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Improving Hemoglobin Level with Increasing Copper, Cobalamin, and Iron Intake of Pregnant Women

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ABSTRACT: Over the past five years, there has been a dramatic increase in anemia problems among pregnant women in Indonesia. Almost half (48.9%) of pregnant women in Indonesia have anemia. Further research is needed to explore the role of additional nutritional deficiencies that cause anemia in Indonesia, apart from iron deficiency. The aim of this research was to determine the characteristics and nutrient intakes affecting pregnant women's hemoglobin levels. A cross-sectional study was carried out from May to October 2019 on 60 pregnant women at Public Health Center Kebon Jeruk, Jakarta. The independent variables were pregnant women's characteristics, intake of energy, protein, folate, vitamin B6, B12 (cobalamin), C, E, iron, copper, and calcium. The dependent variable was hemoglobin level. Multiple regression using dummy variables was used for multivariate analysis. The average age is 28.3±5.5 years old, with no mothers being of risky age. The average hemoglobin (Hb) level is 11.5±1.4 g/dL. The majority of women are in their third trimester (42%). The variables that significantly affect hemoglobin levels are the third trimester, intake of iron, vitamin B12, and copper. Increasing the intake of iron, vitamin B12, and copper effectively improves hemoglobin levels among pregnant women. It is recommended to provide iron tablets in multi-nutrient form, and further research is needed for its effectiveness.

KEYWORDS: anemia, copper, iron, multi-nutrient form, pregnant woman, vitamin B12.

INTRODUCTION

Anemia is a condition characterized by a low hemoglobin level in the blood (WHO, 2011), resulting in a decrease in the quality or quantity of red blood cells, which has an impact on decreasing oxygen delivery to tissues (Chaparro and Suchdev, 2019). Anemia can occur in all age groups but is more common in pregnant women and children (Le, 2016). In normal pregnancy, hemoglobin concentration decreases because of the dilution as circulating blood volume increases (Haider et al., 2013).

Globally 30% of women of childbearing age (15-49 years) suffered from anemia in 2019 (WHO, 2019). The global anemia prevalence is about 9 percent in developed countries and 43 percent in developing countries (Wijayanti and Fitriani, 2019). Meanwhile, national anemia prevalence in women of childbearing age is 31%. Based on Basic Health Research 2018, almost half (48.9%) of pregnant women in Indonesia are anemic (MOH, 2019a). The problem of anemia is considered a high public health problem if the percentage reaches above 20%. Anemia in pregnant women is associated with adverse health effects for both mother and baby, such as mortality, perinatal mortality, growth retardation, and low birth weight, maternal anemia is strongly related to child anemia (Balarajan et al., 2011).

In 2018, maternal deaths in Jakarta increased from 44 to 53 deaths per 100,000 live births. This figure is higher than the maternal mortality rate in Singapore and Malaysia, 7 and 24 per 100,000 live births, respectively. As many as 25% of maternal deaths are caused by bleeding and infection (DKI, 2016). Maternal bleeding and infection may increase due to anemia (Di Renzo et al., 2015).

In Indonesia, research on the many kinds of anemia in pregnant women is very restricted. Thus far, the national initiative to minimize anemia in pregnant women has concentrated solely on the treatment of iron deficiency anemia (IDA) with Iron-Folic Acid (IFA) tablets. The initiative has been functioning for more than three decades, but the anemia problem has not been greatly reduced (Nadiyah et al., 2020).

In addition to iron, other nutrients have important roles in red blood cells and hemoglobin formation, including vitamin B12, copper, vitamin B6, folate, vitamin C (Humayun et al., 2021), vitamin E, and other inhibitory substances (Mahan and Escott-Stump, 2017). The complexity of the causes of anemia is a challenge to effectively address the cause of anemia.

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Accumulating evidence suggests that the proportion of anemia due to ID differs according to geographic setting, the burden of infectious disease, population group, and prevalence of other causes of anemia (Chaparro and Suchdev, 2019). Further research is needed to explore the role of additional nutritional deficiencies. This study examines the effect of the characteristics and intake of essential nutrients on the hemoglobin levels of pregnant women. Using a dietary approach, it would provide an overview of the possibility of deficiency of crucial nutrients that cause anemia, apart from iron deficiency (ID), which needs to be intervened in an anemia reduction program.

This research was located at the Kebon Jeruk Public Health Center (PHC), West Jakarta. It is located in a densely populated area with a middle to lower socioeconomic profile and has the highest number of pregnancy services (120-150 pregnant women per day). This study aims to analyze the factors affecting pregnant women's hemoglobin levels in Kebon Jeruk Sub-District, West Jakarta.

METHODS

Study Design and Sampling

This cross-sectional study was conducted from May to October 2019 at the PHC Kebon Jeruk, West Jakarta. This study included 60 pregnant women selected by purposive sampling technique. The inclusion criteria were pregnant women registered at PHC Kebon Jeruk, performing a hemoglobin check at the time of the study, not on specific diets, and being willing to be a respondent. Pregnant women who suffer from infection were excluded. This research has obtained ethical approval from the Esa Unggul University Code of Ethics Enforcement Council Number 0514-19.496/DPKE-KEP/FINAL-EA/UEU/X1/2019.

Data Collection and Processing

A preliminary study was conducted at the PHC Kebon Jeruk to capture socioeconomic profiles such as the total food expenditure of the household. The independent variables were age, trimester, education, husband's income, nutritional status using upper arm circumference (UAC), height, and nutrient intake. The nutrient intakes studied included energy, protein, vitamin B6, folate, vitamin B12, vitamin C, vitamin E, iron, copper, and calcium intake. The dependent variable was hemoglobin level.

Hemoglobin level was determined using the Hemocue method. A sample of ~10 ml of blood was taken by the analyst laboratory at PHC Kebon Jeruk. The tip of the hemocue cuvette was attached to the surface of the ring finger of the respondent that has been injured and bleeding until the cuvette was filled with blood. Hemoglobin levels will come out on the screen monitor of hemocue.

Informations on gestational and maternal age, husband's income, and education were obtained by interview using a structured questionnaire. The intake of energy and protein was taken using a food recall form 2 x 24 hours, not consecutively. Micronutrient intakes, including iron, vitamin C, folate, vitamin B6, vitamin B12, copper, calcium, and vitamin E intake, were obtained by interview using the Semi-Quantitative Food Frequency Questioner (SQ-FFQ). Information related to compliance with iron-folic acid (IFA) tablet consumption was gathered by interview. Nutrisurvey software and various references such as the Indonesian Food Composition List, Food and Agriculture Organization/FAO-Food Composition List database for Indonesia, multiple journals, and kinds of literature were used to process nutrient intake data.

Data analysis

Data were analyzed using statistical software. Descriptive statistics, including mean, standard deviation, minimum and maximum were determined. Bivariate analysis used Pearson's correlation coefficients for data with normal distribution and Spearman's correlation for otherwise. Multivariate analysis was applied using a multiple dummy regression test with the backward method. The independent variables included trimester, education level, husband's income, upper arm circumference, height, and intake of energy and nutrients (protein, vitamin B6, B12, C, E, folate, iron, copper, and calcium). The backward method is started with a model containing all included variables (full model). Then the least significant variables were removed one by one until reach the best model.

RESULTS AND DISCUSSION

The average age is 28.3±5.5 years old, with no mothers being of risky age. The average hemoglobin (Hb) level is 11.5±1.4 g/dL, with a maximum of 13.9 g/dL and a minimum of 8.8 g/dL. Upper arm circumference is 28.0±4.7 cm on average. It means that, in general, pregnant women do not suffer from chronic energy insufficiency. The average mother's height is 156.0±5.1 cm (Table

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1).

The majority of women are in their third trimester (42%), has a minimum of high school level education (77%) and their husbands earn more than the minimum salary (63%) (Table 2). Despite the fact that the majority of pregnant women had a high education level and family income over the minimum salary, the prevalence of anemia problems in PHC Kebon Jeruk is significant, as seen by 38% of pregnant women suffering anemia. The anemia problem is considered a high public health problem when the percentage reaches above 20% (DI, 2018). Based on the severity of anemia (Shah et al., 2022), anemia in pregnant women at PHC Kebon Jeruk is classified as mild anemia with the lowest hemoglobin level of 8.8 g/dL.

Table 1. Pregnant women's characteristics at PHC Kebon Jeruk in West Jakarta (n=60).

Characteristic	Mean	Std. Deviation	Minimum	Maximum
Age	28.3	5.5	19.0	42.0
UAC	28.0	4.7	20.0	38.0
Height	156.0	5.1	143	165
Hemoglobin	11.5	1.4	8.8	13.9

Table 2. Trimester and socioeconomic among pregnant women at PHC Kebon Jeruk, West Jakarta (n=60).

Variable	n	%
Trimester		
1	17	28
2	18	30
3	25	42
Level of education		
Low		
High	14	23
	46	77
Husband's income		
< Regional minimum wage	22	37
≥ Regional minimum wage	38	63

The regional minimum wage in Jakarta during the study: IDR 3.394.000,-

The average daily energy and protein consumption is 1764.4±361.3 kcal/day and 64.0±11.3 g/day, respectively. The majority of pregnant women do not reach the recommended nutrition adequacy rate for energy and protein intake. The average amount of folate consumed is 462.5±460.8 g. The majority of pregnant women do not get enough folate **(Table 3).** Only 13 pregnant women out of 60 responders take IFA tablets on a daily basis. As many as 78% of pregnant women do not consume daily IFA tablets because they forget, are too lazy to take tablets or dislike it. These causes are similar to those given in Basic Health Research 2018 like forgetting, boredom, nausea and vomiting due to pregnancy, nausea, and constipation, and dislike (13.9%). (MOH, 2019a).

Complaints of nausea, vomiting, and a dislike of the taste of IFA tablets, prompted the issuance of the Regulation of the Minister of Health of the Republic of Indonesia Number 51 in 2016 concerning the Standards of Nutritional Supplementation Products. It states that for the IFA tablets, iron is added in the form of a ferrous fumarate compound to increase compliance (MOH, 2016). However, the IFA tablet with Fe-Fumarate causes a decrease in adherence among pregnant women in Yogyakarta. In contrast, the commercial IFA tablet results in better adherence (Sudargo *et al.*, 2020). The commercial one has a smaller tablet size, a more favorable taste, and fewer side effects. On the other hand, the IFA tablet with ferrous fumarate, which contains multi-nutrients, has a better taste compared to that containing iron and folate only (Fitriana and Pramardika, 2019). The tablets containing multi-nutrients might increase compliance and be more preferred rather than those containing iron and folate, regardless of their iron compound, whether Fe-Fumarate or not.

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The high non-compliance in IFA tablet consumption may cause the majority of respondents to lack folate intake. It's difficult to meet the folate requirement level in pregnant women from only daily food intake because of the increasing folate requirement for both mother and fetus and the sensitivity of folate to the cooking process (heat and dilution). Folate deficiency obstructs red blood cell synthesis (Chen *et al.*, 2019) which is essential for fetal growth in the womb.

Table 3. Energy and nutrient intake among pregnant women at PHC Kebon Jeruk, West Jakarta (n=60).

Intake	Mean	Std. Deviation	Minimum	Maximum
Energy (kkal)	1764.4	361.3	936.4	2698.9
Protein (g)	64.0	11.3	39.9	89.0
Vitamin B6 (mg)	1.7	0.4	1.0	2.8
Folate (µg)	462.5	460.8	90.7	1414.9
Vitamin B12 (µg)	5.5	2.1	1.6	9.2
Vitamin C (mg)	130.2	50.2	28.7	235.0
Vitamin E (µg)	16.5	3.4	11.3	34.9
Iron (mg)	38.8	27.9	9.3	103.5
Copper (µg)	1133.4	266.7	540.0	1811.0
Calcium (mg)	1216.7	242.2	824.1	1807.9

Table 4. Bivariate analysis of sociodemographic, health characteristics, and nutrient intakes with hemoglobin level among pregnant women at PHC Kebon Jeruk, West Jakarta.

Variable	***r***	***p*[a]**
Trimester	-0,504	**0,000**
Level of education	0,363	**0,001**
Husband's income	-0,490	**0,000**
Upper Arm Circumference	-0,088	0,505
Height	0,175	0,181
Intake		
Energy	0,505	**0,000**
Protein	0,429	**0,001**
Vitamin B6	0,796	**0,000**
Folate	0,875	**0,000**
Vitamin B12	0,734	**0,000**
Vitamin C	0,377	**0,003**
Vitamin E	0,479	**0,000**
Iron	0,695	**0,000**
Copper	0,820	**0,000**
Calcium	0,423	**0,001**

[a]Pearson's correlation coefficients for data with normal distribution and Spearman's correlation for the otherwise.

Based on bivariate analysis, trimester, education of pregnant women, and husband's income are significantly related to hemoglobin level in pregnant women (Table 4). The level of education among pregnant women is significantly related to the incidence of anemia. As many as 26% of pregnant women have anemia in the higher education group (senior high school and above). Meanwhile, 79% of pregnant women are anemic in the low education group. The research conducted at PHC Maron, Probolinggo Regency, shows that education does not affect adherence to iron tablet consumption (Shofiana et al., 2018). However,

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the other research observed that formal education is associated with the occurrence of anemia (Widiasih, 2019). The relationship between formal education and the incidence of anemia may be moderated by other factors than compliance with IFA tablet consumption, such as the quality of nutrient intake.

The income of the head of the family or husband was used as an economic profile due to most respondents are housewives. During the research time, the Regional Minimum Wage (RMW) of Jakarta province is IDR 3.394.000,-. The difference in husbands' income (between below and above the minimum wage) is significantly related to the incidence of anemia among their pregnant wives. As many as 73% of pregnant women from the income below RMW group are anemic. This figure is much greater than that of anemic pregnant women (18%) from the income above the RMW group.

A husband's income is a proxy for the economic picture of pregnant women's households. The higher the household income, the more diversified the food consumed by the family. The households with low incomes would only consume certain food products, generally starch sources (Miranti et al., 2016). Based on the preliminary study related to the household total food expenditure, the expenditures for fish and meat are about 18% of the entire food expenditure, including cigarette spending. It is still slightly above the average spending on fish and meat among urban households in West Java Province (13%) in 2015 (Miranti et al., 2016). Fish and meat are sources of heme iron with higher bioavailability than nonheme iron in non-animal protein sources (Mahan and Escott-Stump, 2017).

The median expenditure on fish and meat is IDR 89.000 in a week. During the preliminary study, some pregnant women do not shop for fish and meat for one week. The highest expenditure on fish and meat is IDR 550.000 per week. In general, the meat expenditure increases when the household income increases. Bennett's Law states that the richer a society, the more varied the consumption pattern (Fuglie, 2004).

The proportion of anemic mothers from the normal nutrition status group (UAC≥23.5 cm) is higher (47%) than anemic mothers (8%) from the undernutrition group (UAC<23.5 cm). Upper Arm Circumference (UAC) is a proxy of the risk of chronic energy deficiency (CED) indicator for pregnant women (Ariyani *et al.*, 2012). The nutrition status using the UAC parameter could not describe the problem of anemia. High energy intake often reduces the quality of intake. The food intakes dominated by energy sources are often not rich in micronutrients. In this study, almost half of the total mothers with normal UAC have low hemoglobin levels.

Table 5. Backward multiple dummy regression analysis of the effect of characteristics and nutrient intake on hemoglobin level among pregnant women in Kebon Jeruk sub-district, West Jakarta

Variable	*Unstandardized Coefficients*		*p*[a]
	β	*Std. Error*	
Iron	0,015	0,003	**0,000**
Vitamin B12	0,140	0,043	**0,002**
Vitamin E	0,043	0,023	0,064
Copper	0,002	0,000	**0,000**
Trimester 3	-0,490	0,144	**0,001**

[a] The best fit model comprises third trimester, intake of iron, copper, vitamin B12, and E.

Table 5 shows that the third trimester and intake of iron, vitamin B12, and copper significantly affect the hemoglobin level among pregnant women at PHC Kebon Jeruk (p<0.005). This regression model explains up to 85.7% of the overall factors that affect the hemoglobin level of pregnant women (p=0.000), proved by an R-square value of 0.857. Based on multiple regression analysis, the third trimester significantly affect hemoglobin level. Physiologically pregnant women in the third trimester are susceptible to decreased hemoglobin levels due to hemodilution. However, optimal nutrient intake could maintain the normal hemoglobin level until the third trimester. Research at the PHC Ngorisan Surakarta shows that most (76.5%) pregnant women have normal hemoglobin levels. Some factors affecting their hemoglobin levels are good knowledge, high mother education, having a socio-culture without food abstinence, high compliance (100%) in IFA tablet consumption, having good nutrition status (79.4%), not having infectious or bleeding diseases (100%), having antenatal care > four times (85.3 %) and gestational interval >2 years (82.4%) (Sumiyarsi *et al.*, 2018).

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The other significant variables are iron, vitamin B12, and copper intake. Iron and copper are an essential nutrients for hemoglobin synthesis. Ceruloplasmin, a copper-containing protein, is required to normalize iron mobilization from storage sites to plasma. In a state of copper deficiency, iron could not be released. This results in low serum iron and hemoglobin, even under normal iron stores (Mahan and Escott-Stump, 2017).

Pernicious anemia is megaloblastic macrocytic anemia caused by vitamin B12 deficiency, which is generally due to a lack of intrinsic factor (IF). Vitamin B12 will combine with a protein called IF in the digestive tract so that it can be absorbed further down in the small intestine called the distal ileum. One of the causes of pernicious anemia is the lack of consuming food containing vitamin B12. The food sources of iron and vitamin B12 are generally found in animal foods such as meat, and fish (Damayanti et al., 2018). Animal food intake in Indonesia is still low. Plant foods still dominate protein intake. The intake of animal protein in Indonesia is only 8%, far below Malaysia (28%), the Philippines (21%), and Thailand (20%) (Prasetyo, 2018).

Based on the Executive Summary of Expenditure and Consumption of the Indonesian Population, the average daily protein consumption is 64.64 grams. It was sufficient in quantity based on the established RDA. However, the highest composition of Indonesian protein consumption was grains, as 19.51 grams or about 30 percent of the total protein consumption. Grains are the food sources of vegetable protein. The protein consumption from fish, meat, egg, and milk is 16.67 grams, or only about a quarter of the total protein consumption. It is still less than protein consumption from grains (BPS, 2018). The study of the dynamics of household food consumption patterns in Indonesia indicates that protein consumption tends to increase in line with the increase in income and is still dominated by vegetable food sources rather than animal food (Rachmawati et al., 2021).

After the Covid-19 pandemic, food prices increased and contributed 73.87 percent to the poverty line (BPS, 2021). It is difficult for poor people to reach a balanced diet as a food-based dietary guideline. Research in Bogor showed that dietary habits among pregnant women, regardless of their income-expenditure status, could not meet the RDA (Madanijah et al., 2016). The complexity of nutritional deficiencies may result in anemia. Providing IFA tablets containing only iron and folic acid would be difficult to resolve the high anemia prevalence. It is necessary to provide IFA tablets containing multi-nutrients containing vitamin B12 and copper.

CONCLUSION

The significant factors affecting hemoglobin levels in pregnant women are the third trimester, intake of iron, vitamin B12, and copper. It is necessary to provide IFA tablets containing multi-nutrients containing vitamin B12 and copper due to the low Indonesian animal food consumption. Research on the effectiveness of blood-supplement tablets containing multi-nutrients is still needed.

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