time this study was conducted, 4,890,424 deaths had been reported. In Indonesia, there were 4,235,384 confirmed cases, and 142,999 deaths were reported.⁴ To this date, Dr. Soetomo General Hospital, Surabaya, as the regional referral for COVID-19, has limited data about how COVID-19 affected pregnancy outcomes, particularly birth weight.

According to reports, the first case of COVID-19 was transmitted from animal to human and eventually transmitted among humans. The incubation period occurs on days 3–7, with clinical manifestations that vary from asymptomatic to symptomatic. Some symptoms found in patients infected by COVID-19 are hyperthermia, cough, sneezing, and shortness of breath. Observations of 55,924 patients showed that the most common symptoms were hyperthermia, dry cough, and fatigue.⁵ Other symptoms could be cough with expectoration of sputum, shortness of breath, sore throat, headache, myalgia or arthralgia, chills, nausea/vomiting, nasal congestion, diarrhea, abdominal pain, hemoptysis, and conjunctival congestion. More than 40% of patients had peak temperatures of 38.1–39°C, while 34% had hyperpyrexia, a temperature above 39°C.⁴

Viral infection during pregnancy has been established as one of the risk factors leading to adverse pregnancy outcomes such as abortion, preterm birth, fetal malformation, intrauterine growth restriction (IUGR), and so on.⁶ As the primary receptor of SARS-CoV-2, angiotensin converting enzyme 2 (ACE2) may exacerbate complications. ACE2 expression within the female reproductive tract and placental tissue is also expected to lead to vertical transmission and low birth

weight.⁷ The presence of SARS-CoV-2 has been found in the stroma of the placental villi and the membranes of those who are infected. Thus, a fetus within an infected mother may be exposed to a pro-inflammatory environment via the placenta or fetal tissue or the mother's immune response.⁸

These facts establish that research on COVID-19-infected pregnant women and subsequent birth weight is necessary. This topic has never been studied in Dr. Soetomo General Hospital, Surabaya. This study is expected to provide an overview of the impacts that might occur due to COVID-19 infection during pregnancy and further aid in developing new strategies to prevent its transmission or control the adverse effects it causes.

METHODS

This study employed an observational analytical approach, specifically utilizing a retrospective case-control design. The research sample consisted of 1,302 pregnant women from the medical archives of the Department of Obstetrics and Gynecology Dr. Soetomo General Hospital, Surabaya, between May 2020 and July 2021. The study participants were categorized into two distinct groups. The case group comprised of women confirmed to have been infected with COVID-19 while pregnant, whereas the control group consisted of women who did not test positive for COVID-19 during their pregnancy. Through the application of total sampling, 153 samples were identified who met the case group's exclusion and inclusion criteria. Consequently, the control group also comprised 153 samples. This study had received ethical clearance from the Ethics Committee Dr. Soetomo General Hospital, Surabaya, with letter number 0518/LOE/301.4.2/VII/2021.

Table 1. Operational definitions of research variables

Variable	Operational Definition	Indicator	Test Measurement	Category	Scale
Independent variable: pregnant women with COVID-19	Pregnant women who had the PCR swab test with a positive result	PCR swab laboratory test results	Positive swab PCR	Code 1: asymptomatic Code 2: symptomatic	Nominal
Independent variable: pregnant women without COVID-19	Pregnant women who had the PCR swab test with a negative result	PCR swab laboratory test results	Negative swab PCR	Code 1: yes Code 2: no	Nominal
Dependent variable: birth weight	Neonatal weight was measured at birth or within one hour after birth. Body weight is used to diagnose whether it is normal or low birth weight.	Newborn's birth weight	Newborn's weight in grams	Code 1: birth weight >4,000 gr Code 2: birth weight 2,500–4,000 gr Code 3: birth weight <2,500 gr	Ordinal

PCR: polymerase chain reaction

RESULTS

Table 2 provides information regarding the age of the samples, the gestational age at diagnosis with COVID-19, the gestational age at which the women

delivered their babies, the method of the birth, the perceived symptoms, and the birth weight of the newborns. This data pertains to women with and without COVID-19 admitted to Dr. Soetomo General Hospital, Surabaya, between May 2020 and July 2021.

Table 2. Distribution of research result's frequency

No.	Category	Case	
		N	%
1.	Women with confirmed COVID-19 during pregnancy		
	a. ≤ 20 years old	8	5.2
	b. 21–35 years old	116	75.8
	c. > 35 years old	29	19
2.	Gestational age when the women were first diagnosed with COVID-19		
	a. 1st trimester	0	0
	b. 2nd trimester	6	4
	c. 3rd trimester	130	85
	d. Post date	16	11
3.	Gestational age when the women delivered the newborn		
	a. Immature	4	2.6
	b. Premature	59	38.6
	c. At term	90	58.8
4.	The type of delivery		
	a. Spontaneous	82	53.6
	b. Sectio caesarea	71	46.4
5.	The symptoms perceived by the women who were diagnosed with COVID-19		
	a. Asymptomatic	74	48.4
	b. Symptomatic	79	51.6
6.	Newborns birth weight from the women who were diagnosed with COVID-19		
	a. $> 4,000$ grams	5	3.3
	b. 2,500–4,000 grams	66	43.1
	c. $< 2,500$ grams	82	53.6
7.	Birth weight from the women without COVID-19		
	a. $> 4,000$ grams	22	14.4
	b. 2,500–4,000 grams	103	67.3
	c. $< 2,500$ grams	28	18.3

The effect of perceived symptoms of COVID-19 in pregnancy on birth weight can be seen in Table 3.

Table 3. Cross tabulation of perceived symptoms of women diagnosed with COVID-19 during pregnancy with newborn's birth weight

		Newborn's birth weight			Amount
		$> 4,000$ gr	2,500–4,000 gr	$< 2,500$ gr	
Asymptomatic	Count	5	46	23	74
	Expected count	2.4	31.9	39.7	74.0
Symptomatic	Count	0	20	59	79
	Expected count	2.6	34.1	42.3	79.0
Total	Count	5	66	82	153
	Expected count	5.0	66.0	82.0	153.0

The impact of perceived symptoms of COVID-19 in pregnancy on birth weight

The p-value < 0.001 was obtained using Fisher's exact test, with $\alpha = 0.05$. Since $p < \alpha$, it is hypothetically accepted that perceived symptoms by women who were confirmed with COVID-19 impacted birth weight.

The impact of COVID-19 during pregnancy on birth weight

The impact of COVID-19 infection during pregnancy on a newborn's weight is shown in Table 4.

Table 4. Cross tabulation of pregnant women with or without COVID-19 along with the newborn's birth weight

	Birth weight			Amount
	$> 4,000$ gr	2,500–4,000 gr	$< 2,500$ gr	
Pregnant women with COVID-19	5	66	82	153
Pregnant women without COVID-19	22	103	28	153
Amount	27	169	110	306

Based on the Mann-Whitney statistical test using the Statistical Package for the Social Sciences (SPSS), the p-value was $0.001 < 0.05$. This demonstrates that confirmed COVID-19 infection during pregnancy does have an impact on birth weight.

DISCUSSION

The impact of perceived symptoms of COVID-19 in pregnancy on birth weight

Based on the data collected, it might be inferred that there was a statistically significant correlation between the perceived symptoms reported by pregnant women who tested positive for COVID-19 during their pregnancy and the birth weight of their infants, as indicated by a p-value of 0.001. Symptoms that pregnant women subjectively experience were categorized into two groups, symptomatic and asymptomatic. Approximately 51.6% of the patient population exhibited symptoms, while the remaining individuals were classified as asymptomatic.

A review of the literature indicates there exists a notable correlation between several factors such as individual age, specific comorbidities (e.g., cardiac arrhythmias, depression, and obesity), and the patient's inherent immunological response with the manifestation of symptoms related to COVID-19.^{9,10} When an individual's body encounters an immunogen, it triggers the activation of the immune system, leading to the onset of an immunological response. The immune system serves as a literal mechanism of self-defense that confers positive effects. However, it is important to note that under specific circumstances, it can give rise to adverse consequences.¹¹

The natural immune response begins with the early exposure of immunogens to one's body. If this innate immune system can defend the body from immunogen attacks, one will not become ill when infected (first phase). Conversely, when the natural immune system cannot defend against immunogen attacks, then one will get sick when infected (second phase).¹²

TH17 declines cause an overabundance of pro-inflammatory cytokines in cases of COVID-19. An optimal amount of Treg/Th17 is essential to a fit pregnancy and normal implantation.¹³ Low Treg counts during pregnancy are associated with adverse pregnancy outcomes, such as failures or complications. It follows that pro-inflammatory response towards COVID-19 by maternal, fetal, and trophoblast immune effectors could be risks of obstetric complication and possible short- and long-term hereditary risk.¹⁴ One of these is adverse maternal outcomes such as IUGR, which results in low birth weight.

Despite the limited availability of data about the impact of COVID-19 infection on birth weight in pregnant women, the findings of this study retain relevance to the theory positing that COVID-19 infection during pregnancy could contribute to lower birth weight.

1. The impact of COVID-19 during pregnancy on birth weight

According to the results, p-value = 0.001 means the birth weights of newborns from women diagnosed with COVID-19 during pregnancy are significantly different compared to newborns' birth weights from women who had no history of COVID-19 infection during pregnancy.

The maternal body undergoes some physiological changes during pregnancy to adjust to the growth and development of the fetus. Cytokines are an important component in the processes of pregnancy, such as ovulation, implantation, and delivery. Granulocyte-macrophage colony-stimulating factor, interleukin 3 (IL-3), and interleukin 10 (IL-10) are anti-inflammatory cytokines considered crucial for successful progression of pregnancy as it sustains the functioning of T helper cell 2 (Th2) and regulatory T cells (Treg) 25, 26.¹⁵ Detrimental effects appear to be caused by tumor necrosis factor-alpha (TNF- α) and interferon-gamma (IFN- γ). Complications of pregnancy that affect newborn birth weights, such as recurrences of abortus, preterm birth, premature rupture of membrane, preeclampsia, and IUGR, are associated with an immune response called inflammatory reactions.¹⁶ These reactions can be induced by pro-inflammatory cytokines such as interleukin 1, 2, 8 (IL-1, IL-2, IL-8), TNF- α , and IFN- γ .¹⁷

Pro-inflammatory cytokines (IL-1 β , IL-6, IL-8, and TNF- α) are released by inflammatory mediators stimulated by viral infection, including COVID-19. Cytokines promote the release of corticotropin-releasing hormone (CRH), which could stimulate the fetus' hypothalamic-pituitary-adrenal axis, triggering cortisol and dehydroepiandrosterone sulfate.¹⁸ These hormones are responsible for synthesizing uterotonin (prostaglandins and endothelins) that trigger uterus contractions. Cytokines also play a role in increasing the release of proteases, leading to changes in the cervix and rupture of the amniotic sac, which can affect birth weight.¹⁹

Inflammation also affects fetal development. The development of the nervous system is very sensitive to inflammation during pregnancy. Similar clinical presentations across various viral and protozoan pathogens suggest a common underlying mechanism. A highly coordinated immune response is essential to a fit

pregnancy.²⁰ Cytokines and IFN are important mediators of a healthy pregnancy. This has to do with their ability to alter cellular function drastically, migration, intercellular communication, proliferation, and gene expression. However, if it is uncoordinated or expressed inappropriately, it could be teratogenic and disrupt fetal and placental development, leading to adverse pregnancy outcomes such as low birth weight and even fetal defects.⁸ Investigating how different immune signaling pathways will impact pregnancy and fetal development may provide important insights into adverse pregnancy outcomes and the possibility of further investigation into therapies to prevent pregnancy complications in mothers infected by COVID-19.¹⁰

This study indicated a significant correlation between COVID-19 infection during pregnancy and birth weight. The correlation was evident from the notable difference in birth weight observed between infants born to mothers diagnosed with COVID-19 during pregnancy and those who did not have such a history.

CONCLUSION

Based on the study on the impact of COVID-19 in pregnancy on the birth weight at Dr. Soetomo General Hospital, Surabaya, it can be concluded that most women confirmed to have COVID-19 during pregnancy delivered newborns with birth weights <2,500 grams. Most women gave birth at term (37–42 weeks), followed by premature birth (28–36 weeks), and immature (22–27 weeks). Pregnant women who had confirmed COVID-19 had birth weights between 2,500–4,000 grams. There was a significant impact of women with symptomatic COVID-19 during pregnancy on the birth weight. There was an impact of COVID-19 infection in pregnancy on the birth weight.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Conceived, planned, and finalized the manuscript: ADAAS. Supervised the manuscript and contributed to the interpretation of the results: IAM, BP, DH. Helped in writing the manuscript and provided critical feedback

and thus shaped the analysis: ERD. All authors contributed and approved the final version of the manuscript.

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