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Association between Maternal Hemoglobin Level and Incomplete Abortion in A West Java Tertiary Hospital, Indonesia

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Abstract

Objective: To evaluate the association between maternal hemoglobin concentrations and incomplete abortion.

Methods: An analytic, cross-sectional study with consecutive sampling method was conducted using medical records of 45 pregnant women aged 18–35 years old visiting the Obstetrics and Gynecology Department of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia from January 1, 2017 to December 31, 2019. Participants were grouped into incomplete abortion and non-abortion groups.

Results: Maternal characteristics in the incomplete abortion group showed that the majority of pregnant women in this group were 25.58 years of age, non-anemic (n=37, 82.22%), had no previous spontaneous abortion (n=40, 88.89%), and were nulliparous (n=25, 55.55%) with a mean interpregnancy interval of 4.03 years. The characteristics in both incomplete abortion group and non-abortion group were homogenous in the level of anemia (p-value=0.380), previous spontaneous abortion (p-value=1.00), and interpregnancy intervals (p-value=0.667). The mean hemoglobin concentration for the incomplete abortion group was 11.81 gr/dL (95% CI, 11.30 to 12.26). Heterogenous data was found in age (p-value=<0.001) and parity (p-value=0.002). Parity was a strong confounder, causing the hemoglobin concentration insignificantly associated to incomplete abortion (p-value=0.884).

Conclusion: No statistically significant association is found between hemoglobin concentration and incomplete abortion. Most women with incomplete abortion are around 25 years old, nulliparous, non-anemic with a mean hemoglobin concentration of 11.81 gr/dL with no history of previous abortion, and a rather secure interpregnancy intervals.

Keywords: Anemia, hemoglobin, incomplete abortion, interpregnancy intervals, parity

Introduction

Incomplete abortion is partial expulsion of conception or placenta weighing 500 grams or less with some parts left inside the uterus at gestational age before 20 weeks.[1] The incidence of spontaneous abortion is estimated at 23 million each year, globally.[2] The cause of spontaneous abortion is multifactorial, primarily due to chromosomal anomalies.[3] In Indonesia, according to a meta-analytic study, the most prominent factors are maternal age and parity.[4] Other factors include, education, early menarche, interpregnancy intervals, previous abortion, anemia, infections, hypertension and obesity.[3,4]

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Anemia in pregnancy is a condition in which pregnant women have hemoglobin (Hb) concentration below 11 gr/dL.[5] It can be caused by hemodilution, inadequate intake, heavy menstruation, excretion of iron through sweat, malaria or parasitic infection, and anemia before gestation.[3] The World Health Organization (WHO) states that the global prevalence of anemia in 2019 among pregnant women aged 15 to 49 years is 36.5%.[6] Nationally, the prevalence is 48.9% or 5 out of 10 pregnant women suffer anemia in 2018.[7] A study by Judistiani *et al*.[8] in Padjadjaran University following first-trimester pregnant women, showed an increasing number of anemia in the first trimester from 7.5% to 8.48% in 2020. The increased number is concerning as anemia is related to premature birth, low birth weight, preeclampsia, infections, and cardiac failure which ultimately increases mortality and morbidity rate of mother and baby.[3,9]

Some theories correlate anemia to a decrease in oxygen supply or iron for fetus' development, an increase in oxidative stress production and infection risk, and also a dysfunction in iron-dependent thyroid peroxidase.[10,11] A large-scale study involving almost 4 million women in China shows a significant association between severe anemia (<7 gr/dL) and an increased risk of abortion, while mild anemia (<11 gr/dL) is protective towards abortion.[10] Although various studies had been done regarding anemia and spontaneous abortion, they are rarely being specifically connected with incomplete abortion or using hemoglobin concentration without being categorized, moreover in West Java. Hence, this study aims to evaluate the association between maternal hemoglobin concentration and incomplete abortion.

Methods

This study was an analytic observational study with cross-sectional design using secondary data. Subjects were pregnant women with diagnosis of incomplete abortion (with gestational age <20 weeks) treated at Department of Obstetrics and Gynecology, RSUP Dr. Hasan Sadikin Bandung for 3 years, from 1st January 2017 to 31st December 2019. Data collection was carried out following the obtention of ethical exemption from the Research Ethic Committee Universitas Padjadjaran Bandung (1155/UN6.KEP/EC/2022) and RSUP Dr. Hasan Sadikin Bandung (LB.02.02/X.2.2.1/292/2023).

The inclusion criteria were: (1) pregnant women within 18 – 35 years of age, (2) diagnosed as incomplete abortion confirmed by ultrasound, and (3) recorded hemoglobin concentration when patient first came to the emergency department. The exclusion criteria were: (1) incomplete data such as patients' age, gestational age, and recorded hemoglobin concentration, (2) history of diabetes mellitus and thyroid dysfunction, (3) history of hypertension, (4) multiple gestation, (5) history of lupus, antiphospholipid syndrome, and thalassemia. Data required were age, interpregnancy intervals, and hemoglobin concentration as numerical variables; abortion incomplete, concluded level of maternal anemia, history of previous abortion, and parity as categorical variables. Consecutive sampling technique was used with minimal sample of 35 for each group of incomplete abortion and non-abortion calculated by unpaired numeric formula based on the hemoglobin concentration in a study by Guo *et al*.[12]

Diagnosis of incomplete abortion were confirmed by ultrasound. Hemoglobin concentration were obtained on admission from medical records for incomplete abortion cases. Hospital Information System (SIRS) was used to obtain data for non-abortion cases from women with spontaneous delivery in the same time period. The data presented in mean, median, standard deviation, minimum, maximum values, and further categorized for anemia. Classification of anemia according to WHO consisted of non-anemia (Hb ≥11 gr/dL), mild anemia (Hb 10 – 10.9 gr/dL), and moderate anemia (Hb 7 – 9.9 gr/dL).[5] This study also categorized parity based on number of delivery at gestational age ≥24 weeks as nulliparity (0 child), primiparity (1 child), and multiparity (≥2 children). Qualified data was processed using Microsoft Excel and IBM® SPSS® 26.

Univariate analysis was done to describe subjects' characteristics. Hemoglobin concentration data was tested for its normality using the *Kolmogorov-Smirnov* test. A subsequent bivariate analysis with confidence intervals (CI) of 95% was used to test the hypothesis regarding the association of maternal hemoglobin concentration and incomplete abortion. *Chi Square* test was used for level of anemia and parity, whereas, *Fisher-exact* test was used to analyze number of previous spontaneous abortion. The results were considered statistically significant and interpreted as having cause-effect association

if *p*-value ≤0.05.

Results

Consecutive sampling was taken from secondary data registry and 45 samples were selected in each group of incomplete abortion and non-abortion from 1st January 2017 to 31st December 2019.

Maternal characteristics (Table 1) showed mean age for incomplete abortion group were 25.58 years old. High cases of non-anemia was found in both incomplete abortion and non-abortion groups. Mild and moderate anemia cases was higher among non-abortion group, although not significantly different. Most subjects in both groups had no previous spontaneous abortion. Interpregnancy intervals in abortion incomplete group had mean of 4 years, meanwhile in non-abortion group was 3.45. Both incomplete abortion and non-abortion cases had a high number among women with zero parities, although it was significantly higher in non-abortion group. This study presented that 2 compared groups, incomplete abortion and non-abortion groups, had similar baseline characteristics to be compared in level of anemia (*p*-value 0.380>0.05), number of previous spontaneous abortion (*p*-value 1.00>0.05), and interpregnancy intervals (*p*-value 0.667>0.05). However in both groups, number parity (*p*-value 0.002<0.05) and age (*p*-value <0.001<0.05) were not similar. *Post hoc* test was done to each parity category. The results for nulliparity, primiparity, and multiparity were 1.00>0.05, 0.833>0.05, and 1.00>0.05, respectively. This showed that heterogeneity of parity in the compared groups were significantly associated with the association between hemoglobin concentration and incomplete abortion. Hence, the number of parity could confound and cause no significant association between hemoglobin concentration and incomplete abortion.

The mean and median of hemoglobin concentration in incomplete abortion population was 11.81 gr/dL and 11.80 gr/dL, respectively. In non-abortion population, the mean was 11.90 gr/dL and the median was 12.20 gr/dL. Further analysis was done to define the association between hemoglobin concentration and incomplete abortion after normality test. Non-parametric independent-samples *Mann-Whitney U* test was used due to abortion group was normally distributed and non-abortion group was not normally distributed. This analysis showed

Table 1 Characteristics of the Study Population

Characteristics	Incomplete Abortion (n=45)	Non-Abortion (n= 45)	*p*-value
Age (years)			
Mean (SD)	25.58 (4.59)	29.16 (4.79)	<0.001
Anemia Level, n (%)			
Non-Anemia	37 (82.22%)	32 (71.11%)	
Mild Anemia	2 (4.45%)	5 (11.11%)	**0.380**
Moderate Anemia	6 (13.33%)	8 (17.78%)	
Number of Previous Spontaneous Abortion, n (%)			
0	40 (88.89%)	40 (88.89%)	**1.00**
1	5 (11.11%)	5 (11.11%)	
Interpregnancy Intervals (years)			
Mean (SD)	4.03 (2.86)	3.45 (3.08)	0.667
Parity, n (%)			
Nulliparity	25 (55.55%)	40 (88.89%)	
Primiparity	12 (26.67%)	1 (2.22%)	0.002
Multiparity	8 (17.78%)	4 (8.89%)	

Table 2 The association between Hemoglobin Concentration and Incomplete Abortion

Variable	Hemoglobin Concentration (gr/dL)		95% CI	*p*-value
	Mean (SD)	Median (range)		
Incomplete Abortion	11.81 (1.53)	11.80 (7.60-14.70)	11.30 – 12.26	0.884
Non-Abortion	11.90 (1.68)	12.20 (8.30-14.70)	11.31 – 12.31	

p-value 0.884>0.05, there was no statistical significant association between hemoglobin concentration and incomplete abortion (Table 2).

Discussion

In this study, we found that maternal hemoglobin concentration in early pregnancy was not associated with incomplete abortion. Hemoglobin concentration in incomplete abortion had lower mean number of 11.81 gr/dL compared to non-abortion group of 11.90 gr/dL. Similar difference in concentration was also reported by Guo *et al*.[12] among women treated at the Beijing Obstetrics and Gynecology Hospital, in which first trimester pregnant women had higher mean hemoglobin concentration of 13.22 gr/dL as opposed to women with spontaneous abortion of 12.59 gr/dL. A study by Díaz-López *et al*.[11] in 2021 and Xu *et al*.[10] in 2020 did not correspond to our findings which showed that an increased risk of spontaneous abortion was found in women with severe anemia (*p*-value=<0.001; OR, 1.52; 95% CI, 1.25 to 1.86), low concentration (Hb <11 gr/dL; *p*-value=0.002<0.05) and high concentration (Hb>14 gr/dL; *p*-value=0.012<0.05).

The association result might have appeared due to the fact that women were hemorrhaging for hours to days before hospital admittance, a strong confounding factor of parity and age, and/or other factors that were not established in current study. Moreover, blood tests used as data was taken on the patient's admittance to the hospital, the very first antenatal care (ANC) hemoglobin data were not available as most patients had ANC outside the area of study and some may not even seek any care at all. Although current study showed that most pregnant women in first trimester had hemoglobin concentration above lower cutoff of 11 gr/dL determined globally, this number was still lower compared to other pregnant women outside of Indonesia. This might be due to the fact that there were differences in demography, climate, lifestyle, and health-seeking behaviors. Low hemoglobin level during adolescence (aged 10-18 years) was said to be carried over to adulthood and contribute to anemia in pregnancy, hence it had become important to prepare early in reaching adequate hemoglobin level for preconception.[13]

Mean age for incomplete abortion cases was 25 years, which was younger than non-abortion cases. A study in Norway showed an absolute lowest risk of spontaneous abortion in pregnant women 27 years of age, ranging among women of 25–29 years old.[14] A case-control study by Yanti L.[15] showed that maternal age had significant positive correlation with spontaneous abortion (*p*-value=<0.01; r=0.297), although another study showed that there was no significant correlation (OR, 1.587; *p*-value=0.202<0.05).[16] Findings in the current study might show that women with more mature age had a more solid plan to conceive, therefore they were more open in finding support or information, restricting their daily activities and sought more care or supplementations in order to achieve a successful pregnancy.

Most women in incomplete abortion group fell in non-anemia category and this corresponded with a study done at Bahagia General Hospital in Makassar, but did not correspond with a study done in Kediri district in 2017, where the highest occurrence of abortion happened in subjects with severe anemia (59.5%; ρ value=0,000<0,05; r=0.504).[17,18] The non-anemic state presented by most subjects might suggest that they had received adequate care in terms of Fe or multi-vitamins supplementations, nutritious intake and healthy lifestyle. Although, the number of hemoglobin concentration alone could not be accounted for adequate iron stores. Several mechanism due to anemia and iron deficiency in pregnancy could cause

spontaneous abortion. Hypoxic state due to decreased in oxygen supply could stimulate the production of cortisol by fetus which disturbed fetal development and estrogen-progesteron function, that caused cervix dilation and myometrium contraction.[11,19] Increased oxidative stress could disturb trophoblast invasion and the development of spiral arteries which were not yet embedded firmly.[18] Therefore, explained the early expulsion of conception.

Most subjects with incomplete abortion had no history of previous spontaneous abortion (88.89%), corresponded with a study done in the same Bandung region which showed higher number of subject in incomplete abortion group without previous abortion of 56.98% (p-value=0.111>0.05) at Al-Ihsan Regional General Hospital with no significant correlation.[20] Another study by Arnianti *et al*.[21] in 2021 had different results which abortion group with previous abortion had percentage of 56.5% and increased risk of 2.97 times (95% CI, 1.05 to 8.37) for subsequent abortion. History of spontaneous abortion did not determined that the subsequent pregnancy would end in another abortion, although it would increase the risk up to 20%.[3] It was speculated that history of spontaneous abortion could cause trauma physically and psychologically. Curettage could scar the endometrium, leading to suboptimal condition for the fetus and placenta to grow. The preceding loss could lead to stress, substance abuse, and unhealthy lifestyle that could put current pregnancy at risk.

According to the interpregnancy intervals, subjects with incomplete abortion had mean intervals of 4 years differing from 4 months to 9 years. A case-control study by Purwaningrum *et al*.[22] stated that pregnant women with interpregnancy intervals of less than 6 months or more than 48 months had a four-fold increased risk (OR, 4.2; p-value=0.01<0.05) of spontaneous abortion rather than intervals between 6 to 48 months. Mremi *et al*.[23] in 2022 found that interpregnancy intervals was significantly correlated with anemia post-partum and was 10 times higher in women who had less than 2 years between pregnancies. Pregnancy had been progressively using maternal iron stores for the development of the fetus in each trimester, hence it would be deficient by the end of the term. It was said that the body needed at least eight weeks to return red blood cells volume and hematocrit to normal, not to count other events that could make the wait time longer, such as anemia during pregnancy, blood loss during delivery, post-partum hemorrhage, and lochia that happened for weeks.[3] A big gap between pregnancies (>5 years) was also considered to be a risk due to an increased in maternal age and the need for the uterine wall to adjust as if it was the first pregnancy. Hence, preconception counseling and supplementations became important to anticipate such factors that could contribute to spontaneous abortion.

Incomplete abortion most often occurred in nulliparity or women who were pregnant for the first time (55.56%). These findings corresponded to a study done in Mojokerto in 2022 which stated that first pregnancy had risk for abortion (42.4%).[24] Different results were reported from a study in Al-Ihsan General Hospital Bandung in 2020 that multiparity had higher number (66.67%) among women with incomplete abortion and more number of parity was causing higher proportion of abortion (p-value=0.08<0.05).[20] This study, supported by another study in Nepal showed that parity was a significant predictor of hemoglobin concentration, as well as maternal age.[25] Increasing parity numbers could lead to decrease hemoglobin concentration and serum ferritin in the subsequent pregnancy due to inadequate replenishment from the preceding spent of iron stores, which was also influenced by interpregnancy intervals.[4]

This study concludes that there is no significant association between maternal hemoglobin concentration in early pregnancy and incomplete abortion. This study also reveals that parity could be a strong confounder and prevalence of anemia in pregnant women in RSUP Dr. Hasan Sadikin Bandung is low, hence can be a factor in explaining the non-association. This study has several limitations. Most subjects are not anemic and study populations are quite different as data for incomplete abortion were taken from medical records and non-abortion were taken from SIRS. Hemoglobin concentration data from the very first antenatal care cannot be acquired considering the subjects were receiving care outside of the study location. A limited period of time and being single-centred have made the sample study small and might not accurately reflect the actual condition. Future studies are suggested to be multi-centred and have a longer period of time in hope that more precise results can be obtained. It is recommended to do analysis solely among pregnant women with anemia.

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