

Maternal Anemia in Patients with Preterm Delivery in Indonesia

Nastiti Hemas Mayangsari, Donel Suhaimi

Departement of Obstetrics and Gynecology, Faculty of Medicine, Universitas Riau, Indonesia

Abstract

Preterm delivery remains one of the leading causes of fetomaternal morbidity and mortality worldwide. Anemia during pregnancy is also a significant concern, and may contribute to adverse pregnancy outcomes including preterm birth, intrauterine growth restriction (IUGR), and postpartum hemorrhage (PPH). This study aimed to assess the prevalence of maternal anemia in women with preterm delivery and to evaluate its association with preterm-related complications. A retrospective cross-sectional study was conducted at the Obstetrics and Gynecology Department of Arifin Achmad Hospital, Pekanbaru, Indonesia. Anemia was defined according to the CDC criteria as hemoglobin levels below 11 g/dL in the first and third trimesters or below 10.5 g/dL in the second trimester. Data were collected from medical records of 654 preterm deliveries, of which 359 met the inclusion criteria. Among these, 204 women (56.82%) had anemia, while 155 women (43.18%) had normal hemoglobin levels. A significant association was found between anemia and preterm delivery ($p=0.010$). Maternal anemia was associated with preterm premature rupture of membranes (PPROM) ($p=0.035$, contingency coefficient=0.110, 95% CI). These findings suggest that maternal anemia is significantly correlated with preterm birth and its complications, particularly PPRM. Screening and early management of anemia in pregnancy may help reduce the risk of preterm delivery and improve maternal and neonatal outcomes.

Keywords: Anemia, hemoglobin, preterm birth, pregnancy complications, premature rupture of fetal membranes

Introduction

Preterm delivery remains one of the leading causes of maternal and perinatal morbidity and mortality worldwide.¹ Each year, more than 15 million preterm births occur globally, where 60% of the occurrence occurs in African and Asian countries. In 2015, Indonesia ranked ninth among countries with the highest number of preterm births, with a national incidence exceeding 15%.² The 3rd target of the Sustainable Development Goals (SDG) aimed to ensure healthy lives and promote well-being for all ages. Appropriate action in prevention, management, and care for preterm babies can reduce infant mortality and morbidity, along with reducing economic burden of preterm birth for families and the national health system.

The World Health Organization (WHO) has

issued various approaches to reduce preterm delivery, including nutritional support for pregnant women.² The amount of protein, calcium, and phosphorus become inadequate for the growth of preterm infants, such that fortification is recommended when enteral feeding is established. Recently, intestinal obstruction due to calcium soap formation has been reported. All the reported cases were fed fortified thawed human milk. It has not been elucidated how human milk fortifier reacts with milk fat globules (MFGs). Maternal Anemia is one of the main health problems that can be addressed with nutrition support. Centers for Disease Control and Prevention (CDC) defines anemia as a hemoglobin level below 11 g/dL (hematocrit <33%) in the first and third trimesters, or a hemoglobin concentration below 10.5 g/dL (hematocrit <32%) in the second trimester.³ WHO estimates that 35-75% of pregnant women in developing and 18% in developed countries suffer from anemia.³ However, although previously suspected, the relationship between preterm delivery and anemia is still not clearly

Corresponding Author:

Nastiti Hemas Mayangsari
Departement of Obstetrics and Gynecology,
Faculty of Medicine, Universitas Riau, Indonesia
Email: nastitimayangsari@gmail.com

defined.^{4,5}

A study by Ren et al. showed a relationship between anemia in the first trimester with risk of preterm delivery, IUGR, and low birth weight.^{6,7} This study compares the prevalence of anemia in women with preterm delivery. However, further research is needed to validate this relationship, particularly in the Indonesian population. To support holistic care and evidence-based clinical practice in the local context, this study aimed to compare the prevalence of maternal anemia in women with preterm delivery and explore its potential association with preterm-related complications.

Methods

This was a retrospective cross-sectional observational study conducted at the Obstetrics and Gynecology Department of Arifin Achmad Hospital, Pekanbaru, Indonesia. The study protocol was reviewed and approved by the Ethical Review Board for Medicine & Health Research, Medical Faculty Riau University, Indonesia. Data were collected from medical records of patients who delivered preterm from July 2018 to February 2021. A total of 654 patients aged ≥ 16 who gave birth prematurely (gestational age < 37 weeks) based on the patient register data was enrolled in this research. Exclusion criteria included multifetal pregnancies, polyhydramnios, poor obstetric history with a history of cervical incompetence, uterine or other abnormalities, and termination

with medical indications for both mother and fetus are excluded.

Inclusion patients were classified into anemic and non-anemic groups based on their hemoglobin levels. The limit value of hemoglobin in this study used CDC which defines anemia as a hemoglobin level below 11 g/dL (hematocrit $< 33\%$) in the first and third trimesters, or a hemoglobin concentration below 10.5 g/dL (hematocrit $< 32\%$) in the second trimester, considering the hemoconcentration condition in the second trimester of pregnancy.

Statistical analysis was performed using SPSS version 25.0. One sample Chi-Square test was used to evaluate the prevalence of anemia among patients with preterm delivery. Additional analyses assessed gestational age at delivery, the association between maternal anemia and the premature rupture of membranes, and differences in leukocyte counts between groups. A p-value < 0.05 was considered statistically significant.

Results

Of the 654 patients registered for preterm delivery, 359 met the inclusion criteria and were included in the data analysis. A total of 204 (56.82%) women had low hemoglobin concentrations, compared to 155 (43.18%) women with normal count. A statistically significant number of premature delivery patients with anemia was found ($p=0.010$). Patients were grouped into Anemia and Non-

Table 1 Baseline Characteristics of Study Participants

Characteristics	Mean $\pm$ SD		Frequency (n)		p-value
	Anemia (n=204)	Non-anemia (n=155)	Anemia (n=204)	Non-anemia (n=155)	
Age	29.4 $\pm$ 6.5	28.7 $\pm$ 6.3			0.706*
Gestation					
First			60	63	
Second			48	32	
$\geq$ Third			92	58	0.168†
No data			4	2	
Education					
Elementary			14	14	
Primary School			40	23	
High School			94	69	0.054†
Bachelor			46	48	
No data			10	1	

*Independent t-test; † Chi-square test

Table 2 Analysis of Anemia in the Study Population

	Frequency (n)		p-value	Contingency Coefficient
	Anemia (n=204)	Non-Anemia (n=155)		
Preterm Classification				
Extremely Preterm	14	24	0.031*	0.138
Very Preterm	57	40		
Late Preterm	133	91		
PPROM				
PPROM	115	70	0.035*	0.110
Non-PPROM	89	85		

* Chi-square test

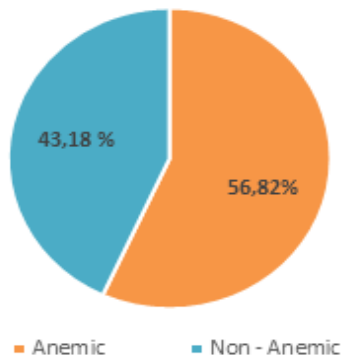


Figure 1 Prevalence of Anemia in Patients With Preterm Delivery

Anemia groups.

Hemoglobin and leukocyte levels were analyzed between the groups. Patients in the anemia group showed significantly lower hemoglobin (Hb) levels, with an average level

of 9.55 g/dl ($p=0.001$). However, there is no difference in the leukocyte count between the two groups ($p=0.142$).

Baseline characteristics between both groups were analyzed, with parameters such as

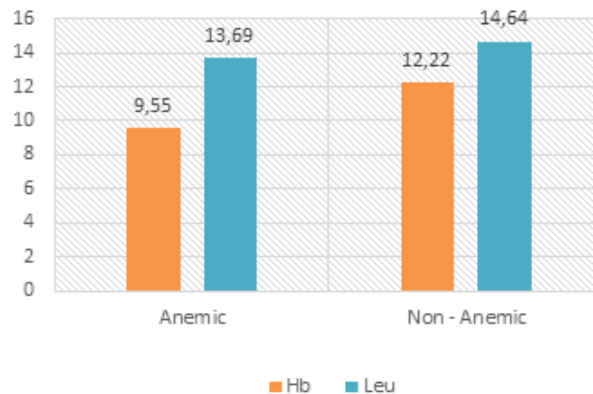


Figure 2 Hemoglobin and Leukocyte Levels in Patients With Preterm Delivery

* $p=0.010$ for hemoglobin (independent t test); † $p=0.142$ for leukocytes (independent t test)

age, gestation, and education level. There is no meaningful difference in baseline characteristics between both groups. It can be concluded that age, gestation, and education did not influence the incidence of anemia among premature birth patients.

In this study, most preterm deliveries occurred during the late preterm period, with a statistically significant difference between groups ($p=0.031$). Furthermore, a significant association was found between anemia and the occurrence of preterm premature rupture of membranes (PPROM) ($p=0.035$, Contingency Coefficient = 0.110, 95% CI).

Discussion

Preterm labor is a major reproductive health and half of the total cases are with unknown causes.⁸ Many studies regarding the relationship between anemia and adverse pregnancy outcomes have ended up with inconsistent findings. Baseline characteristics between both groups were analyzed, with parameters such as age, parity, and educational level. There's no important distinction of pattern characteristics between both groups. It concluded these parameters did not impact the frequency of anemia among preterm birth patients. This finding is different from the findings in other studies that found a strong association between preterm birth, anemia and maternal factors such as sociodemographic, psychological, genetic, paternal, and environmental elements. A study from Khezri⁸ reported a significant relationship between preterm delivery and spousal age that might be due to the influence of genetic factors that contribute to the incidence of anemia and preterm delivery. The finding of no correlation between educational status and the anemia event in preterm delivery is also inconsistent with the finding of a previous study that education contributes to mothers' lifestyle and nutritional status related to better knowledge about maternal health. The discrepancies in this finding may be due to the strong heterogeneity in the risk profile of anemia and the incidence of preterm birth. Studies indicate that anemia that contributes to the increased risk of preterm birth is the one that starts from the first trimester of pregnancy and this one is correlated with the knowledge and longer exposure window.^{9,10}

This study found that 56.82% of women with preterm labor had anemia. This supports previous findings by Kempinen et al., who

reported that anemia in pregnancy significantly increased the risk of preterm delivery (OR 1.90; 95% CI: 1.15–2.81) and preterm birth itself associated with an increased risk of neonatal mortality and morbidities such as impaired cognition, poor nutrition, neurological disorder and other chronic conditions that may lead to death.^{11–13} Khezri et al.⁸ also found a strong relationship between anemia and preterm birth. Anemia during pregnancy had about 2.69 higher odds of becoming preterm delivery compared to the non-anemic groups.

The timing and duration of anemia appear to be important. Anemia that appeared in all three trimesters of pregnancy was related to an increased risk of preterm delivery. On the other hand, anemia in mid-and late pregnancy was related to diminished ones. There were patterns of increased risk for PPRM in connection to anemia presentation in the early half or all through pregnancy. Anemia in early pregnancy or all through pregnancy may represent pre-existing, or early onset and determined iron deficiency state rather than hemodilution. In turn, it seems to actuate maternal contamination, hypoxia, and oxidative stress, and trigger the unconstrained onset of preterm birth.¹⁰

Anemia increases the risk of preterm birth by inducing low-grade chronic hypoxia, which reduces nutrition and oxygen-delivery capacity, causing an imbalance in placental oxygen and fetal demand and resulting in fetal stress. In addition, anemia might increase the risk of maternal stress and the release of Corticotropin-Releasing Hormone (CRH). It can cause a series of effects that lead to the activation of labor initiation.^{14,15}

This study also found a statistically significant association between anemia and the incidence of PPRM ($p=0.035$). This is consistent with findings from previous studies, including one in Belitung, where anemic pregnant women were found to have a threefold increased risk of PPRM. Other studies have reported that approximately 59% of anemic pregnant women experienced membrane rupture.^{14,15}

Tissue hypoxia, especially in the amniotic membrane will trigger oxidative stress. This situation increases mitochondrial activity and Reactive Oxygen Species (ROS) production. Collagen is the primary target for oxidative stress reactions. Increased ROS will cause the degradation of amniotic membrane collagen and premature rupture of membranes.^{14,16}

Within the recent study, a few qualities and restrictions ought to be considered. A solid point

of this study is the sample size which includes 3 years total sample from a referral hospital in Riau province. This study also confined some factors that could interfere with the result of the study. The limitation of this study was this study was conducted retrospectively so there was a limitation in controlling confounding variables. Further research is recommended by performing a multivariable examination thus an obvious relationship between maternal anemia in pregnancy with preterm labor will be clearly defined.

In conclusion, this study demonstrates that maternal anemia is significantly associated with preterm delivery and the occurrence of PPRoM. Management plan should address the occurrence, and actively screen and manage co-occurrence of anemia in premature birth patients. PPRoM should be expected as a possible complication of premature birth with anemia.

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