



Factors Affecting The Incidence of Anemia in Pregnancy During The COVID-19 Pandemic

Juvita Tri Rahmawati¹, Lucia Sincu Gunawan²✉, Rumeyda Chitra Puspita³

¹⁻³ Universitas Setia Budi, Indonesia

✉ sincugunawan@gmail.com, Telp: +62816674427

Received: 20 July 2023/Accepted: 26 February 2024/Published Online: 29 February 2024

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Abstract

Pregnancy-related anemia increases the risk of low birth weight, early delivery, and deformities in the fetus. It can also add to the financial burden on families and society. The most reliable way to track the health of expectant mothers and avoid pregnancy-related issues would be to look for the prevalence of anemia. The COVID-19 pandemic has impacted pregnant women. In Kalijambe Indonesia between 2019 and 2020, the percentage of pregnant women with anemia rose from 38.33% to 49.21%. In the COVID-19 pandemic situation with social activity restrictions, decreasing family income, and limited access to health services, suffering from COVID-19 are risk factors for increasing the incidence of anemia in pregnancy. This study aimed to determine factors affecting the incidence of anemia in pregnancy during the COVID-19 pandemic in Karangrejo District, Magetan Regency. This research was an analytical observational study. The sample was selected by purposive sampling with a sample size of 52 study subjects. Data were analyzed using logistic regression analysis with SPSS. Factors that increased the incidence of anemia in pregnancy during the COVID-19 pandemic were pregnancy interval (OR=17.67; CI 95%= 1.01 to 116.00; p=0.049), gestational age (OR=11.39; CI 95% 1.12-116.00; p= 0,040), animal protein intake (OR= 0.25; CI 95% 0.03 – 2.38; p= 0,044), iron supplementation (OR= 108.47; CI 95% 2.36 – 4978.68; p= 0,016), consumption of tea (OR=36,89; CI95% 1.57 to 868.41; p=0.025). Mothers' education, family income, parity, frequency of ANC visits, and COVID-19 morbidity do not significantly affect the incidence of anemia in pregnancy. Pregnancy interval, gestational age, tea consumption, animal protein intake, and iron supplementation in Karangrejo District, Magetan Regency were found to have an impact on the incidence of anemia in pregnancy.

Keywords: Anemia; Pregnancy; COVID-19; Women's Health; Iron Supplementation

INTRODUCTION

Anemia during pregnancy is linked to unfavorable pregnancy outcomes and is a public health concern, particularly in developing nations like Indonesia. (Stephen et al. 2018). The WHO defines anemia in pregnancy as having a hemoglobin concentration of less than 11 g/dl in pregnant women (Aji et al. 2020). The physiological changes that occur during pregnancy are a significant factor in anemia, regardless of any other factors. Throughout pregnancy,

levels of hemoglobin, red cell mass, and plasma volume rise. However, the rise in plasma volume is disproportionately larger than the rise in hemoglobin or red cell mass, leading to what they called a "oligocythemich hypervolemia." Pregnancy generally causes a 30-to 50% increase in blood volume over baseline. The viscosity of the mother's blood is decreased by these hemodilutional alterations, which should enhance uteroplacental perfusion (James 2021).

The etiology of anemia during pregnancy in developing nations is complex and includes chronic diseases like HIV and TB, anemia brought on by parasite infections like malaria and hookworm, and micronutrient deficiencies of iron, folate, and vitamins A and B12 (Stephen et al. 2018). Iron deficiency is the primary cause of anemia in pregnant women (Aji et al. 2020). Due to the iron requirements of both the mother and the fetus, pregnant women are susceptible to iron deficiency anemia (James 2021).

The COVID-19 pandemic has impacted pregnant women. During the COVID-19 pandemic, in Kalijambe, Indonesia the prevalence of anemia in pregnancy grew considerably; from 2019 to 2020, the percentage of pregnant women with anemia went from 38.33% to 49.21% (Surya et al. 2021). A hyper-inflammatory condition linked to elevated amounts of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and ferritin characterizes such severe COVID-19 infections. Typical changes in iron homeostasis brought on by inflammation include decreased intestinal iron absorption and increased iron uptake and retention in macrophages. Because of this, there is less iron in the blood and less iron available for erythropoiesis, which uses it to make hemoglobin. Anemia of inflammation in COVID-19 is caused by cytokine-mediated suppression of erythropoiesis, delayed erythrocyte half-life, and decreased biological activity of the red cell hormone erythropoietin (Bellmann-Weiler et al. 2020).

Another concern is the COVID-19 pandemic created a stressful environment that prevented pregnant mothers from getting routine Antenatal Care (ANC). Maternal mortality occurred due to the inability to access proper health care, such as suspicion of being infected from COVID-19, and limited healthcare personnel and facilities (Surya et al. 2021).

Pregnancy-related anemia is known to have detrimental effects on the health of both the mother and

the unborn child and to raise the risk of both (Stephen et al. 2018). In Indonesia, anemia during pregnancy accounts for 305 out of every 100,000 live births as an indirect cause of maternal death (Surya et al. 2021). Comorbid conditions such as arterial hypertension, cardiovascular disease, and chronic renal disease were more common in anemic patients and are recognized risk factors for COVID-19-associated mortality. (Bellmann-Weiler et al. 2020). Pregnancy-related anemia may be linked to a higher severity of COVID-19 due to altered immune systems, physiological and anatomical abnormalities, hormonal imbalances, and increased expression of ACE2 (Surya et al. 2021). Understanding the factors influencing anemia cases during the COVID-19 pandemic is crucial for anticipating future occurrences and addressing existing factors to reduce the incidence of anemia in pregnant women. This is essential as it can have significant implications for both the mother and the developing fetus, impacting the overall growth and development of the child. This study aimed to determine the factors that influence the incidence of anemia in pregnancy during the COVID-19 pandemic in Karangrejo District, Magetan Regency.

METHOD

This study was quantitative, and used an analytical survey approach with a cross-sectional design. The survey uses questionnaires that are arranged based on the independent variables studied, while the dependent variable is measured by examining Hb levels. The sample was selected by purposive sampling with a sample size of 52 subjects. The population in this study were pregnant women who got the ANC in Karangrejo District. The sample size was determined based on the population of pregnant women who got ANC at Karangrejo District, Magetan Regency from March to May 2022, which amounted to 60 individuals. The number of subjects was 52 pregnant women.

Pregnant women who were willing to participate in the first through third trimester met the inclusion criteria. Exclusion criteria were: pregnant women who have chronic diseases (Thalassemia, Leukemia, TBC, Malaria). The type of data used in this study was primary data.

Pregnancy-related anemia was the dependent variable, and it was determined by measuring hemoglobin levels using specimens of capillary blood and POCT. Independent variables were parity, pregnancy interval, gestational age, family income, mother's education, frequency of ANC visits, consumption of tea, animal protein intake, iron supplementation, and COVID-19 morbidity.

Anemia is a condition of lack of hemoglobin which is characterized by hemoglobin (Hb) levels in the blood less than normal (less than 11g/dL). Hemoglobin level was determined from capillary blood from a finger prick with a measuring tool (EasyTouch® GCHB) measurement scale of categorical data (0: nonanemic dan 1: anemia). Parity is the number of children born alive or dead. Assessed by asking mother's birth history (0: low risk, one child, and 1: high risk, two or more children). Pregnancy interval is the time interval between the last birth and the current pregnancy (0: low risk (>2 years) dan 1: high risk(<2 years). Gestational age is the number of weeks of this current pregnancy, calculated from the first day of her last menstruation (0: low risk, in 1st trimester; and 1: high risk, in 2nd or 3rd trimester). Family income is the monthly income a family earns (0: high income, which is higher than regional minimum wage, and 1: low income, below regional minimum wage). Education level is the level of formal education of the mother (0: high education, which is senior high school or college, and 1: lower education level, which is elementary education or junior high school). The Ante Natal Care (ANC) is a visit of pregnant women to a health service center for pregnancy checks, at least 1 time in the 1st

and 2nd trimesters and 2 times in the 3rd trimester (0: yes/regularly dan 1: no/irregularly). Animal protein intake is defined as a daily diet containing chicken/fish/meat/eggs at least 3 times a week (0: consumption of animal protein at least 3 times a week, and 1: no consumption or less than 3 times a week). Consumption of tea is the habit of drinking tea every day, either together with the main meal or not (0: no drinking tea/ not every day dan 1: every day). Iron supplementation is the habit of taking iron tablets as directed by a doctor or midwife (0: regularly dan 1: irregularly). The data were collected by using a questionnaire. Healthcare professionals at the public health centers used capillary blood drawn from a finger prick (EasyTouch® GCHB) to measure the subject's Hb content. The data that has been obtained was processed using SPSS. Univariate analysis was employed in the data analysis (categorical scale variables were defined in terms of n and percent, while continuous scale variables were characterized in terms of mean, SD, minimum, and maximum). Chi-square was used to statistically assess bivariate analysis, which is the association between two variables using a categorical scale—that is, the difference in the percentage between two or more groups. the relationship's size as measured by the odds ratio, or OR. Logistic regression analysis was employed in multivariate analysis.

RESULT AND DISCUSSION

The characteristics of the subjects can be seen in Table 1, where the majority of subjects who took part in the study were in the third trimester of pregnancy (55.8%), where the risk of anemia increases along with the physiology of pregnancy.

Table 1. Subject Characteristics

Characteristics	Category	Frequency	Percentage
Gestational Age	1 st Trimester	1	1.9 %
	2 nd Trimester	22	42.3 %

Characteristics	Category	Frequency	Percentage
Gestational Age	1 st Trimester	1	1.9 %
	3 rd Trimester	29	55.8 %
	2-3	24	46.2 %
Parity	1	28	53.8 %
	2-3	24	46.2 %
Pregnancy interval	High risk (<2 years)	22	42.3 %
	Low risk (>2 years)	30	57.7 %
Education level	Junior HS	11	21.2 %
	Senior HS	39	75.0 %
	College	2	3.8 %
Family income	Less than regional minimum wage	30	57.7 %
	Equal or higher than the regional minimum wage	22	42.3 %

Based on Table 1, it can be seen that most of the subjects were in the first pregnancy (53.8%). For subjects in the second and third pregnancies, most of the pregnancies were more than 2 years apart (57.7%), thereby reducing the risk of the pregnancy itself. Most of the subjects had senior high school education (75.0%) and only 2 subjects (3.8%) had higher education. Most of the family income was still below the regional minimum wage (57.7%).

Based on the findings of the measurement of hemoglobin levels, Table 2 below indicates that up to 34 (65.4%) of the subjects have anemia, and up to 18 (34.6%) do not.

Table 2. Univariate Analysis of Anemia Distribution

Description	n	%
Non Anemia	18	34.6
Anemia	34	65.4
Total	52	100

Several causal factors of anemia during pregnancy are a lack of consumption of foods rich in iron, especially derived from simple animal protein, iron deficiency due to increased iron requirements in pregnancy, iron loss in excessive bleeding, including bleeding from menstruation before, and frequent birth with short intervals (Astuti and Kulsum 2018). The cause of high incidence of anemia in women can also be caused by malaria, worm infections, or other infections that occur even before pregnancy (Indrawatiningsih et al. 2021).

Table 3 below presents there was effect of the ANC on the incidence of anemia. Visiting ANC regularly reduced the risk of anemia in pregnancy by 0.27 times compared to subjects who visited ANC irregularly years (OR= 0.27; p= 0.03). There have been numerous limitations on practically all community services, including maternity and newborn health services, throughout this COVID-19 pandemic. As a result of their fear of contracting an infection, expectant mothers avoided visiting the public health center and other medical institutions (Mera, Marhama; Anes 2022) In pandemic, access to the healthcare system is restricted, particularly to preventative and reproductive healthcare, show that obstetric care is especially vulnerable (Connor et al. 2020).

There was an effect of the pregnancy interval on the incidence of anemia. Pregnancy intervals of more than 2 years reduced the risk of anemia in pregnancy 0.08 times compared to subjects having pregnancies less than 2 years (OR= 0.08; p= 0.001).

Table 3. Bivariate analysis

Variable	Anemia				OR	p
	Non Anemia		Anemia			
	n	%	n	%		
Family income						
< minimum wage	9	17.3	21	40.4	0.62	0.414
≥ minimum wage	9	17.3	13	25.0		
Parity						
1 st	10	19.2	18	34.6	1.11	0.857
2 nd -3 rd	8	15.4	16	30.8		
Visiting ANC						
Regularly	12	23	12	23	0.27	0.03
Irregularly	6	11	22	43		
Pregnancy Interval						
High risk	2	3.8	20	38.5	0.08	0.001
Low risk	16	30.8	14	26.9		
Consumption Tea						
No	10	19.2	7	13.5	4.82	0.011
Yes	8	15.4	27	51.9		
Animal protein intake						
No	8	15.4	28	53.8	5.83	0.005
Yes	10	19.2	6	11.5		
Iron supplementation						
No	1	1.90	20	38.5	0.41	<0.001
Yes	17	32.7	14	26.9		
Covid-19 morbidity						
No	17	32.7	33	63.5	0.52	0.641
Yes	1	1.90	1	1.90		

The consumption of tea increased the risk of anemia in pregnancy 4.82 times more likely compared to subjects who did not consume tea (OR= 4.82; p= 0.011). Pregnant women's diet affects not only the health of the fetus but also the pregnancy and the mother. An expectant mother's diet serves as the unborn child's primary source of nutrients. Knowing what foods are healthiest for both the expectant mother and the developing kid is crucial for expectant mothers as it can promote both parties' well-being (Mera, Marhama ; Anes 2022).

There was an effect of animal protein intake on the incidence of anemia. It reduced the risk of

anemia in pregnancy by 5.83 times, compared to subjects who did not consume animal protein (OR= 5.83; p= 0.005). Parallel to other researchers, respondents with less protein intake are 6 times more at risk of anemia than respondents with sufficient protein intake (Machmud, Hatma, and Syafiq 2019).

There was an effect of iron supplementation on the incidence of anemia. The iron reduced the risk of anemia in pregnancy 0.41 times compared to subjects who did not consume iron supplements (OR= 0.41; p= <0.001). The coverage of pregnant women receiving iron supplements in Indonesia in 2017 reached 80.81 percent, but this has not yet achieved the target of the strategic plan (Renstra) of 90 percent (Mera, Marhama ; Anes 2022).

The incidence of anemia was not significantly impacted by COVID-19 infection (OR= 0.52; p= 0.641). This was contrary to similar research which stated anemia was more often present in pregnant mothers with a history of SARS-CoV-2 infection during pregnancy (42.1% vs. 29.3%, p = 0.018) (Uta et al. 2022). In theory, the COVID-19 virus causes inflammation that has a significant impact on erythropoiesis through a variety of pathways. Abnormal iron metabolism mediated by interleukin (IL)-6 overproduction and pro-inflammatory cytokines such as interferon- γ , IL-1, IL-33, and tumor necrosis factor (TNF)- α are two of the main causes of this inflammation. The latter may shorten the lifespan of erythrocytes and have inhibitory effects on precursor and erythroid progenitor cells (Bergamaschi et al. 2021). Certain viruses attach to transferrin receptor type 1 to infect iron-acquiring cells, while other viruses target hepcidin and the Human Homeostatic Iron regulator Protein (HFE) genes in an attempt to cause iron overload in cells to aid in their survival and multiplication (Menshawey et al. 2020). Cytokine storm raises the possibility of miscarriage and can lead to the development of multiple organ dysfunction

syndrome in both the fetus and the expectant mother. Specifically, hypoxia and uncontrollably distributed inter-tissue iron redistribution are caused by erythrocyte breakdown brought on by severe inflammation (Gromova et al.2020). Studies have shown that about 50% of COVID-19 patients have decreased hemoglobin (Hb). In an instance of acute immunological activation, an inflammatory anemia may arise; this defense mechanism entails low circulating iron to stop the virus from infecting the organs while boosting cellular immunity. This anemia's pathogenesis includes decreased erythropoietic progenitor cell proliferation, decreased erythropoietin stimulation, and a decrease in erythrocyte half-life. Reticulum-endothelial system cells' heightened iron retention is the cause of the iron homeostasis imbalance in inflammation. Ferritin levels, an acute phase reactant, are extremely elevated in COVID-19 patients (Urrechaga et al. 2020). In respect to COVID-19 infection, a robust relationship was found between iron, IL-6, and hepcidin. Hepcidin production is triggered by the virus's release of IL-6, which results in hyperferritinemia and iron-restricted erythropoiesis (Abu-Ismael et al. 2023).

A diagnosis for iron deficiency is ferritin less than 30 ug/L. Elevated ferritin levels in COVID-19-positive patients do not rule out iron deficiency (Malinowski and Murji 2021). Hyper-ferritinemia is a response of excess iron load, characterizes with pathogenic role on the ground of its immunomodulatory properties, which has already been described as a cardinal feature of COVID-19. Interestingly, however, the global COVID-19 tracker shows that nations with greater economic status—such as the United States, Canada, Europe, and Australia—have significantly lower rates of iron deficiency anemia (IDA), despite having higher COVID-19 case fatality rates (CFRs). Conversely, low-income nations, such as India and Africa (the world's poorest continent), which

have greater rates of IDA, are less likely to contract COVID-19 and have lower levels of COVID-19-related CFR, which is roughly half that of their higher income counterparts (Ghosh et al. 2021). More evidence was gathered to show that iron-chelation helps the host by lowering the quantity of viral proteins and nucleic acids, which in turn lowers viral release and replication. Furthermore, low iron levels may suppress the production of adhesion molecules necessary for the attachment and internalization of viruses (Menshawey et al. 2020).

The results of the multivariate analysis of the factors that influence the incidence of anemia in pregnancy are presented in Table 4 below. There was an effect of gestational age on the incidence of anemia. The 3rd trimester pregnant women were 11.39 times more likely to get anemia than the 1st-trimester pregnant women (OR= 11.39; 95% CI= 1.12 to 116; p= 0.040). The physiological changes in pregnancy that start in the sixth week of pregnancy and peak in the 26th week, when Hb levels decline, are the reason behind the increased incidence of anemia with increasing gestational age (Astuti and Kulsum 2018). Compared to the first and second trimesters, the third trimester had a higher rate of anemia (Karami, et al.2022). The plasma volume keeps increasing until weeks 32 to 34, when it reaches a plateau. Increased erythropoietin levels in response to increasing placental lactogen and progesterone cause the activation of erythropoiesis, which happens at a little later stage. Typically, by week 36, there is a 25% rise in red blood cell production, which began at week 16 and has been steadily increasing ever since (Agarwal and Rets 2021).

There was an effect of pregnancy interval on the incidence of anemia. Pregnancy intervals of more than 2 years were 17.67 times more likely to reduce the risk of anemia than subjects having next pregnancies less than 2 years (OR= 17.67; 95% CI= 1.01 to 116; p= 0.049). For pregnant women who had a pregnancy

interval too close, maintaining their nutritional status was quite difficult, because they might still be breastfeeding, and their needs and resources were focused on the first child so they were at risk of anemia (Prahesti, Indarto, and Akhyar 2016). Younger age group and high parity were the risk factors that were significantly associated with antenatal anemia (Abd Rahman et al. 2022).

There was an effect of animal protein intake on the incidence of anemia. Consumption of animal protein was 0.25 times more likely to reduce the risk of anemia than subjects who did not (OR= 0.25; 95% CI= 0.03 to 2.38; p= 0.044). Protein serves as a building and regulatory agent. It also plays a part in the delivery of iron to the bone marrow, which is necessary for the production of red blood cells, and it maintains human health by supplying the molecular precursors of amino acids. Consuming protein, particularly from animal sources, helps the body absorb iron more readily. As a result, eating too little protein can lower hemoglobin levels, which can lead to anemia (Machmud et al. 2019). Pregnant women who have difficulty eating large quantities can be given high-protein snacks eel cookies that are proven to increase body weight of pregnant women with chronic protein energy deficiency (Pratiktowati, D et al. 2020). Locally made snacks with a composition of corn flour, soy flour, yellow pumpkin flour, katuk leaf flour, margarine, refined sugar, and chicken eggs can also improve the nutrition of pregnant women as indicated by an increase in upper arm circumference and body weight (Putri, R. et al 2019).

In impoverished nations, iron supplementation is highly advised. Almost all women should receive effective therapy with oral or parenteral preparation, depending on their gestational age and hemoglobin level. Iron supplementation is the preferred course of treatment (Amrale, Ahire, and Vairage 2019). There was an effect of iron supplementation on the

incidence of anemia. Without iron supplementation, anemia increased 108 times more than subjects who got iron supplementation (OR= 108.47; 95% CI= 2.36 to 4978.68; p= 0.016). Among patients prior to providing supplements, 18% had anemia on admission compared with 11% with iron-containing supplements dispensed (risk ratio [RR], 0.61; 95% CI, 0.56-0.66) (Thiele et al. 2023).

The reluctance to consume iron supplements in pregnant women is due to the side effects of iron tablets such as nausea, vomiting, stomach cramps, heartburn, and constipation. Family support was an important factor in encouraging pregnant women to consume iron supplements regularly (-Anggraini, Wulandari, and Arisanti 2022). To reduce side effects, oral ferrous iron supplements should be taken daily or every other day and comprise 40–100 mg of elemental iron. Products with sustained release or enteric coatings are not as well absorbed; that is, their activity begins farther from the duodenum. Patients should take oral iron and vitamin C (250–500 mg) on an empty stomach, if tolerated, one hour before or two hours after calcium, antacids, proton pump inhibitors, thyroxine, tea, coffee, milk, soy, and eggs in order to maximize absorption. Two to four weeks after the start of treatment, the hemoglobin level should be measured to assess the response to oral iron (Malinowski and Murji 2021).

Intolerance to iron and non-compliance in some women may make oral iron therapy inadequate and these can be benefited from parenteral iron therapy (Satyanarayana et al. 2017). Oral iron therapy had statistically significantly better efficacy in improving serum ferritin levels (Natarajan and Baskaran 2021). Adherence to taking iron tablets can be improved by audio-visual media-based counseling (Jannah and Arini Murni 2019). Even if a pregnant woman stops menstruating, additional iron is still needed for fetal growth, placenta, and increased maternal blood volume. This amount is close to 1000 mg of iron,

greater compared to early pregnancy. This iron requirement during pregnancy increased from 0.8 mg daily in the first trimester to 6.3 mg daily in the third trimester (Astuti and Kulsum 2018).

Table 4. The results of multilevel multiple logistic regression analysis

Independent Variables	OR	95% CI		p
		Lower limit	Upper limit	
Gestational age	11.39	1.12	116.00	0.040
Pregnancy interval	17.67	1.01	116.00	0.049
Consumption of animal protein	0.25	0.03	2.38	0.044
Iron supplementation	108.47	2.36	4978.68	0.016
Consumption of tea	36.89	1.57	868.41	0.025
Visiting ANC	13.50	0.94	94.23	0.056

n observation = 52

There was an effect of the consumption of tea on the incidence of anemia. Consumption of tea was 36.89 times more likely to increase the risk of anemia than subjects who did not consume tea (OR= 36.89; 95% CI= 1.57 to 868.41; p= 0.025). The literature suggests that drinking tea may increase the risk of anemia by absorbing iron-based nutrients. Tea has several ingredients, including tannin and phytate, which can prevent the body from absorbing iron. Tannin which is not broken down by the digestive system forms a complex bond with iron. As a result, the iron complex loses its usefulness and is eliminated from the body as excrement. The prevalence of tea drinking is indirectly linked to the increased effects of anemia on expectant mothers, as well as low birth weight, preterm, and mortality (Machmud et al. 2019). Pregnant women who drink tea or coffee after meals and who eat a diet lacking in variety run a higher risk of developing anemia (Hanifah, Lilik, et al. 2021).

CONCLUSION

Factors affecting the incidence of anemia in pregnancy during the COVID-19 pandemic were pregnancy interval (OR=17.67; CI 95%= 1.01 to 116.00; p=0.049), gestational age (OR=11.39; CI 95% 1.12-116.00; p= 0,040), animal protein intake (OR= 0.25; CI 95% 0.03 – 2.38; p= 0,044), iron supplementation (OR= 108.47; CI 95% 2.36 – 4978.68; p= 0,016), consumption of tea (OR=36,89; CI95% 1.57 to 868.41; p=0.025). Mothers' education, family income, parity, frequency of ANC visits, and COVID-19 morbidity do not significantly affect the incidence of anemia in pregnancy. The limitations of the study were the small sample size and potential confounding factors that have not been recognized.

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