

## Research Article

## The Role of Ferritin Levels Serum of Third Trimester Obese Pregnant Women in Neonatal Outcome

### *Peran Kadar Feritin Serum pada Perempuan Hamil Trimester Tiga dengan Obesitas terhadap Luanan Bayi*

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#### Abstract

**Objective:** To determine relation of obesity to serum ferritin levels in third trimester pregnant women and neonatal outcome at Rumah Sakit Umum Daerah (RSUD) dr. Zainoel Abidin Banda Aceh.

**Methods:** This was a prospective. The study was conducted in January-November 2019 at RSUD dr. Zainoel Abidin Banda Aceh. Total of 38 patients with 34-40 weeks gestational age with obesity were included in the study. Univariate analysis is presented in the frequency distribution table. Bivariate analysis to test study hypotheses using Spearman's Rank Correlation. P-values > 0.05 were considered significant. The degree of correlation is determined based on the value of the correlation coefficient  $r$ .

**Result:** Spearman test showed no correlation between obesity variables and ferritin reserve status ( $p$ : 0.068). Correlation between obesity variable and the infant APGAR value was significant ( $p$ : 0.032) and the strength of correlation was weak ( $r$ : 0.349). Chi-Square test results showed no correlation between obesity and infant birth weight ( $p$ : 0.369). Relationship of serum ferritin levels with APGAR no significant ( $p$  > 0.05). Serum ferritin levels with birth weight also did not significant ( $p$  > 0.05).

**Conclusions:** This study shows that obesity in pregnancy has an effect towards the incidence of asphyxia in newborns an increase in serum ferritin or the incidence of macrosomia in newborns.

**Keywords:** APGAR, birth weight, ferritin, obesity.

#### Abstrak

**Tujuan:** Mengetahui hubungan obesitas terhadap kadar feritin serum pada ibu hamil trimester ketiga serta neonatal outcome di Rumah Sakit Umum Daerah (RSUD) dr. Zainoel Abidin Banda Aceh.

**Metode:** Penelitian analitik observasional menggunakan desain kohort prospective. Penelitian ini dilaksanakan pada Bulan Januari sampai November 2019 di RSUD dr. Zainoel Abidin Banda Aceh. Sebanyak 38 pasien dengan usia kehamilan 34-40 minggu dengan obesitas diikutsertakan dalam penelitian. Analisa univariat disajikan dalam tabel distribusi frekuensi. Analisa bivariat untuk menguji hipotesis penelitian menggunakan Spearman's Rank Correlation. P-value > 0,05 dianggap signifikan. Derajat korelasi ditentukan berdasarkan nilai koefisien korelasi  $r$ .

**Hasil:** Uji hipotesis Spearman menunjukkan korelasi antara variabel obesitas dengan status cadangan ferritin tidak bermakna ( $p$ : 0,068). Korelasi antara variabel obesitas dengan nilai APGAR bayi bermakna ( $p$ : 0,032) dan kekuatan korelasi lemah ( $r$  : 0,349). Hasil uji hipotesis Chi-Square menunjukkan korelasi antara variabel obesitas dengan nilai berat badan lahir bayi tidak bermakna ( $p$ : 0,369). Hubungan kadar serum ferritin dengan nilai APGAR menunjukkan hasil tidak bermakna ( $p$  > 0,05). Kadar serum ferritin dengan berat badan lahir bayi juga memiliki hubungan yang tidak bermakna ( $p$  > 0,05).

**Kesimpulan:** Penelitian ini menunjukkan bahwa korelasi antara obesitas dengan status cadangan ferritin tidak bermakna. Korelasi antara obesitas dengan nilai APGAR bayi bermakna dan kekuatan korelasi lemah, sedangkan dengan Berat Badan Lahir tidak bermakna. Kadar serum ferritin dengan nilai APGAR dan BBL bayi memiliki hubungan yang tidak bermakna.

**Kata kunci:** APGAR, berat badan lahir, feritin, obesitas.

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## INTRODUCTION

Obesity is excess fat in parts of body that can cause health problems, morbidity, mortality and has become one of the global health problems in the 21st century.<sup>1</sup> Increased prevalence of obesity occurs in many circles, one of which is women in reproductive age, especially during pregnancy.<sup>2</sup> Prevalence of obesity during pregnancy ranges from 1.8-25.3%.<sup>1</sup> Prevalence of obesity in adult women in Indonesia increases every year to reach 32.9% in 2013.<sup>3</sup>

Pregnancy and obesity have opposite effects on regulation of iron homeostasis and nutritional status. Increased need for iron in mothers occurs during pregnancy which has implications for anemia during pregnancy. Obesity changes iron homeostasis mediated by inflammatory mediators. Study showed an increase in ferritin serum levels in obese pregnant women,<sup>4</sup> whereas a different.<sup>5</sup>

Obesity not only affects ferritin levels, but also can have bad implications for fetus. Increased inflammatory mediators in obese mothers during pregnancy can affect intrauterine environment and interfere with fetal development. Mothers who have a BMI  $\geq 25$  kg/m<sup>2</sup> during pregnancy are at high risk for giving birth to babies with low APGAR score at minutes 1 and 5.<sup>6</sup>

The study results are in line, also found that obese mothers had a greater risk of giving birth to macrosomia babies which could increase risk of the labor complications such as shoulder dystocia and perineal tears.<sup>7</sup> Based on results of studies conducted above, we were interested in examining the relationship of obesity to serum ferritin levels in third trimester pregnant women and neonatal outcome at RSUD dr. Zainoel Abidin Banda Aceh.

## METHODS

We used prospective study design. This study uses non probability sampling techniques with quota sampling. This study was conducted in January-November 2019 at RSUD dr. Zainoel Abidin Banda Aceh. A total of 38 patients were taken with inclusion criteria 34-40 weeks gestational age with obesity, pregnant women in the latent and active labor phase, single pregnancy, pregnancy control patients and childbirth at RSUDZA, and were willing to participate in the study.

Patients with premature rupture of membranes with signs of intestinal uterine infection, preeclampsia and eclampsia, premature rupture of premature membranes, fetuses with congenital abnormalities, patients with a history of diabetes mellitus and hypertension before pregnancy, and mothers with severe anemia were excluded in this study.

Variables used in this study were Body Mass Index (BMI), serum ferritin levels, and Neonatal Outcomes (birthweight, and APGAR score). Univariate analysis is presented in frequency distribution table. Bivariate analysis to test study hypotheses using Spearman's Rank Correlation. P-values  $>0.05$  were considered significant. Degree of correlation is determined based on the value of the correlation coefficient *r*. (*r* 0.0 -  $<0.2$  (very weak), 0.2 -  $<0.4$  (weak), 0.4 -  $<0.6$  (moderate), 0.6 -  $<0.8$  (strong) , 0.8-1.00 (very strong).

## RESULTS

This study was conducted in RSUD dr. Zainoel Abidin Banda Aceh from January-November 2019 and found as many as 38 subjects. Characteristics of respondents are presented in Table 1.

**Table 1.** Characteristics of Study Subjects

	Amount (N = 38)	(%)
<b>Age (y.o)</b>		
21-25	2	5.3
26-30	13	34.2
31-35	13	34.2
36-40	9	23.7
41-45	1	2.6
<b>Parity Status</b>		
Primipara	7	18.4
Multipara	31	81.6
<b>Gestational Age (week)</b>		
Preterm ( $<37$ )	9	23.7
Early term (37-38)	22	57.9
Full term (39-40)	6	15.8
Late term (41)	1	2.6
Post term ( $> 42$ )	0	0
<b>Hemoglobin levels (gr/dL)</b>		
Anemia ( $<11$ )	27	71.1
Not Anemia ( $> 11$ )	11	28.9
<b>Delivery Method</b>		
Pervaginam	17	44.7
<b>Ferritin Serum <math>\mu\text{g/L}</math></b>		
Low ( $<12$ )	5	13.2
Normal (12-150)	30	78.9
High ( $>150$ )	3	7.9
<b>Neonatal Outcome</b>		
<b>Apgar Score</b>		
Severely Depressed (0-3)	1	2.6
Moderately depressed (4-6)	13	34.2

Excellent Condition (7-10)	24	63.2
<b>Baby Birth Weight (gr)</b>		
Low (< 2500)	22	57.9
Normal (2500-4000)	11	28.9
More (> 4000)	5	13.2
<b>Stage of Obesity</b>		
Obesitas stg I	11	28.9
Obesitas stg II	22	57.9
Obesitas stg III	5	13.2

Most age groups in this study are 26-30 and 31-35 years. Majority of respondents included in multipara (81.6%). Gestational age at time of delivery in the majority of respondents was 37-38 weeks (57.9%) with the highest number of labor methods (55.3%). Majority of study respondents had anemia (71.1%).

Spearman hypothesis test results showed no correlation between obesity variables and ferritin reserve status (p: 0.068).

**Table 2.** Results of Correlation Obesity Analysis and Serum Ferritin Levels

Obesitas	Ferritin Serum						Total		P-value
	Low		Normal		High				
	n	%	n	%	n	%	n	%	
Stage I	0	0	10	26.3	1	2.6	11	28.9	0.068
Stage II	3	7.9	17	44.7	2	5.3	22	57.9	
Stage III	2	5.3	3	7.9	0	0	5	13.2	
Total	5	13.2	30	78.9	3	7.9	38	100	

Spearman hypothesis test results showed a correlation between the obesity variable with a significant infant APGAR value (p: 0.032) and weak correlation strength (r: 0.349).

**Table 3.** Results of Obesity Correlation Analysis and Infant APGAR Value

Obesitas	Apgar Score						Total		R	P-value
	Excellent Condition		Moderately Depressed		Severely Depressed					
	n	%	n	%	n	%	n	%		
Stage I	9	23.6	2	5.3	0	0	11	28.9	0.349	0.032
Stage II	14	36.9	7	18.4	1	2.6	22	57.9		
Stage III	1	2.6	4	10.6	0	0	5	13.2		
Total	24	63.1	13	34.3	1	2.6	38	100		

Results of bivariate analysis of the relationship of serum ferritin levels with infant birth weight showed no significance (p> 0.05). Data analysis results can be seen in full in Table 4.

**Table 4.** Results of Correlation Analysis of Serum Ferritin Levels and Infant Birth Weight

Ferritin Serum	Birth Weight						Total		P-value
	Low		Normal		High				
	n	%	n	%	n	%	n	%	
Low	4	10.5	2	5.3	0	0	6	15.8	0.673
Normal	17	44.7	7	18.4	4	10.5	28	73.7	
High	2	5.3	2	5.3	0	0	4	10.5	
Total	1	60.5	13	29	24	10.5	38	100	

## DISCUSSION

Pregnant women with iron deficiency can experience increased maternal and fetal mortality during prenatal and perinatal periods.<sup>8</sup> Pregnancy in obese women can have bad implications for their health during pregnancy and even fetuses in the womb.<sup>9</sup> The results of this study found 38 respondents were trimester pregnant women third who underwent labor in the delivery room and operating room RSUDZA with the category of obesity nutritional status.

The average age of study respondents was 25-35 years with multigravida parity status (81.6%), the results of this study are 6.558 samples, 17% of them were obese and the average age was 30.5 (+5.8).<sup>10</sup> The average gestational age of the study respondents was 37-38 weeks, this result of 4.438 pregnant women respondents with the category of overweight and obese the majority giving birth to babies at 38 weeks gestation.<sup>11</sup> Different which shows that 28% of mothers with a BMI >30.0 give birth prematurely on medical indications and 18% spontaneously give birth.<sup>12</sup> According to the American College of Obstetricians and Gynecologist (ACOG) obesity increases the risk during pregnancy one of which is frequent premature birth occur due to an increased incidence of preeclampsia in obesity.<sup>13</sup>

The mean of study respondents had anemia (Hb <11 mg/dl). To assess whether Body Mass Index or BMI in early pregnancy can affect the risk of anemia in respondents in the form of pregnant women from Indonesia and Ghana with prospective cohort study methods, found that in comparison In both of the study groups, a higher weight in early pregnancy affected higher Hb levels so that the risk of anemia was lower. Meanwhile, if the initial weight is low or the BMI under the category of underweight reflects poor nutritional intake, including intake of various important micronutrients that play a role in the haematopoiesis process.<sup>14</sup>

Majority of respondents in this study had normal ferritin serum. This can occur due to an increase in the regulation of hepsidin which is induced by IL-6 as one of the inflammatory mediators that is triggered due to excess adipose tissue in obese patients.<sup>15</sup> Hepsidin is a hormone that regulates cellular iron exports, where the expression of hepsidin is feedback regulated by iron concentration, erythropoietic processes, and inflammation. Chronic low-level inflammation associated with obesity can increase the

regulation of hepsidin, and inhibit the absorption of iron in the intestine and release of iron from both the liver and spleen macrophage storage, thereby reducing circulating iron concentration which is characterized by an increase in sTfR and a decrease in serum iron, whereas ferritin can increase or remain in normal concentration.<sup>16</sup>

A total of 55.3% of respondents in this study gave birth using the method of Mandarin. This can happen because respondents of this study are pregnant women who have risk factors, namely obesity. The majority of respondents in this study gave birth to babies with excellent condition (63.2%). Yeşilçiçek Çalik study (2018) in Turkey, from 27 study samples with obesity category (BMI > 30) 16 of them (59.3%) gave birth to babies with APGAR score 7-10.<sup>16,17</sup>

Based on the results of this study, if we look at the correlation of obesity variables and the status of ferritin reserves which were tested using Spearman's Rank showed no significant correlation (p: 0.068 and r: 0.063). Pregnancy and obesity have opposite effect on hepsidin which is a hormone regulator of iron levels in the body and consequently affects regulation on iron homeostasis and nutritional status. Increase in adipose tissue activity of chronic low-level inflammation and involves the removal of cytokines as mediators of information, one of which is interleukin 6 (IL-6) and leptin, thus affecting the effectiveness of the ferroportin membrane which causes internalization and degradation of ferroportin and iron resistance in enterocytes. This causes the absorption and mobilization of iron from the liver and macrophages as storage will decrease.<sup>18</sup>

Influence of obesity on Apgar Score in this study has a significant value with weak correlation strength. Obesity in pregnant women can affect the neonatal condition in various ways.<sup>10</sup> Obesity in pregnancy increases the incidence of morbidity in the fetus, thereby affecting the baby's outcome (APGAR and birth weight). Obese female placenta has more lipids that can affect placental pathogenesis through inflammation and oxidative stress.<sup>19</sup> Placental dysfunction disrupts the health condition of the fetus in the womb due to changes in metabolism, inflammation, and endothelial dysregulation in placental tissue which contribute to an increased risk of asphyxia. Pregnancy complicated by obesity can increase the risk of umbilical cord twisting.<sup>20</sup>

Environmental placental lipotoxicity is influenced by obesity that occurs in mothers

with a metabolic profile that can increase inflammation and oxidative stress, as well as a decrease in angiogenesis regulators. This can cause intrauterine growth restriction (IUGR) or intra uterine fetal growth disturbance.<sup>21</sup> Mechanisms that can affect neonatal outcome are pathomechanisms of anemia that occur due to increased levels of hepsidin which can reduce the amount of iron available to be released into the circulation, thereby affecting the synthesis of hemoglobin and production of erythrocytes.<sup>22</sup> Decreased hemoglobin levels cause a decrease in oxygen transport and treatment of the fetus, thereby supporting the occurrence of hypoxic conditions in the fetus.<sup>23</sup>

Direct evidence for the effect of lipotoxicity in pregnancy with obesity on neonatal outcomes is directly lacking, studies are currently only linking lipotoxicity to dysfunction in the placenta. The placenta can cause metabolic abnormalities to the fetus through intra utero, so the consequences can affect the health of children widely. Because of its considerable potential to harm both mother and baby, studies of the level, causes and effects of lipotoxicity in obese pregnancies continue.<sup>13</sup>

Based on an article review study, of about 34 articles that examined the relationship between maternal BMI and infant birth weight, around 15 studies evaluated the relationship between maternal BMI and LBW. The total of subjects included in the study metanalyst review was around 313.569 and using the reference category of mothers with normal BMI, it was found that no relationship was found between the incidence of infants with low birth weight with obese mothers.<sup>24</sup>

## CONCLUSION

This study shows that the correlation between obesity and ferritin reserve status is not significant. The correlation between obesity with a baby's APGAR value is significant and the strength of the correlation is weak, whereas with BBL it is not significant. Serum ferritin levels with APGAR and BBL values of infants have no significant relationship.

## SUGGESTION

This study is expected to be continued by looking at other variables such as complications of placental disorders, inflammatory markers and other variables.

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