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Relationship between Exposure to COVID-19 and Hemoglobin Levels in Pregnant Women

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ABSTRACT

Background: Mothers who are exposed to COVID-19 have an impact on decreasing HB levels causing anemia thereby increasing the risk of morbidity and mortality in mothers during childbirth. Purpose: To determine the relationship between exposure to COVID-19 during pregnancy and hemoglobin levels in the Bantul II Health Center area. **Methods:** This study is a quantitative study with a retrospective cohort study design. The sample in this study was 26 pregnant women in each group (exposed and not exposed to COVID-19), selected based on inclusion criteria with simple random sampling. This research was conducted in the Bantul II Health Center area from October 2021 – February 2022. Data was collected by measuring Hb levels and filling out questionnaires. Data were analyzed by independent t-test and correlation. **Results:** There was no difference in the average Hb level in pregnant women who were exposed and not exposed to COVID-19 (Mean difference = 0.785; 95% CI = -0.164-1.734; p=0.103). Meanwhile, for the external variables, namely age (p=0.839), parity (p=0.565), nutritional status (p=0.233), and consuming Fe tablets (p=0.286) in the case group, age variable (p=0.492), parity (p=0.34), nutritional status (p=0.511) in the control group was not associated with a decrease in Hb levels. The variable consuming Fe tablets (p=0.049) in the control group was associated with a decrease in Hb levels. **Conclusion:** Pregnant women experience a decrease in Hb levels not due to exposure to COVID-19. Age, parity, nutritional status, and consumption of Fe tablets had no relationship with the decrease in Hb levels.

Introduction

Coronavirus Disease 2019 (COVID-19) is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS Cov-2). The disease is a new type of disease that attacks the respiratory system. The average incubation period of the disease is 5-6 days, with the longest incubation period being 14 days. Symptoms can include coughing, runny nose, fever, sore throat, up to the most severe is ISPA [1]. Patients who have co-morbidities (comorbid), elderly, pregnant women are at greater risk of experiencing death [2]. However, some cases do not experience the above symptoms and appear healthy [1].

COVID-19 disease was first recorded as a new disease in the city of Wuhan, China. China reports a pneumonia-like illness of unknown cause. The addition of cases shows an exponential trend. The spread of COVID-19 which was originally local transmission has changed to imported cases between countries [3]. The World Health Organization (WHO) designated COVID-19 as a Public Health Emergency of International Concern (PHIC) in January 2020 [4].

Based on WHO data, in May 2021 there were more than 153 million cases of COVID-19 with 3.2 million deaths. Of these cases, 23.1 million were cases in the Southeast Asia region [5]. Indonesia first confirmed a case of COVID-19 on March 2, 2020 with two sufferers who were suspected of being infected by a Japanese citizen. After that, it was reported that there were additional new cases and deaths every day spread across 34 provinces [6].

Based on data from the DIY COVID-19 Task Force, the number of confirmed cases from the first case to August 4 2021 in Indonesia was 3,325,567 cases. This data is supported by the number of confirmed cases in the Special Region of Yogyakarta of 124,009 cases (3.5%) [7]. The number of confirmed cases in Bantul Regency until 3 August 2021 was 44,091 cases [8]. The number of pregnant women in Bantul Regency is 7,120 people with a total of 432 confirmed cases of COVID-19. This data is supported by the number of pregnant women confirmed with COVID-19 at the Bantul II Health Center as many as 28 people.

Pregnant women who are infected with COVID-19 result in anxiety, severe respiratory complications [9], and increase the risk of delivery by caesarean section [10]. In rare cases, exposure to COVID-19 can cause preterm delivery, fetal distress, and giving birth to LBW babies [11]. In addition, exposure to COVID-19 can reduce Hemoglobin levels [12]. In a study with a sample of 41 people, divided into 2 groups, the average hemoglobin level in mild cases of COVID-19 was 13.3 g/L, while the average hemoglobin level in severe cases was 12.2 g/L [13]. Another study with a sample of 67 patients stated that the mean hemoglobin level in the ICU patient group was 13.2 g/L and in the non-ICU patient group was 14.2 g/L [14].

Decreased HB levels in pregnant women cause anemia which has an impact on increasing the risk of morbidity and mortality in mothers during childbirth [15]. Anemia in pregnancy has a negative effect, especially during pregnancy, childbirth and the puerperium. Anemia in pregnant women has the opportunity to experience bleeding during childbirth resulting in death [16].

Anemia in pregnancy can cause premature labor, abortion, infection, hydotidiform mole, hyperemesis gravidarum and premature rupture of membranes [17]. Based on the problems above, the researchers wanted to know the relationship between exposure to COVID-19 and hemoglobin levels during pregnancy in the Bantul II Health Center area. So that it is expected to provide benefits in the form of knowledge for pregnant women who are exposed to COVID-19 and the impact of decreasing Hb levels.

Materials and Method

This research is a quantitative study with a retrospective cohort research design. The sample in this study were pregnant women who were exposed and not exposed to COVID-19. Respondents were selected based on inclusion criteria with simple random sampling. The minimum sample size in this study was 22 people in each group (exposed and not exposed to COVID-19) so that there were 26 pregnant women per group. This research was conducted in the Bantul II Health Center area from October 2021 – February 2022. The variables for this study consisted of independent variables: exposure to COVID-19; dependent variable: hemoglobin level; confounding variables: Consumption of Fe Tablets, nutritional status, parity, and age of the mother. Data was collected by measuring Hb levels and filling out questionnaires. Data were analyzed by independent t-test and correlation "using SPSS ver. 17". This research has received ethical approval no. e-KEPK/POLKESYO/0831/XI/2021 by the Health Research Ethics Committee Poltekkes Kemenkes Yogyakarta.

Results and Discussion

Results

Based on the research, it was found that in the case group, the age of the respondents ranged from 23-40 years, with the majority having D1/D3/S1 education (50%), as housewives (57.69%), and domiciled in Ringinharjo Village (53.85%). The majority of pregnant women are in the 3rd trimester (57.69%), and have no history of parity or 1 time (42.31%). Pregnant women have more nutritional status (61.54%), consuming less than 90 iron tablets during pregnancy (57.69%).

Whereas in the control group, the age of the respondents ranged from 21-39 years, with the majority having high school/vocational high school education (80.77%), as housewives (IRT) (80.77%), and domiciled in Ringinharjo Village (69.23%)). The majority of pregnant women are in the second trimester (53.85%), and have no history of parity (46.15%). Pregnant women have more nutritional status (61.54%), consuming more than 90 iron tablets during pregnancy (88.46%).

Based on the results of the pearson correlation bivariate test, it was found that consumption of Fe tablets in the control group was associated with Hb levels of pregnant women ($p<0.05$). Meanwhile, age, parity, trimester, iron consumption, nutritional status in the case group, age, parity, trimester, nutritional status in the control group were not related to Hb levels of pregnant women ($p>0.05$). The results of the chi-square test showed that there was no relationship between education, occupation, and domicile with Hb levels in both the case and control groups ($p>0.05$) (Table 1).

Table 1. Characteristics of Respondents

Variable	Exposure group (Covid) N = 26		p-value	Non-exposed group (not covid) N=26		p-value
	n/ $\bar{x}$	%		n/ $\bar{x}$	%	
Age	($\bar{x}$=30, 23-40 years)			($\bar{x}$=30, 21-39 years)		
20-30 years	13	50	0.839	16	61.54	0.492
31-40 years	13	50		10	38.46	
Education						
Junior High School	1	3.85		0	0	
Senior High School	12	46.15	1.000	21	80.77	1.000
D1/D3/S1	13	50		5	19.23	
Work						
Housewife	15	57.69		21	80.77	
Workers/Private	8	30.77	0.385	4	15.38	0.423
Teacher/Police	3	11.54		1	3.85	
Address						
Sabdodadi	3	11.54		1	3.85	
Bantul	9	34.62	0.077	7	26.92	0.5
Ringinharjo	14	53.85		18	69.23	
Trimester	($\bar{x}$=2.46)			($\bar{x}$=2.5)		
1	3	11.54		0	0	
2	8	30.77	0.652	14	53.85	0.881
3	15	57.69		12	46.15	
Parity	($\bar{x}$=0.77)			($\bar{x}$=0.89)		
0	11	42.31		12	46.15	
1	11	42.31	0.565	6	23.08	0.34
2	3	11.54		7	26.92	
3	1	3.85		1	3.85	
IMT	($\bar{x}$=26.42)			($\bar{x}$=25.7)		
Normal (18,5 – 24,9)	10	38.46	0.233	10	38.46	0.511
Over (25,0-29,9)	16	61.54		16	61.54	
Fe consumption	($\bar{x}$= 83.46)			($\bar{x}$=96.35)		
<90 tablet	15	57.69	0.286	3	11.54	**0.049***
≥90 tablet	11	42.31		23	88.46	

$\bar{x}$ = average

*p<0.05 = statistically meaningful

Based on Table 2, it was found that there was no difference in the average hemoglobin (Hb) level in the group of pregnant women who were exposed and not exposed to COVID-19 (Mean difference = 0.785; 95% CI = -0.164-1.734; p>0.05).

Table 2. Differences in average Hb levels in pregnant women between groups exposed and not exposed to COVID-19

Kadar Hb	Mean ± SD	Mean ± SD difference	P Value	CI 95%
Case	1.027 ± 1.773	0.785 ± 0.472	0.103	-0.164-1.734
Control	0.242 ± 1.631			

Based on Table 3, it was found that Fe consumption had a very weak relationship to a decrease in Hb levels and was statistically significant (r = 0.389; p <0.05). Meanwhile, age (r = 0.100), parity (r = 0.048), nutritional status (r = 0.093) had a very weak relationship but not statistically significant.

Table 3. Relationship between External Variables and Decreased Hb Levels in Pregnant Women Who Are Exposed and Not Exposed to COVID-19

Variabel	r*	P value
Age	0.100	0.480
Parity	0.048	0.736
Nutritional Status/IMT	0.093	0.511
Fe Consumption	0.389	**0.004****

*r = relationship power

**p<0.05 = statistically meaningful

Discussion

Based on the research conducted, it was found that 52 pregnant women respondents were domiciled in the Bantul II Health Center area. The results showed that in the case group, the age of the respondents ranged from 23-40 years, with the majority having D1/D3/S1 education (50%), as housewives (57.69%), and domiciled in Ringinharjo Village (53.85%). The majority of pregnant women are in the 3rd trimester (57.69%), and have no history of parity or 1 time (42.31%). Pregnant women have more nutritional status (61.54%), consuming less than 90 iron tablets during pregnancy (57.69%).

Whereas in the control group, the age of the respondents ranged from 21-39 years, with the majority having high school/vocational high school education (80.77%), as housewives (IRT) (80.77%), and domiciled in Ringinharjo Village (69.23%). The majority of pregnant women are in the second trimester (53.85%), and have no history of parity (46.15%). Pregnant women have more nutritional status (61.54%), consuming more than 90 iron tablets during pregnancy (88.46%).

The results showed that the youngest respondent was 23 years old and the oldest was 40 years old with an average age of 30 years in the case group. In the control group, the youngest respondent was 21 years old and the oldest was 39 years old with an average age of 30 years. Bivariate tests showed that age had a very weak relationship to a decrease in Hb levels, but it was not statistically related in the case group (r = -0.042; p>0.05) and the control group (r = 0.141; p>0.05). This shows that age does not affect Hb levels in pregnant women who are exposed to Covid-19.

This is in line with a study which stated that age had nothing to do with the incidence of anemia in third trimester pregnant women with the majority aged 21-35 years [46-47]. However, it is different from other studies where the majority of respondents aged 21-35 years stated that maternal age is related to Hb levels. The age of 21-35 years is a very mature productive age from a biological and mental point of view, so the potential for anemia is smaller [49].

Mother's age can affect the decrease in Hb levels. If the mother is less than 20 years old, physically her reproductive system is immature, as well as her psychology so that she has the potential to experience disturbances in her intake of nutritious food [21]. Intake that is not supported properly has an impact on decreasing Hb levels. Meanwhile, if the mother is too old (>35 years), she is at risk of contracting an infectious disease, making her susceptible to anemia [51].

The majority of mothers have never given birth (nullipara) (42.31%) or have given birth once (primipara) (42.31%). In this study, statistically, parity history had no relationship with decreased Hb levels and the relationship was shown to be very weak in the case group (r = -0.118; p>0.05) and the control group (r = 0.195; p>0.05). So, pregnant women who are exposed to Covid-19 and experience a decrease in Hb levels are not affected by a history of parity.

In line with research with parity respondents who were the first time pregnant or gave birth. This study showed that there was no relationship between parity and the incidence of anemia 47.52. Parity is related to the level of knowledge, where mothers who are pregnant or giving birth for the first time tend to have less knowledge than experienced pregnant women [53]. So that the behavior and fulfillment of nutrition is not optimal [54].

However, it is inversely proportional to other studies which state that pregnant women with high parity or multiparas have a relationship to the incidence of anemia. Supported by mothers who have previously experienced anemia in previous pregnancies, then in subsequent pregnancies more and more iron is needed [55]. During pregnancy the mother's body will use up iron reserves due to bleeding during childbirth [51]. The amount of iron released when the mother gives birth reaches 250 mg [55]. So that if pregnancies occur repeatedly, and are not supported by balanced nutrition, iron will decrease [49].

Most pregnant women have more nutritional status (61.54%). Statistically, the nutritional status taken from the value of Body Mass Index (BMI) has a weak and negative relationship, and not significant in the case group (r = 0.243; p>0.05) and the control group (r = -0.135; p> 0.05). These results reinforce the two variables above that good maternal nutritional status is not associated with decreased Hb levels.

These results are in line with a study in which the majority of respondents had normal BMI and were not associated with the incidence of anemia with reference to Hb levels [56]. A good nutritional status of the mother indicates that the mother's intake needs are met, including Hb levels [57]. Thus, the decrease in Hb levels that occurred in the respondents in this study was not caused by the nutritional status of the mother.

However, these results are not in accordance with other studies where the majority of respondents have normal nutritional status and are associated with the incidence of anemia in third trimester pregnant women [58]. Mothers with normal nutritional status but experiencing anemia can be caused by the poor quality of the food consumed or not containing iron [59].

Anemia in pregnant women is caused by low nutritional status due to a lack of iron intake [60]. Pregnancy provides physiological changes to a woman. During her pregnancy, the mother's body will need 20-30% more blood to be shared with the fetus. If this is not supported by increased consumption of nutritious foods, vitamins and iron tablets, a deficiency in Hb levels will occur [49].

Prevention of anemia can be done by fulfilling protein and folic acid intake [61]. Thus, mothers can consume foods from protein that contain iron such as liver and meat [62]. While intake of folate such as vegetables, fruits, and nuts [61]. Fulfillment of iron and folic acid can increase Hb levels by 0.720 g/dL in mothers [63].

Pregnant women who regularly take blood booster tablets will increase their Hb levels [59]. In this study, the majority of pregnant women consumed less than 90 iron tablets during pregnancy (57.69%). This is influenced by several pregnant women who are still in their first trimester, so that Fe consumption has not reached 90 tablets. The results of the bivariate test showed that Fe consumption had a very weak and negative relationship, and was not statistically related in the case group (r = 0.218; p>0.05). Meanwhile, in the control group there was a statistical relationship (r = 0.39; p <0.05).

One study stated that there was no difference in the average Hb level in pregnant women who regularly and did not regularly consume Fe tablets with normal levels [46]. Similar studies state that there is no relationship between nutrient intake and the incidence of anemia [64]. Other research states that pregnant women who are sufficient to meet their iron intake also experience anemia [65]. In contrast to research where the majority of pregnant women did not adhere to taking Fe tablets (<60 tablets) had an impact on the incidence of anemia (p<0.05) [62].

Iron intake for Women of Reproductive Age (WUS), namely aged 19-49 years, must be sufficient for 18 mg with an additional 9 mg for pregnant women in trimesters 1 and 262. The iron needed by pregnant women is 7 mg/day. So that the total requirement for iron is 800-1200 mg [55].

After conducting a bivariate test, it was found that there was no difference in the mean hemoglobin (Hb) levels of pregnant women who were exposed and not exposed to Covid-19 (95% CI = -0.164-1.734; p>0.05) (Table 3). These results are in line with other studies which state that there is no relationship between C-Reactive Protein (CRP) and Hb levels [66].

During pregnancy, the mother experiences a process of hemodilution or adjustment to the mother's physiology to reduce the workload of the heart due to hypervelomy. This adjustment has an impact on decreasing Hb levels [67]. One study stated that anemia occurs in pregnant women when they enter the second trimester due to blood dilution, blood that is not comparable to plasma, lack of iron in the body[68]. As the gestational age increases, the need for iron increases. If pregnant women do not balance it with a good diet and take iron tablets, Hb levels will decrease and have a negative impact on the health of the mother and fetus [69].

In addition, there was no difference in the mean results in this study possibly due to the homogeneity of the sample characteristics of both the case and control groups. The difference between the two groups was the consumption of Fe tablets which affected Hb levels. Thus, the absence of a difference in average Hb levels in the two groups was not only caused by exposure to Covid-19, but also other factors such as hemodilution and lack of consumption of Fe tablets.

However, it is inversely proportional to other studies which state that there is a relationship between the incidence of anemia and the incidence of Covid-19 [70-71]. Other research also states that a decrease in Hb levels occurs in a short time after a person is diagnosed with Covid-19 infection [72]. People infected with Covid-19 experience a decrease in Hb levels more than other types of pneumonia [73].

Pregnant women who are exposed to Covid-19 have an impact on decreasing Hb levels due to the body's response where SARS-CoV-2 infection interferes with erythropoiesis and reduces hemoglobin levels [74]. When the Covid-19 virus enters the body, the virus secretes CRP in the form of CD147 and CD26 which enters the erythroblasts of the spinal cord and replicates the virus then destroys the function of hemoglobin [75]. When the body experiences an acute inflammatory process and infection, the body reacts by releasing iron to protect the body from excessive invasion66.

One study found that 92.8% of pregnant women experienced anemia because integrated ANC services did not run optimally during the Covid-19 pandemic. ANC services aim to provide Communication, Information, and Education (IEC) to pregnant women regarding nutritional intake, physical health of mothers and babies, and psychological services [76]. Lack of education and knowledge can affect the pattern of mother's behavior during pregnancy [77]. However, the Government has given directions so that ANC services can continue as they should by complying with the health protocol [76].

Conclusion

Based on the research that has been done, it can be concluded that there is no difference in the average Hb level between pregnant women who are exposed and not exposed to COVID-19. Age, parity, nutritional status, and consumption of Fe tablets had no association with a decrease in Hb levels. The suggestions that researchers can give are giving the Covid-19 vaccine to boosters as a prevention for pregnant women so they don't get infected with Covid-19 infection, monitoring the condition of the mother and baby. It is recommended that village midwives work together with cadres to be able to carry out home visits to at-risk pregnant women, carry out regular Hb level measurements, provide counseling services about food diversity that supports increasing Hb levels and foods that prevent iron absorption in the body, and provide nutritional supplementation pregnant women, especially Fe tablets and folic acid. In addition, carrying out strict monitoring with village midwives and companion cadres regarding adherence to taking Fe tablets every night via WhatsApp groups consisting of pregnant women.

Declaration

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Conflicts of Interest: The authors declare no conflict of interest.

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