

Haemoglobin Level of Pregnant Women was Associated with History of Anemia During Adolescent Period: Findings from the Indonesia Family Life Survey



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ABSTRACT

Introduction: Low hemoglobin levels in pregnant women are global health problem that adversely affect the mother's and newborn's health. There is no study proving the effect of anemia during adolescence in pregnancy, especially in Indonesian population. This study aimed to investigate the effect of anemia in adolescence on the hemoglobin level during pregnancy, using Indonesian Family Life Survey (IFLS) data.

Methods: This retrospective cohort study used the 1997, 2007 and 2014 IFLS data. The hemoglobin levels in adolescents aged 10-18 years were obtained from the IFLS-II data in 1997. Then, the hemoglobin levels during pregnancy from the same individuals were tracked from the IFLS-IV in 2007 and IFLS-V in 2014. Data from 210 subjects were included in the analysis as these subjects had the complete data on hemoglobin levels during adolescence and pregnancy and all other considered confounding variables, such as maternal age, iron protein, vitamin C consumption, education, working status, residence, socioeconomic status, gestational age at data collection, parity, antenatal care, iron supplement consumption. Data was analyzed by T tests, Pearson's correlation tests and General Linear Model.

Results: The mean hemoglobin levels of pregnant women was 11.23 g/dL with standard deviation 1.271 and the prevalence of anemia during adolescence was 34.3%. There was a significant difference of 0.447 g/dL in the average hemoglobin levels in pregnant women with and without history of anemia during adolescence ($p=0.023$). The hemoglobin levels in pregnant women also differed among trimesters of gestational age ($p=0.001$). After being controlled for vitamin C and protein consumption, anemia status during adolescence still has a significant effect on lowering hemoglobin level during pregnancy.

Conclusion: Anemia during adolescence negatively impacts pregnant women's hemoglobin levels. Prevention programs for anemia in pregnant women should be started from adolescence period.

Keywords: Adolescents, hemoglobin level, anemia, pregnancy, gestational age.

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INTRODUCTION

Hemoglobin is essential for oxygen circulation from the lungs to all cells in human body.^{1,2} Low hemoglobin levels lead to multiple adverse health problems and additional costs to the health system and society.^{3,4} Pregnancy is the most vulnerable phase in the life cycle to experience low hemoglobin level.⁵ Pregnant women with low hemoglobin levels have a higher risk for postpartum hemorrhage and maternal death.⁶⁻¹² It has not been proven that a history of anemia during adolescence is the main cause of a low hemoglobin level during pregnancy. However, a study showed that anemia condition in adolescence continually

impact the health status in the following phase of life, which is the preconception stage to pregnancy.¹³

Low hemoglobin levels in adolescents affect oxygen transport in the blood which lead to lower physical and mental capacity, and result in a decrease in quality of life.¹⁴ Low hemoglobin levels during the pregnancy would also threat newborns' health. The newborns of mothers with low hemoglobin levels are more likely to experience premature birth, low birth weight, and death.^{6,8,15,16} They also have a higher chance to have brain and body cell growth problems and acquire nutritional problems, including stunting and wasting.¹⁷⁻²⁰ This condition could

continually decrease the immune system protecting the children from infection and hinder the intelligence quotient (IQ) development at school age period.¹⁷⁻²⁰ In the long term, these children would have a higher risk of low cognitive and motoric performance and acquire neurophysiologic impairment.^{21,22}

The prevalence of low hemoglobin levels among pregnant women is approximately 40% or 614 million worldwide.²³⁻²⁵ Most of these problems occur in Low and Middle-Income Countries (LMICs), including countries in Southeast Asia.^{26,27} The prevalence of low hemoglobin levels among pregnant women in Indonesia is among the world's highest. The

2018 Indonesian Basic Health Survey (RISKESDAS) revealed that the prevalence of low hemoglobin levels among pregnant women has increased from 37.1% in 2013 to 48.9% in 2018.²⁸ Therefore, pregnant women in Indonesia are considered the most vulnerable population to have severe health problems.²⁹

Previous studies have identified several factors influencing the hemoglobin levels among pregnant women. Low hemoglobin levels among pregnant women is influenced by the lack of nutritional reserves in the body and a history of low hemoglobin levels before pregnancy.^{30,31} History of low hemoglobin levels during the adolescent and preconception period increases the risk of having low hemoglobin levels during pregnancy.⁶ RISKESDAS data showed that a total of 32% of adolescents had low hemoglobin levels in 2018.³² This condition could continue up to pregnancy period and would cause long-term negative impacts for women and their children.³³

The Indonesian government has implemented several measures to reduce the prevalence of low hemoglobin levels among pregnant women. However, the programs have not shown promising results. The intervention still focuses only on the pregnancy period instead of using a life-cycle approach. Although hemoglobin levels maintenance during adolescence has been well known, the study analyzing the hemoglobin level during pregnancy using a life-cycle approach is still lack of numbers. This study aimed to investigate the effect of anemia status during adolescence on pregnant women's hemoglobin levels in Indonesia.

METHODS

Study Design and Participants

This study used a fixed retrospective cohort study design on longitudinal data from the Indonesian Family Life Survey (IFLS), a multilevel, multi-topic, and large-scale survey in Indonesia, which provides extensive information, including household and community-facility aspects. IFLS data were collected through a thorough process of enumerators selections and trainings to ensure data validity. The results of this survey contained data of the same individual in

several batches to analyze the dynamics of the individual's behavior. It has been carried out in five batches from IFLS-I to IFLS-V, conducted in 1993, 1997, 2000, 2007, and 2014, respectively. IFLS data is publicly accessible. Therefore, there is no need to collect informed consent from the participants and approval from institutional review board for this secondary data study.

In this study, we observed the hemoglobin levels of adolescent girls aged 10-18 years from IFLS-II in 1997 as the baseline data. Then, the hemoglobin levels from the same individuals were tracked in IFLS-IV and IFLS-V data if they were in the pregnancy states. Moreover, we also extracted the confounding variables from the surveys. The authors determined several inclusion criteria for the subjects, including women aged 10-18 years in the IFLS-II (1997), and being pregnant

during the data collection of the IFLS III (2007) or IFLS IV (2014). We excluded the participants with incomplete hemoglobin levels data. We found a total of 210 eligible participants for this study (Figure 1).

Measurements

The dependent variable of this study was the hemoglobin levels during pregnancy, obtained from the IFLS-III or IFLS-IV. The hemoglobin levels of the capillary blood from the participants were measured using HemoCue, which comprised a micro cuvette and a photometer. The hemoglobin levels were assessed in g/dL.

The sociodemographic characteristics during adolescents were included in the models as the covariates, including age (years), education attainment (diploma/college, senior high school, junior high school, elementary school, and no school), working status (working and not working),

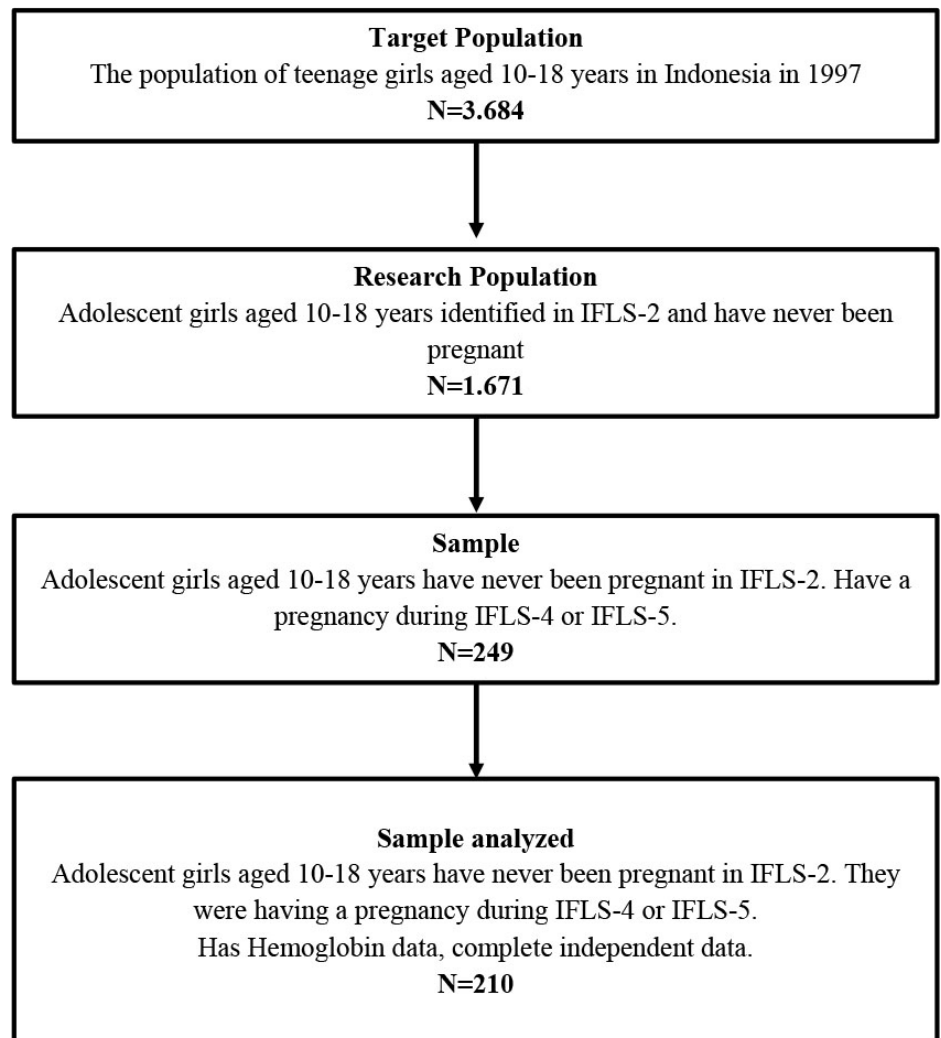


Figure 1. Population and sample flowchart of the study.

residences (village and city), and economic status (from the quartile 1: the poorest to the quartile 5: the richest). The predictive variable was the anemia status during the adolescent period, which obtained from the IFLS-II in 1997. The hemoglobin levels in all waves of IFLS were examined by the same method.

Gestational age at the date of data collection was counted and then classified into three categories (trimesters I, II or III). The subjects were classified as multiparous if they had ever given birth to more than one alive child, while the others were called primiparous. The consumption of iron-folate tablets and antenatal examination were categorized into dichotomous variables, with yes and no answer choices. The frequency of food consumption containing protein, iron, and vitamin C in the past seven days was also recorded. The subjects who had consumed poultry meat, fish or beef were included in the category of iron-source food consumption; and fruits such as mango, papaya and carrot were included in vitamin C-source food consumption.

Statistical Analysis

Univariate analysis was conducted to describe hemoglobin levels and maternal age. Education attainment, working status, economic status, marital status, residence locations, gestational age, parity, antenatal examination, iron supplement consumption, and types of food intake were shown in frequency distribution.

In bivariate analysis, we used the independent T-tests, one-way ANOVA, and Pearson Correlation tests, to determine the correlation between the independent variables with the hemoglobin levels during pregnancy. The independent variables with *p* values of <0.05 in the bivariate analysis and the ones considered as important variables were entered into the multivariate analysis. General Linear Models (GLMs) were run to find the best final model. All of the analysis were performed using Stata ver. 17 and IBM SPSS ver. 28.

RESULTS

Characteristics of the 210 subjects are shown in Table 1. Most of the subjects had a high school education (39.05%), did not

Table 1. Characteristics of participants (n=210).

| Variables | | n | % |
|-----------------------------|---------------------------|-----|------|
| Level of education | No School | 2 | 1.0 |
| | Elementary school/MI | 35 | 16.7 |
| | Junior high school | 54 | 25.7 |
| | Senior high school | 82 | 39.0 |
| | Diploma/ College | 37 | 17.6 |
| Working Status | Not Working | 127 | 60.5 |
| | Work | 83 | 39.5 |
| Residence | Village | 93 | 44.3 |
| | City | 117 | 55.7 |
| Socio-Economic | Quantile 1 | 29 | 13.8 |
| | Quantile 2 | 53 | 25.2 |
| | Quantile 3 | 37 | 17.6 |
| | Quantile 4 | 60 | 28.6 |
| | Quantile 5 | 31 | 14.8 |
| Gestational Age | 1 st Trimester | 55 | 26.2 |
| | 2 nd Trimester | 77 | 36.7 |
| | 3 rd Trimester | 78 | 37.1 |
| Parity | Primiparous | 89 | 42.4 |
| | Multiparous | 121 | 57.6 |
| Antenatal Check-up | No | 16 | 7.6 |
| | Yes | 194 | 92.4 |
| Consumption of iron tablets | No | 71 | 33.8 |
| | Yes | 139 | 66.2 |
| Teenage Anemia Status | Anemia | 72 | 34.3 |
| | Not Anemia | 138 | 65.7 |
| Teens Residence | Village | 112 | 53.3 |
| | City | 98 | 46.7 |
| Youth Socio-Economic | Quantile 1 | 60 | 28.6 |
| | Quantile 2 | 39 | 18.6 |
| | Quantile 3 | 46 | 21.9 |
| | Quantile 4 | 50 | 23.8 |
| | Quantile 5 | 15 | 7.14 |

n, number of participants

work (60.5%), and lived in urban areas (55.7%). At adolescent age, 34.3% of the subjects suffered from anemia, 53.3% lived in rural areas, and 28.6% were poor (in the 1st quintile). Table 2 shows the maternal hemoglobin levels, age, iron supplement consumption and food consumption frequencies. Those continuous data were normally distributed.

This study found significant differences

in the average hemoglobin levels between pregnant women with and without anemia during adolescence period (*p*= 0.023) and between gestational ages (*p*= 0.001), which can be seen in Table 3. Table 3 also shows that there was no difference in the mean hemoglobin levels of pregnant women among the categories of these independent variables of education level (*p*= 0.480), employment status (*p*= 0.682),

Table 2. Description of maternal hemoglobin levels, age and food consumption.

| Variables (units) | Range | Mean | SD |
|--|---------|------|-----|
| Hb levels of pregnant women (g/dl) | 7 - 15 | 11.2 | 1.2 |
| Age of pregnant women (years) | 18 - 35 | 26.7 | 3.8 |
| Consumption of iron source food (days/week) | 0 - 7 | 2 | 1.5 |
| Consumption of protein source food (days/week) | 0 - 7 | 4 | 1.7 |
| Consumption of vitamin C source food (days/week) | 0 - 7 | 3 | 1.7 |

Hb: hemoglobin; SD: standard deviation

Table 3. Distribution of average hemoglobin levels of pregnant women based on predictor variables.

| Variables | Categories | Pregnant women's hemoglobin levels | | |
|-----------------------------|---------------------------|------------------------------------|-----|---------|
| | | Mean | SD | p-value |
| Adolescent's Anemia Status | Anemia | 11.0 | 1.3 | 0.023 |
| | Not Anemia | 11.4 | 1.2 | |
| Level of education | No School | 11.9 | 0.7 | 0.480 |
| | Elementary school/MI | 11.2 | 1.4 | |
| | Junior high school | 11.2 | 1.3 | |
| | Senior high school | 11.3 | 1.2 | |
| | Diploma/ College | 10.9 | 1.2 | |
| Working Status | Not working | 11.3 | 1.3 | 0.682 |
| | Work | 11.2 | 1.2 | |
| Residence | Village | 11.0 | 1.3 | 0.059 |
| | City | 11.4 | 1.2 | |
| Socio-economic status | Quantile 1 | 10.8 | 1.2 | 0.498 |
| | Quantile 2 | 11.3 | 1.4 | |
| | Quantile 3 | 11.3 | 1.1 | |
| | Quantile 4 | 11.3 | 1.3 | |
| | Quantile 5 | 11.3 | 1.1 | |
| Gestational age | 1 st Trimester | 11.8 | 1.1 | 0.001 |
| | 2 nd Trimester | 11.1 | 1.1 | |
| | 3 rd Trimester | 11.0 | 1.1 | |
| Parity | Primiparous | 11.3 | 1.3 | 0.410 |
| | Multiparous | 11.2 | 1.3 | |
| Antenatal check-up | No | 11.6 | 1.1 | 0.182 |
| | Yes | 11.2 | 1.3 | |
| Consumption of iron tablets | No | 11.5 | 1.3 | 0.052 |
| | Yes | 11.1 | 1.2 | |

Hb, hemoglobin; SD, standard deviation

place of residence ($p= 0.059$), socio-economic status ($p= 0.498$), parity ($p= 0.410$), antenatal check-up ($p= 0.182$), and consumption of iron tablets ($p= 0.052$). Table 4 shows a weak and negative correlation pattern between hemoglobin levels of pregnant women and protein consumption ($r= -0.178$, $p= 0.010$).

Table 5 shows the results of the multivariate analysis with GLM. The study found a significant effect of adolescent's anemia status on hemoglobin levels of pregnant women with a p -value of 0.013. The mean hemoglobin levels of pregnant women who had a history of anemia during their adolescence was 0.45 g/dL,

lower than the ones who did not have a history of anemia after controlling for variables of gestational age, intake of protein sources, and intake of vitamin C sources.

DISCUSSION

The purpose of this study was to predict the hemoglobin level during pregnancy using historical data on anemia status during adolescence period in Indonesian population. This study confirmed that anemia history during adolescence could indicate the hemoglobin level during pregnancy. Pregnant women with a history of anemia in adolescence period have lower hemoglobin levels than pregnant women without a history of anemia. Although it has not been established that the history of anemia during the adolescent period is the only factor for a low hemoglobin level during pregnancy, this study emphasizes that adequate hemoglobin should be prepared as early as possible, starts from adolescence period.

This study supported the findings of the previous study using focus group discussion method with 11 experts in women and child health, nutrition, clinical psychology, and education fields, showed that the anemia condition that occurred during adolescence would not only affect their health status at that time but would also continue to affect their health status in preconception phase to pregnancy.¹³ In addition, adolescent girls with anemia were at risk of having low hemoglobin levels in adulthood, especially during pregnancy. The physiological change (i.e., low hematocrit) during pregnancy can further strengthen this risk, causing pregnant women to be more susceptible to decreased hemoglobin levels.³⁴

Individual nutritional status and the risk of nutritional problems in the next life cycle are interrelated.³⁴ This cycle begins in women at childbearing age who have dietary issues and are at risk of experiencing similar nutritional problems when entering the pregnancy phase, resulting in the birth of children who grow up with dietary issues.³⁴ Low hemoglobin levels are among the most common nutritional problems experienced by adolescent girls and pregnant women worldwide.²⁴

Table 4. Correlation analysis of food intake and maternal age with hemoglobin levels of 210 pregnant women.

| Variables (unit) | <i>r</i> | <i>p</i> -value |
|--|----------|-----------------|
| Intake source of iron (day/week) | 0.001 | 0.989 |
| Protein source intake (day/week) | -0.178 | 0.010 |
| Intake of vitamin C sources (day/week) | 0.125 | 0.070 |
| Mother's age (years) | 0.018 | 0.920 |

r, correlation

Table 5. Results of general linear model analysis of pregnant women's hemoglobin levels based on hemoglobin levels during adolescence.

| Predictor variables (unit) | | Pregnant women's hemoglobin levels | | | |
|-----------------------------------|---------------------------|------------------------------------|-----------|-----------------|-------|
| | | β | 95% CI | <i>p</i> -value | |
| Teenage anemia conditions | Not anemia | | reference | | |
| | Anemia | -0.45 | -0.80 | -0.10 | 0.013 |
| Gestational age | 1 st Trimester | | reference | | |
| | 2 nd Trimester | -0.61 | -1.03 | -0.19 | 0.005 |
| | 3 rd Trimester | -0.64 | -1.06 | -0.22 | 0.003 |
| Protein source intake (day) | | -0.14 | -0.24 | -0.05 | 0.004 |
| Intake of vitamin C sources (day) | | 0.17 | 0.02 | 0.32 | 0.030 |

Model summary $r^2 = 0.13$, p -value=0.000.

β , beta coefficient; CI, confidence interval.

Adolescence is the critical period to build adequate iron stores as the main component of hemoglobin formation, which may determine hemoglobin levels during pregnancy.³⁵ Another previous study also found that women who entered the early stages of pregnancy with adequate iron stores were less likely to experience low hemoglobin levels during pregnancy.³⁶ Ensuring adequate hemoglobin levels as early as possible during adolescence can have a long-term positive impact on the born children. Previous studies reported that a decrease in hemoglobin concentration in the preconception phase contributed to an increased risk of low birth weight³⁷, risk of preterm birth^{37,38}, and a decrease in birth length and head circumference of the newborns.³⁹

This current study reported a significant association between gestational age and hemoglobin levels of pregnant women. In each different trimester of pregnancy, there was a decrease in hemoglobin level. At the second trimester of pregnancy, the hemoglobin levels decreased by 0.608 g/dL from the level at the first trimester. The most significant decrease was in the third

trimester, which was 0.644 g/dL lower than the second trimester. This study results were similar to some previous studies that showed the prevalence of pregnant women with low hemoglobin levels was about 3 times higher in the third trimester compared to the first trimester.^{40,41} The tendency of higher prevalence of pregnant women with low hemoglobin levels at older gestational age can be caused by several factors. As gestational age increases, both mother and fetus increase oxygen consumption, which is associated with significant hematological changes.⁴⁰ In addition, pregnant women also experience a significant increase in red blood cell mass and a slight increase in plasma volume. This condition triggers a decrease in the hemoglobin concentration ranged from 1-2 g/dL at the end of the second and third trimesters due to hemodilution.⁴²

An increase in nutritional needs for older gestational age also triggers low hemoglobin levels. Fetal growth requires a lot of nutrients, including iron⁴³, which increase iron requirements during pregnancy until 2- or 3-fold.⁴⁰ A study stated that a significant increase

in iron requirements during pregnancy was starting from 0.8 mg/day in the first trimester to 3.0-7.5 mg/day in the third trimester.⁴⁴ Pregnant women with low hemoglobin levels in the third trimester were at risk for a decrease in birth weight, birth length, head and chest circumference of their newborns.^{45,46}

In addition to protein intake, intake of energy, vitamin A, iron (Fe) and iron absorption inhibitors has an impact on the hemoglobin levels of pregnant women. Pregnant women with higher energy intake were found to have greater hemoglobin levels.⁴⁸ We determined that these previous findings could be the reason of the negative relationship found in this study. Although pregnant women consume sufficient amount of protein, their hemoglobin levels will typically stay low because poor energy intake prevents the body from converting protein into hemoglobin. This study found that most of the subjects had a low intake of Fe and vitamin C. Unfortunately, there were no further details about total energy intake and Fe absorption inhibitors usage in the IFLS. Furthermore, the measurement of protein intake was only performed based on the frequency of weekly protein consumption without any exact amount of consumption. These reasons caused limitation in data analysis, which further affected the study results.

Vitamin C is one of the micronutrients, which help iron absorption, especially when the body has a low iron intake. The presence of vitamin C in the food consumed increases stomach acidity, transfers iron from plasma to ferritin, and facilitates the iron reduction from ferric to ferrous form, which results in four times faster iron absorption in the small intestine.⁵⁴ An increase of 25-50 mg vitamin C consumption is known to raise iron absorption in the body.⁵⁵ Based on the results, consuming food containing vitamin C at every meal is highly recommended because it will increase the average hemoglobin level by 0.168 g/dL. Our results supported the previous study, which found that pregnant women at 16-32 weeks of gestation showed a higher hemoglobin levels when they were given iron tablets supplemented with vitamin C compared to those who were only given

iron tablets.⁵⁶ Another interventional study found a significant increase of 3.21 g/dL in the hemoglobin level of pregnant women with anemia after being given vitamin C supplementation.⁵⁷

In clinical setting, the results of the study can be used as a reference for anemia control programs for pregnant women. Some interventions to reduce the prevalence of low hemoglobin levels in pregnant women need to be started as early as possible, since adolescence period. These interventions are relatively easy and safe and have positive long-term impacts on the pregnancy outcomes.³⁷ These approaches will not rule out the efforts that focus on pregnant women but will complement ongoing efforts to overcome anemia problems at every stage of life.⁵⁸ Anemia prevention from adolescence period also gives benefits for pregnancy preparation since predicting the start of the pregnancy in women is difficult.⁵⁸ The period between adolescence and prior to pregnancy, is a critical time for women to maintain their hemoglobin levels. The duration of treatment to improve hemoglobin levels might not be long enough if the treatment was started from the time when the women realized that they are pregnant. Besides, the adequacy of protein and vitamin C intakes is also important to avoid low hemoglobin levels during pregnancy and improve pregnancy outcomes.

The strength of this study is related to large sample size obtained from nationwide survey, resulting in adequate statistical power, and generalizable findings. In addition, this survey used valid instruments and trained personnel. This study has several limitations that need to be considered. Firstly, self-reported food intake might result in information bias. Secondly, the interaction between low hemoglobin levels during pregnancy and its predictors could not be entirely determined since the IFLS questionnaires only covered limited variables.

CONCLUSIONS

This study found that history of anemia in adolescence period negatively affects pregnant women's hemoglobin levels. Pregnant women with history of anemia at adolescence period have lower

hemoglobin levels of 0.447 g/dL compared to pregnant women without history of anemia. Maternal hemoglobin levels will decrease along with increasing gestational age, with the lowest level at the third trimester. Consumption of vitamin C sources increases the average hemoglobin level of pregnant women by 0.168 g/dL.

The intervention to prevent low hemoglobin levels in pregnant women in Indonesia should be started from the adolescence period. Adequate iron supplementation and nutritional intake are also important to ensure adequate hemoglobin levels during adolescence until pregnancy.

AUTHOR CONTRIBUTIONS

SRTH, conceived the study design, data extraction and analysis, and paper writing. A, MIK, and SAN, performed the data analysis and interpretation, and paper writing. All authors have read and agreed to the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable.

INFORMED CONSENT STATEMENT

Not applicable.

DATA AVAILABILITY STATEMENT

The data analyzed in this study are publicly open data. Interested parties can apply on the website to obtain the data.

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