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THE RELATIONSHIPS BETWEEN PRE-PREGNANCY BODY MASS INDEX WITH HEPCIDIN AND FERITIN LEVELS

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ABSTRACT

Pregnancy with anemia is often occurs. An estimated 38% of pregnant women in the world are anemic. Pregnant women who have a normal pre-pregnancy Body Mass Index (BMI) have more iron stores. Being overweight, especially obesity, is associated with systemic inflammation, thereby increasing hepcidin and ferritin, which disrupt hemoglobin synthesis. This study aims to analyze the relationship between pre-pregnancy BMI with hepcidin and ferritin levels This research is an observational analytic study with a cross sectional approach. The population is anemia pregnant women and the number of samples is 24 peoples. Blood collection, pre-pregnancy BMI data collection and hemoglobin level checks were carried out at Pauh Padang Health Center. Hemoglobin levels were examined with a hematology analyzer. Hepcidin and ferritin were examined using the ELISA method at the Biomedical Laboratory of Andalas University. The pre-pregnancy BMI variable was divided into 2 categories, namely non-overweight (≤24.99) and overweight (≥ 25.00). Data analysis was performed by univariate and bivariate. The results showed that the mean hepcidin in the overweight group (39.70 ± 6.97 ng / ml) was higher than the mean hepcidin in the non-overweight group (36.88 ± 5.83 ng/ml). The median ferritin in the overweight group 17,33 (4.97-26.21) ng/ml was higher than the median ferritin in the non-overweight group (5.49 (1.01-53.26) ng / ml). That showed no significant relationship between pre-pregnancy BMI and hepcidin (p = 0.69) and no significant relationship between pre-pregnancy BMI and ferritin(p = 0.69).

Keywords : ***Pre-Pregnancy BMI, Hepcidin, Feritin***

INTRODUCTION

Pregnancy with anemia is often occurs. It is estimated that 38% of pregnant women in the world are anemic, or the equivalent of 32 million pregnant women have anemia. Anemia contributes to 20% of maternal deaths in Africa and Asia. (Tan et al, 2020). The results of Indonesian Basic Health Research show a significant increase in the prevalence of anemia in pregnant women in Indonesia, 37.1% (2013) to 48.9% (2018). (Kemenkes, 2013; Kemenkes, 2018). Pregnancy anemia resulting in poor pregnancy outcomes for both mother and fetus, including infection, premature rupture of membranes, fetal growth restriction, fetal hypoxia, preterm birth, low birth weight and fetal death. In low and middle income countries, 12% of low birth weight, 19% of preterm births, and 18% of perinatal deaths, are due to anemia during pregnancy. (Tan et al, 2020)

One of the risk factors for anemia in pregnant women is the condition of nutritional status before pregnancy. The pre-pregnancy Body Mass Index (BMI) represents the mother's metabolic and nutritional conditions during pregnancy. Pregnant women who have a normal BMI before pregnancy may have more iron stores. Conversely, pregnant women who have a prepregnancy BMI less than normal, may experience iron deficiency during pregnancy. On the other hand, being overweight, especially obesity is associated with systemic inflammation thereby increasing hepcidin and ferritin. The increase in hepcidin and ferritin, leads to low iron absorption and disruption of hemoglobin synthesis. (Tan et al, 2018)

Obesity increases fat tissue deposits which leads to increased expression of proinflamatory cytokines, including Interleukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α) (Triyonate and Apoina, 2015). IL-6 induces transducer and transcription activator (STAT3) bind signals to the hepcidin promoter which ultimately increases hepcidin expression. Hepcidin is a hormone that regulates systemic iron. This increase in hepcidin causes hypoferremia, characterized by an increase in sTfr and a decrease in serum iron, while ferritin also increases. (Rahma et al, 2018; Quijano et al, 2019,)

This study aims to analyze the relationship between pre-pregnancy BMI with hepcidin and ferritin levels.

STUDY DESIGN AND METHODS

This study is an observational analytic study with a cross sectional comparative approach to see the differences in hepcidin and ferritin levels in the non-overweigth pre-pregnancy BMI and overweight pre-pregnancy BMI groups. The population in this study were anemia pregnant women and the number of samples is 24 people that was taken by consecutive sampling technique. Blood samples, pre-pregnancy BMI, and hemoglobin levels were collected and checked at the Pauh Padang Public Health Center. Hemoglobin levels were checked with a hematology analyzer. The examination of serum hepcidin and serum ferritin was carried out using the ELISA method at the Biomedical Laboratory of Andalas University. The pre-pregnancy BMI variable was divided into 2 categories, namely non-overweight (≤24.99) and overweight (≥ 25.00). Data analysis was performed by univariate and bivariate. Univariate analysis was presented in terms of frequency and percentage for the pre-pregnancy BMI variable, while the hepcidin and ferritin levels were presented in the form of means. Bivariate analysis was carried out to see the relationship between pre-pregnancy BMI with hepcidin and ferritin levels. Independent T test was used to analyze the relationship between prepregnancy BMI and ferritin because the data were normally distributed, while for the association between pre-pregnancy BMI and hepcidine levels, the Mann Whitney test was used because the data were not normally distributed.

RESULTS

A. Respondents Characteristics

Table 1. Characteristics of respondents based on BMI, hepcidin and ferritin levels

Variable	F	%	Mean ± SD (ng/ml)
Pre-pregnancy BMI			
Non overweight	8	75	
Overweight	16	25	
Hepcidin levels			37,59 ± 6,1
Feritin levels			14,46 ± 13,4

Table 1. shows that most respondents (75%) have BMI non-overweight. However, less than half of the respondents (25%) have a BMI overweight. Table 1 also shows that the mean hepcidin levels of all respondents were 37.59 ± 6.1 ng / ml and the mean ferritin levels of all respondents were 14.46 ± 13.4 ng / ml.

B. The Relationships between Pre-pergnancy Body Mass Index With Hepcidin And Ferritin Levels

Table 2. Relationships between Pre-pergnancy BMI With Hepcidin And Ferritin Levels

	Non Overweight	Overweight	p

	Median (min-maks) ng/ml	Mean±SD ng/ml	Median (min-maks) ng/ml	Mean±SD ng/ml	
Hepcidin	38,24 (16,36-43,32)	36,88±5,83	38,38 (30,02-48,12)	39,70±6,97	0,69
Ferritin	5,49 (1,01-53,26)	13,87 ± 14,71	17,33 (4,97-26,21)	16,22 ± 9,5	0,66

Table 2 shows that the mean hepcidin level in the overweight group (39.70 ± 6.97 ng / ml) was higher than the mean hepcidin level in the non-overweight group (36.88 ± 5.83 ng / ml). The median hepcidin level in the overweight group was almost the same as the hepcidin level in the non-overweight group, namely 38.38 (30.02-48.12) ng / ml for the overweight group and 38.24 (16.36-43.32) ng / ml for the overweight group. The statistical test showed that there was no significant association between pre-pregnancy BMI and hepcidin levels (p = 0.69). Table 2 also shows that the median ferritin level in the overweight group was higher than the ferritin level in the non-overweight group, namely 17.33 (4.97-26.21) ng / ml for the overweight group and 5.49 (1.01-53, 26) ng / ml for the overweight group. The statistical test showed that there was no significant relationship between pre-pregnancy BMI and ferritin levels (p = 0.66).

The results of this study are in line with what Quijano (2019) found in pregnant women in Mexico, that there was no significant relationship between pre-pregnancy BMI and hepcidin levels (p value = 0.23) and there was no significant relationship between pre-pregnancy BMI and ferritin levels with (p value = 0.89). Quijano's (2019) study found the median hepcidin was higher in the obese group (958 (6.21-15.67)) than the non-obese group (8.04 (5.88-11.86)). Likewise with ferritin levels, Quijano (2019) found that the median ferritin in the obese group (40.60 (19.40-96.15)) was higher than the median for the non-obese group (39.30 (27.60-65.05)).

DISCUSSION

Rahma (2018) also found the same thing in Medan Indonesia, namely that there was no significant relationship between pre-pregnancy BMI with hepcidin levels and ferritin levels (p = 0.58 and p = 0.59). Rahma (2018) found the median hepcidin in the obese group (7.08 (2.14-78.18) slightly higher than the median hepcidin in the non-obese group (6.24 (1.01-90.18)). Meanwhile, the median ferritin in the obese group (20.57 (3.66-102.25) was higher than the median ferritin in the non-obese group (15.00 (2.90-98.15)).

Dao et al (2013) also found that the mean hepcidin of obese pregnant women was higher than the mean hepcidin of lean women (13.5 ± 9.0 ng ml vs 5.1 ± 2.7 ng ml). Cao et al (2016) found that there was a weak positive correlation between pre-pregnancy BMI and serum hepcidin serum at midgestation in Rochester, New York. However. This association lost significance after controlling for maternal age, race, gestational age at midgestation, weight gain at midgestation, and iron intake. This study found a 50% increase in hepcidin in both grade 2 and grade 3 obese respondents compared to the lean group. Although this increase did not reach statistical significance, the results of this study suggest higher hepcidin levels in obese individuals and support the idea that certain levels of adiposity lead to significant increases in hepcidin.

Obesity causes fat deposits in the body. These fat deposits will induce the release of inflammatory markers cytokines, including Interleukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α) (Triyonate, 2015). These cytokines will stimulate the release of hepcidin from the liver and adipose tissue. High hepcidin will inhibit the functional activity of ferroportin. This inhibits the absorption of iron in enterocytes and the release of iron in reticuloendothelial macrophages, resulting in decreased plasma iron (hypoferremia) and impaired iron metabolism. If iron

metabolism is disturbed, then iron deficiency occurs. (Sal et al, 2018; Mc.Clung and Karl, 2008; Lopez et al, 2011;)

The degree of chronic inflammation in obese conditions includes a mild degree of inflammation, so that obesity does not really increase the expression of hepcidin. This is except for the category of the highest degree of obesity (pre-pregnancy BMI ≥ 35 kg / m2). In these conditions, it shows high adiposity which affects iron homeostasis and changes in ferritin concentration. (Quijano et al, 2019). Differences in hepcidin levels can be influenced by various things such as nutritional factors (dietary patterns) due to obesity in western populations which generally occur in socioeconomic conditions. low, and possibly genetic factors. In addition, during pregnancy, there is suppression of hepcidin as an effort / response of the body to maximize the availability of iron so that hemoglobin levels can be maintained, so that hepcidin levels in obese pregnant women do not increase significantly (Weiss and Goodnough, 2005)

There was no significant difference in ferritin between the two groups because ferritin levels were more influenced by nutritional intake, especially iron intake. In addition, ferritin acts as an acute phase protein in the non-overweight and non-overweight groups. There was no sharp difference in the increase in ferritin in the obese group because the study subjects were healthy subjects who did not experience inflammation or infection. (Rahma, 2018)

CONCLUSSION

The conclusions of this study are that there is no significant relationship between pre-pregnancy BMI and hepcidin levels and there is no significant relationship between pre-pregnancy BMI and ferritin levels.

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