

Research Article

## Ferritin Level Decreased between the Second and Third Trimester of Pregnancy

### *Kadar Feritin Menurun pada Kehamilan Trimester II dan III*

Ramli, Hermie MM Tendean, Rudy A Lengkong

*Department of Obstetrics and Gynecology  
Faculty of Medicine University of Sam Ratulangi/  
Prof. Dr. R.D. Kandou General Hospital  
Manado*

#### Abstract

**Objective:** To know the change in ferritin level in second and third trimester of pregnancy.

**Methods:** This study was a cohort study. The level of ferritin was estimated in the second trimester of pregnancy and examined again in the third trimester of pregnancy. Data processed and analyzed by statistically.

**Result:** The number of sample in this study was 30 patients. From this study, we found that the Ferritin level in second to third trimester of pregnancy was decreased in 28 patients (93.3%) and increased in 2 patients (6.7%). This result showed that ferritin serum level in second and third trimester would significant difference ( $p < 0.001$ ). This different can be showed in media ferritin serum level in second trimester higher than third trimester (31.10 ng/ml > 22.20 ng/ml).

**Conclusion:** There was a significant decrease in the level of ferritin from the second to third trimester. This could be caused by the occurrence of hemodilution reaching its peak at 28-32 weeks of pregnancy, increasing the need of iron intake. This could also be caused by an imbalanced diet of the mother.

[Indones J Obstet Gynecol 2013; 37-2: 77-81]

**Keywords:** ferritin, pregnancy

**Correspondence:** Ramli, Jln. Manibang I Malalayang II Manado 95263 Sulawesi Utara. Mobile: 085394375055  
Email: ramli\_obsigin@yahoo.com

#### Abstrak

**Tujuan:** Mengetahui perubahan kadar feritin pada kehamilan trimester dua dan tiga.

**Metode:** Penelitian ini bersifat kohort, di mana subjek penelitian yang memenuhi kriteria inklusi, dilakukan pemeriksaan kadar feritin pada kehamilan trimester kedua dan kemudian dilakukan lagi pemeriksaan kadar feritin saat kehamilan trimester ketiga. Data diproses dan dianalisa secara statistik.

**Hasil:** Jumlah sampel yang didapat dan memenuhi kriteria inklusi dalam penelitian ini sebanyak 30 orang. Dari hasil penelitian ini didapatkan terjadi penurunan kadar feritin dari ibu hamil trimester dua ke trimester tiga sebanyak 28 ibu (93,3%) dan terdapat 2 ibu (6,7%) yang mengalami kenaikan. Hasil tersebut menunjukkan bahwa kadar feritin serum pada trimester dua dan tiga berbeda sangat bermakna ( $p < 0,001$ ). Perbedaan ini dapat dilihat pada nilai median kadar feritin serum trimester dua lebih tinggi dibandingkan dengan trimester tiga (31,10 ng/ml > 22,20 ng/ml).

**Kesimpulan:** Terdapat penurunan secara bermakna kadar feritin ibu hamil trimester dua ke trimester tiga yang disebabkan oleh kebutuhan akan zat besi yang meningkat pada kehamilan, di mana hal ini disebabkan karena adanya hemodilusi yang mencapai puncaknya pada usia kehamilan 28 - 32 minggu dan adanya proses transfer zat besi ke janin selain itu dapat juga disebabkan oleh faktor komposisi diet yang buruk.

[Maj Obstet Ginekolog Indones 2013; 37-2: 77-81]

**Kata kunci:** feritin, kehamilan

## INTRODUCTION

In pregnancy, the blood volume is increasing in every trimester. Starting in the first trimester, it increases for 20%, 40% in the second trimester, and 50% until the midst of third trimester. Afterwards until delivery, the blood volume will not increase, making the total volume increase of 42%.<sup>1</sup>

In addition, there is an increasing rate of erythropoiesis in pregnant woman, which would increase the number of erythrocyte. The rate will differ at each pregnancy age. In first trimester the

erythrocyte production was slow, but in second trimester to third trimester, its speed will increase sharply.<sup>2</sup>

Initially, haemoglobin will still be in normal range. But it will then decrease to the lowest level in the end of second trimester and increase before delivery.<sup>2</sup>

Iron daily recommendation in the first trimester of pregnancy is relatively low, about 0.8 mg. but this number would increase in the second and

third trimester, to about 3 to 7 mg. The iron absorption ratio will not increase accordingly on pregnant women, only 2-3 mg will be absorbed from 10 mg oral intake. Even in women with adequate iron reserve in the beginning of pregnancy, there still will be several phases of iron deficiency. Increasing iron necessity is due to decreasing ferritin level. In the first trimester of pregnancy, the level of ferritin is about 100 ng/ml, in second trimester it will decrease into about half, and in the third trimester it will decrease for another 30% so the in the end, the ferritin level is under of 20 ng/ml.<sup>3</sup>

Iron deficiency is the most common nutrition problem in every corner of the world, affecting about 25% world population.<sup>4</sup> Specifically, pregnancy women has a high risk for iron deficiency and iron deficiency anemia due to the increasing iron necessity. Prevalence of Iron deficiency anemia in pregnant women is about 35% - 75% (average 56%), while in industry country the prevalence is about 18%.<sup>4</sup>

Haemoglobin, haematocrit, and erythrocyte level are the functional component of an assessment that estimated the level of iron storage.<sup>4</sup> In fact, the alteration of iron storage and functional iron component deficiency has a different picture. The level of haemoglobin, haematocrit and number of erythrocyte would influenced by hemodilution in pregnancy.<sup>3</sup>

Ferritin is a protein that is rich in iron (iron storage protein) that was produced by several tissue including the liver, bone, and placenta. Lower level of ferritin was a sensitive indicator for iron deficiency states.<sup>5</sup>

Several studies have proved that ferritin serum is a non-invasive test that is useful for pregnancy. Ferritin serum concentration decreases after 12 weeks of pregnancy with relatively constant rate until the 32<sup>nd</sup> weeks, where the level would decreased to less than 20 ng/ml even in pregnant women who has consumed iron supplementation. In healthy adult, the concentration of ferritin serum has a correlation with iron storage in bodies. Iron storage of 8 mg is equal with 1 ng/ml of ferritin serum. Based on this calculation 100 mg of iron is equal with 125 ng/ml of ferritin serum. Average level of ferritin serum in healthy women equal with < 500 mg of iron storage.<sup>6</sup>

## METHOD

This was a cohort study, where the subjects who filled the inclusion criteria, were undergoing ferritin level examination in second and third trimester of pregnancy. Data were then processed and analysed statistically.

The number of subjects in this study was 30 people who agreed to participate and signed the informed consent. The subject characteristic, including age, gravid, education, occupation as well as the ferritin level in second and third trimester, was showed in table form.

## RESULT

This study was performed from November 2012 to January 2013. Subjects have received explanation about benefit, objective and study method that being used and sign informed consent to participate in this study.

**Table 1.** Subject characteristic based on age, gravid, educational background and occupation (n = 30).

Age (Years)	n	%
< 20	3	10
20- 35	24	80
> 35	3	10
Gravid	n	%
1	13	43.3
2 - 3	16	53.4
3	1	3.3
Education	n	%
Elementary	3	10
Junior high school	1	3.3
Senior high school	23	76.7
Bachelor	3	10
Occupation	n	%
House wife	25	83.3
Private	2	6.7
State enterprise worker	2	6.7
University student	1	3.3

The subjects' age ranged from 19 to 39 years old. Most subjects (80%) were 20 to 35 years old. Sixteen subjects (53.4%) had 2-3 previous pregnancies. Most subjects (76.7%) were graduated from senior high school and most (83.3%) were a housewife.

**Table 2.** The ferritin level in second to third trimester of pregnancy (n = 30)

Variation of ferritin level	n	%
Decreases	28	93.3
Increases	2	6.7
<b>Total</b>	<b>30</b>	<b>100</b>

From this study, it was found that in 28 patients (93.3%) the ferritin level was decreasing, while in 2 patients (6.7%), the level was increasing instead.

**Table 3.** Decreased of ferritin level in second to third trimester (n = 28)

Decreased of ferritin level	n	%
< 5 ng/ml	3	10.7
5 - 10 ng/ml	12	42.9
> 10 ng/ml	13	46.4
<b>Total</b>	<b>28</b>	<b>100</b>

In this study, we found that 13 patients (46.4%) experienced a decrease in ferritin level in second to third trimester for more than 10 ng/ml.

**Table 4.** Results from ferritin level different test in second and third trimester

Trimester	On average	Standard Deviation	Median	Wilcoxon test
II	35.04	20.987	31.10	- 3.569 (p < 0.001)
III	34.27	44.189	22.2	

Based on Kolmogorov-Smirnov test (appendix) it showed that ferritin serum level in second and third trimester was not distributed normally (p < 0.05). Thus, we analysed the differences of ferritin serum level test in second and third trimester by Wilcoxon Signed Ranks test. The result showed that level of ferritin serum in second and third trimester was significantly different (p < 0.001). The ferritin serum level in the second trimester is higher compared with in the third trimester (31.10 ng/ml > 22.20 ng/ml).

## DISCUSSION

The subjects' age ranged from 19 to 39 years old. Most subjects (80%) were 20 to 35 years old. Sixteen subjects (53.4%) had 2-3 previous pregnancies. Most subjects (76.7%) were graduated from senior high school and most (83.3%) were a housewife. Age, gravid, educational background and occupation could influence the iron storage/ferritin level in pregnant women. In the younger age group lower ferritin level can be caused by the additional iron need for body metabolism in growing period and vital organ preparation.<sup>7</sup>

Iron storage would decrease in women who ever had childbirth since they need longer time to replace it, approximately  $\pm$  3 - 6 months. The women with shorter interval between pregnancies could have even lower iron storage, since the storage had not been fully replenished when it was used again for the next pregnancy.<sup>8</sup>

Pregnant women with a lower level of education could have a lower ferritin/iron storage level of the body because of the lack of knowledge about diet that would be needed to fulfil the iron necessity. Pregnant women that worked in stressful job rarely pay attention to her intake thus also influencing the nutrient, including iron, status. Economic and social factor are also another important factors because it influence nutrient intake.<sup>9</sup>

From 30 respondents, 28 respondents had decreasing ferritin level and 2 respondents had increasing ferritin level. The decreasing ferritin serum level can be caused by the increasing need of iron in second trimester, imbalanced diet, and hemodilution in pregnancy.<sup>7</sup>

Decreasing ferritin serum depends on how much the iron storage is in the beginning of pregnancy, and also influenced by iron supplementation in pregnancy period.<sup>10</sup>

Increasing ferritin serum level in pregnancy can be caused by several factors, including infection, gestational diabetic, premature parturition and also preeclampsia.<sup>11-13</sup> In this study we found that 2 pregnant women experienced an increasing level of serum ferritin, which could be caused by infection, premature parturition and preeclampsia.

Most patients (46.4%) in this study experienced a decrease in ferritin level in second to third trimester for more than 10 ng/ml. This can be caused by hemodilution that peaks in 28 - 32 weeks preg-

nancy age, the increasing rate of iron transfer to fetus and also a fall in iron absorbing ability that can be influenced by several substance.<sup>14</sup>

In this study we found 3 women with the greatest decrease of ferritin serum level (-30 ng/dl until -60 ng/dl). There are several factors which can explain this phenomena, including normal range ferritin level. There is no reference regarding the expected decrease in ferritin serum level in second and third trimester and the normal range of ferritin serum level in the second and third trimester. Huch R found that ferritin serum level decreased in pregnancy, and reaching the lowest point in second and third trimester.<sup>10</sup>

Analysis of decreasing ferritin serum level can be performed by subtracting the highest number of ferritin serum level with its consumption. This can be individualized.<sup>15</sup> In this study, we did not study about the fetus' body weight. thus we can't conclude whether there is a correlation between the decrease of maternal ferritin serum level with birthweight. The decreased of ferritin serum level were different in each subject, and that can be influenced by another variable, i.e. nutrient and diet supplementation and blocked iron absorption.<sup>16</sup> However, in this study, we did not studied about correlation between the iron daily intake and ferritin serum level.

Based on Wilcoxon Signed Ranks test, we found that median level of ferritin in second trimester was 31.10 ng/ml and median level of ferritin in third trimester was 22.20. This result showed that ferritin serum level in second and third trimester was significantly difference ( $p < 0.001$ ). The level of ferritin serum in second trimester is significantly higher than in third trimester, so we can conclude that ferritin level serum decrease significantly.

In second trimester, ferritin serum level decreased consistently, up to 50% of the normal range. This change is caused by hemodilution and iron mobilization from the storage to fulfil the increasing iron need in pregnancy.<sup>17,18</sup> For this period, iron storage in pregnancy women would decreased.<sup>19</sup>

This study result is similiar with another study's. Hou Jr showed that pregnant women in their first trimester had a higher ferritin serum level compared with non pregnant women. While in second and third trimester they found significantly decreasing ferritin serum level. Ferritin serum level

in non-pregnant group was  $\pm 63$  ng/ml. In first trimester, the level of ferritin serum would increase to  $\pm 97.4$  ng/ml, significantly different compared to ferritin serum in non-pregnant women. Then it would decrease to  $\pm 22.2$  ng/ml in the second and  $\pm 14.7$  ng/ml in the third trimester.<sup>20</sup>

Breymann C showed that ferritin serum level in the beginning of normal pregnancy was higher than in non-pregnant women. In pregnant women, ferritin serum concentration reached its highest point in 12 - 16 weeks gestational age, then decrease accordingly to fetus growth and reached its lowest level in third trimester.<sup>21</sup>

Study by Ichsan showed that the older the gestational age, the lower of average ferritin serum level, meaning that the iron storage would be depleted as the pregnancy continued. From this study it was also found that ferritin level in pregnant women was  $20.21 \pm 19.53$  ng/ml. In first trimester of pregnancy ferritin level was  $52.86 \pm 47.88$  ng/ml, in second trimester was  $26.81 \pm 22.97$  ng/ml, while in third trimester was  $13.93 \pm 7.95$  ng/ml. So they concluded that the ferritin level in pregnant women would decrease based on fetus development.<sup>22</sup>

Mastiadji in 2001, showed that "ferritin level in pregnant women was associated with haemoglobin, haematocrit, and erythrocyte level. The ferritin level is lower in the third trimester than in the second trimester. They found that ferritin level in third trimester of pregnancy was  $\pm 21.698$  ng/ml and in second trimester of pregnancy was  $\pm 24.268$  ng/ml."<sup>23</sup>

## CONCLUSION

There is a significant decrease of ferritin level in pregnancy women between second to third trimester. Highest ferritin serum level were different in each individual and that can be influenced by nutrient and diet intake that the rate of iron absorption. As suggestion, ferritin level examination can be used as one of supporting examination in establishing the diagnosis and treatment of iron deficiency anemia in pregnant women.

## REFERENCES

1. Decherney AH, Goodwin TM, Nathan L, Laufer N. Maternal physiology during pregnancy. In Current Diagnosis and Treatment Obstetrics and Gynecology. 10<sup>th</sup> edition. Apleton and Lange. 2007: 149-57.

2. Laubach J, Bendell J. Hematologic changes in pregnancy. In: Hoffman: Hematology Basic principles and practice. 5<sup>th</sup> ed. Churchill Livingstone. 2008: 92-107.
3. Beaton GH. Iron Need During Pregnancy: Do We Need to Rethink Our Targets. *Am J Clin Nutr* 2000; 72: 265-71.
4. Scholl TO. Iron status during pregnancy: setting the stage for mother and infant. *Am J Clin Nutr*. 2005; 81: 1218-22.
5. Beaton G. Iron need during pregnancy: do we need to rethink our target. *Am J Clin Nutr*. 2000; 72: 254-7.
6. Irshad G, Jafri SA, Kousar S, Ali I. Significance of serum ferritin in diagnosis of iron deficiency anemia in pregnant females of Pakistan. *Professional Med J Sep*. 2011; 18: 475-8.
7. Beard JL. Effectiveness and Strategies of Iron Supplementation During Pregnancy. *Am J Clin Nutr*. 2000; 71: 1288-94.
8. Meier PR. Prevention of iron deficiency anemia in adolescent and adult pregnancies. *Clin Med Res*. 2003: 29-36.
9. Ronnenberg AG, Wood RJ, Wang X. Preconception hemoglobin and ferritin concentrations are associated with pregnancy outcome in a prospective cohort of Chinese women. *J Nutr*. 2004; 134: 2586-91.
10. Huch R, Breyman C. Anemia in pregnancy and the puerperium. 1<sup>st</sup> ed. Unimed. Bremen. 2005: 32-7.
11. Chen X, Scholl TO. Elevated serum ferritin concentrations are associated with increased risk of gestational diabetes: Camden Study. *Diabetes* 2003; 52: 407-10.
12. Siddika A, Nasrin B, Shamim S, Begum N, Nahar N, Begum SR. Serum Ferritin Level In Preterm Labor. *Bangladesh J Obstet Gynecol*, 2009; 24: 14-7.
13. Scholl TO. High third-trimester ferritin concentration: associations with very preterm delivery, infection, and maternal nutritional status. *Obstet Gynecol* 1998; 92: 161-5.
14. Riswan M. Anemia defisiensi besi pada wanita hamil di beberapa praktek bidan swasta dalam Kotamadya Medan. *Bagian Ilmu Penyakit Dalam FK USU*. 2003: 16-9.
15. Raza N, Sarwar I, Munazza B, Ayub M, Suleman M. Assessment of iron deficiency in pregnant women by determining iron status. *Hazara University, Mansehra, Pakistan. J Ayub Med Coll Abbottabad*. 2011; 23: 36-40.
16. Assessment of the prevalence of iron deficiency anemia, by serum ferritin, in pregnant women of Southern Iran, Mehran Karimi, Raheem Kadivar, Hooman Yarmohammadi. Hematology Research Center, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. Department of Pediatrics, Division of Infectious diseases, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran, *Med Sci Monit*, 2002; 8(7): 488-92.
17. Lao TT, Tam KF, Chan LY. Third Trimester Iron Status and Pregnancy Outcome in Non-anemic Women; Pregnancy Unfavorably affected by Maternal Iron Excess *Hum Reprod*. 2000; 15: 1843-8.
18. Irshad G, Jafri SA, Kousar S, Ali I. Significance of serum ferritin in diagnosis of iron deficiency anemia in pregnant females of Pakistan. *Professional Med J* 2011; 18(3): 475-8.
19. Karimi M, Kadivar R, Yarmohammadi H. Assessment of the prevalence of iron deficiency anemia, by serum ferritin, in pregnant women of Southern Iran. *Med Sci Monit*. 2002; 8(7): 488-92.
20. Hou JR, Cliver SP, Tamura T, Johnston KE, Goldenberg R. Maternal serum ferritin and fetal growth. *Obstet Gynecol*. 2000; 95: 447-52.
21. Breyman C. Iron deficiency and anaemia in pregnancy: modern aspects of diagnosis and therapy. *Blood Cells Mol Dis*. 2002; 29: 506-16.
22. Ichsan T. Gambaran Feritin Serum sebagai Penilaian Cadangan Besi pada Wanita Hamil dibandingkan dengan Parameter Hematologi lainnya. Tesis, Bagian Obstetri dan Ginekologi FK USU, Medan. 1996: 40-9.
23. Masiadji B. Hubungan kadar hemoglobin, hematokrit, dan jumlah eritrosit dengan kadar feritin pada kehamilan trimester II dan III. *Bagian Obstetri Ginekologi FK Undip*. 2001: 34-6.