

Estimation of Hcpidin Level and Its Correlation With Iron State in Pregnant Women

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Abstract

This study aimed for determination of serum hepcidin level and its association with iron state in pregnant women with and without anemia. This study comprises 86 pregnant women divided into two groups, the first group comprises 49 pregnant women without iron deficiency anemia, the second group comprises 37 pregnant women with iron deficiency anemia. Blood was drawn from all pregnant women for determination of serum ferritin and hepcidin concentrations. The results establish a significant decrease in serum ferritin and hepcidin concentrations in pregnant women with anemia as paralleled with pregnant women without anemia. The outcomes of linear regression analysis demonstrate a significant positive association between serum ferritin and hepcidin concentrations in both study groups. In conclusion, measurement of serum hepcidin level is an important parameter for evaluation the iron state in pregnant women.

Keyword: Pregnancy, Anemia and Hcpidin

الخلاصة

الهدف من هذه الدراسة لتعيين مستوى الهبسيدين وعلاقته مع حالة الحديد في النساء الحوامل اللواتي لا يعانين من فقر الدم و النساء الحوامل اللواتي يعانين من فقر الدم. تضمنت الدراسة 86 من النساء الحوامل قسمن على مجموعتين، المجموعة الاولى تضمنت 49 امرأة حامل لا يعانين من فقر الدم، المجموعة الثانية تضمنت 37 امرأة حامل يعانين من فقر الدم. عينات الدم تم الحصول عليها من كل النساء الحوامل لتعين تركيز الفريتين و الهبسيدين. نتائج هذه الدراسة بينت ان هناك نقصان ملحوظ في التركيز المصلي للفريتين و الهبسيدين في مجموعة النساء الحوامل اللواتي يعانين من فقر الدم عند مقارنتها مع مجموعة النساء الحوامل اللواتي لا يعانين من فقر الدم. نتائج تحليل الانحدار الخطي بينت ان هنالك ارتباطاً معنوياً موجبا بين التركيز المصلي للفريتين و التركيز المصلي للهبيديدين في كلا مجموعتي الدراسة. نستنتج ان قياس مستوى الهبسيدين هو عامل مهم لتقييم حالة الحديد في النساء الحوامل.

الكلمات المفتاحية: الحمل، فقر الدم و الهبسيدين

Introduction

Iron deficiency anemia is highly widespread during pregnancy. In developed and developing countries, iron deficiency anemia is connected with higher maternal and perinatal morbidity and mortality (1). Iron is an important element for the growth and function of brain. Also, it sustenance energy metabolism in neuron and synthesis of neurotransmitters (2).

The control of body iron based on duodenal absorption through an active transport. In the diet, iron is generally exist in the ferric form (Fe^{+3}). The ferric is reduced to ferrous form (Fe^{+2}) by duodenal cytochrome b reductase

enzyme. Ferrous is passed through the cell membrane of enterocytes by divalent metal transporter 1 (3, 4). Inside the enterocyte, the iron bind with the protein apoferritin to form ferritin. The iron is transferred from the enterocyte to circulation by ferroportin, and then the iron is bound with transferrin for transport and storage. In the target cells the transferrin-bound iron enters these cell by receptor-mediated endocytosis. The essential regulator of iron is a hepcidin (3, 5).

Hepcidin is a peptide composed from 25 amino acids, it is produced by the liver and noticeable in urine and

blood (6, 7). When hepcidin released into the circulation, it binds with ferroportin, and recognized in the enterocytes basal membrane, hepatocytes, spleen and macrophages. Hpcidin activates lysosomal degradation of ferroportin (8, 9). This study aimed for determination of serum hepcidin level and its association with iron state in pregnant women with and without anemia.

Materials and Methods

This study comprises 86 pregnant women distributed into two groups, the first group comprises 49 healthy pregnant women without iron deficiency anemia aged from 19 to 30 years, the second group comprises 37 pregnant women with iron deficiency anemia aged from 21 to 33 years. The cases are selected by gynecologist in several health centers in AL-Hilla city and the pregnant women that suffering from any disease (such as diabetes mellitus, hypertension and asthma) or have taken a medication were excluded from this study.

A five milliliters of blood was drained by vein puncture from all pregnant women after an overnight fast and the blood was divided into two

parts, the first part includes three milliliters of blood placed in plain tube and this used for determination of serum ferritin and hepcidin concentrations while the second part includes two milliliters of blood placed in EDTA containing tube for determination of serum hemoglobin concentration. Serum ferritin and hepcidin concentration are determined by ELISA kit. Statistical analyses were done by SPSS.

Results

The parameters of pregnant women with and without anemia presented in table (1-1). The outcomes of the current study establish a significant decrease ($P < 0.05$) in serum ferritin and hepcidin concentrations in pregnant women with anemia as paralleled with pregnant women without anemia as mentioned in figure (1-1) and figure (1-2) respectively.

The outcomes of linear regression analysis (table 1-2) demonstrate a significant positive association between serum ferritin and hepcidin concentration in both study groups.

Table (1-1) Parameters of the Pregnant Women With and Without Anemia

Character	Pregnant without anemia	Pregnant with anemia
Number	49	37
Age (year)	26.8 ± 4.94	27.16 ± 5.10
Gestational age (week)	31.95 ± 2.72	33.01 ± 2.51
Hb (g/L)	12.61 ± 1.22	9.7 ± 0.91 (*)

(*) This means significant value ($P < 0.05$) as paralleled with pregnant without anemia

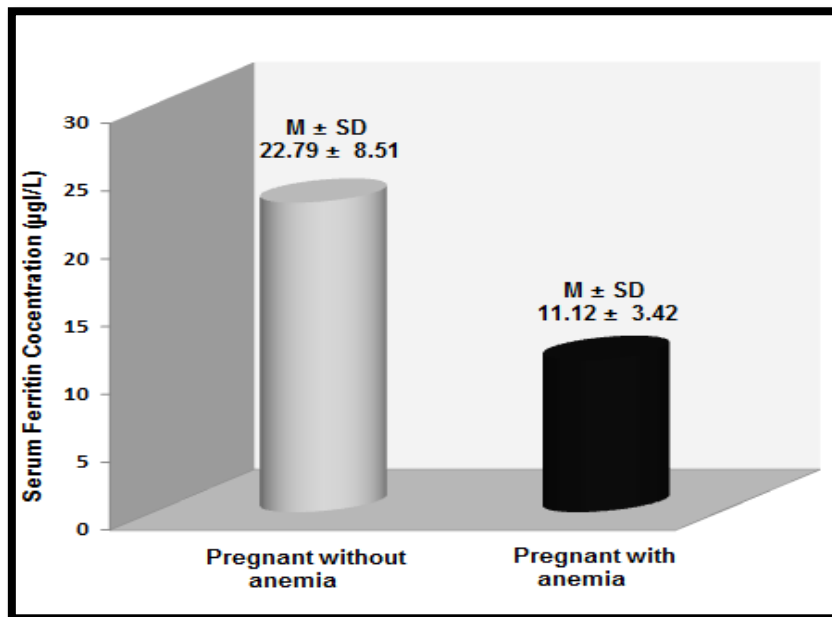


Figure (1-1): Ferritin Level in Pregnant Women With and Without Anemia

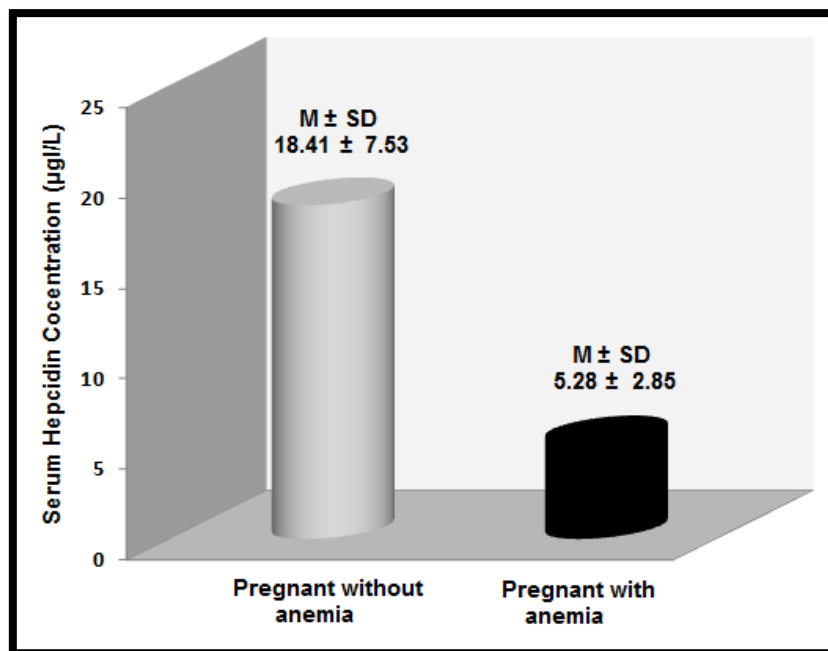


Figure (1-2): Hepcidin Level in Pregnant Women With and Without Anemia

Table (1-2) Correlation Between Hepcidin and Ferritin Levels in Pregnant Women With and Without Anemia Groups

Character	Serum Hepcidin Concentration (r)	
	Pregnant Women Without Anemia	Pregnant Women With Anemia
Serum Ferritin Concentration	0.47*	0.43*

(* This means significant association ($P < 0.05$))

Discussion

There are several factors can lead to iron deficiency anemia such as insufficient nutrition intake, raising the physiological demand of the nutrient (pregnancy) and elevation of iron losses. In pregnancy, the requirements to iron increased by about tenfold; thus, the pregnant women are mainly at hazard of emergent iron deficiency anemia (10, 11, 12).

Hepcidin plays an essential role in regulation of iron in the body through suppression of iron absorption from intestine and releasing of iron from macrophages (13, 14). The production and secretion of hepatic hepcidin is controlled by circulating iron. The decline in hepcidin levels were detected in persons with the iron depleted stores, this lead to stimulate the iron release to the bloodstream through ferroportin (which is act as iron exporter), while the increase in hepcidin levels decrease the absorption of iron in enterocytes by inactivating the ferroportin (15, 16, 17).

This study shows a significant decrease in serum ferritin and hepcidin levels in pregnant women with anemia as paralleled with pregnant women without anemia. The current outcomes are covenant with the outcomes of Manolov V. study (18) wherein the serum ferritin and hepcidin levels were significantly decreased in the in a group of pregnant women with anemia as compared to the group of pregnant women without anemia. The present study shows a significant positive association between serum ferritin and hepcidin concentrations in study groups. The existing results are in consistence with the outcomes of Amat B. (19) and Albendary E. (20) studies wherein serum ferritin levels were positively associated with hepcidin levels.

In this study, the decrease in serum ferritin level in pregnant women with anemia indicate that the decline in

iron store which suppresses the hepatic hepcidin secretion. The decreasing in serum hepcidin level activates ferroportin to increase iron absorption from intestine. This reason interpret the significant decrease in serum ferritin and hepcidin levels in pregnant women with anemia, also the positive association between serum ferritin and hepcidin concentration in both study groups.

Conclusions

In conclusion, measurement of serum hepcidin level is an important parameter for evaluation the iron state in pregnant women.

References

1. Lawrence P. Iron deficiency in pregnancy. *Obstet Med.* 2010; 3: 17-24.
2. Shafir T., Angulo-Barroso R., Jing Y., *et al.* Iron deficiency and infant motor development. *Early Hum Dev.* 2008; 84 (7): 479-485.
3. Crook M. *Clinical Biochemistry and Metabolic Medicine.* 2012; 8th ed. 21: 312.
4. Ganz T. Hepcidin and its role in regulating systemic iron metabolism. *Am J Hematol.* 2006; 1: 29-35.
5. Oates P. The relevance of the intestinal crypt and enterocyte in regulating iron absorption. *Pflugers Arch.* 2007; 455: 201-213.
6. Roy C. and Andrews N. Anemia of inflammation, the hepcidin link. *Curr Opin Hematol.* 2005; 12: 107-111.
7. Jayantha A., Arvind S., Vijay M., *et al.* Presence of hepcidin-25 in biological fluids: Bile, ascetic and pleural fluid. *World J Gastroenterol.* 2010; 16 (17): 2129-2133.
8. Manuel M., Isabel V., and José A. An update in iron physiology *World J Gastroenterol.* 2009; 15 (37): 4617-4626.
9. Nemeth E., Tuttle M., Powelson J., *et al.* Hepcidin regulates cellular iron efflux by binding to ferroportin and inducing its internalization. *Science.* 2004; 306: 2090-2093.

10. Dawn Koenig M., Tussing-Humphreys L., Day J., *et al.* Hepcidin and iron homeostasis during pregnancy. *Nutrients*. 2014; 6: 3062-3083.
11. Sawada T., Konomi A., and Yokoi K. Iron deficiency without anemia is associated with anger and fatigue in young Japanese women. *Biol Trace Elem Res*. 2014; 159: 22-31.
12. Klajnbard A., Szecsi P., Colov N., *et al.* Laboratory reference intervals during pregnancy, delivery and the early postpartum period. *Clin Chem Lab Med*. 2010; 48 (2): 237-248.
13. Hoppe M., Lönnerdal B., Hossain B., *et al.* Hepcidin, interleukin-6 and hematological iron markers in males before and after heart surgery. *J Nutr Biochem*. 2009; 20:11-16.
14. Fleming M. The regulation of hepcidin and its effects on systemic and cellular iron metabolism. *Hematology American Society Hematology Education Program*; 2008; 151-158.
15. Collins J., Wessling-Resnick M., and Knutson M. Hepcidin regulation of iron transport. *J Nutr*. 2008; 138: 2284-2288.
16. Wrighting D. and Andrews N. Iron homeostasis and erythropoiesis. *Curr Top Dev Biol*. 2008; 82: 141-167.
17. Ganz T and Nemeth E. Hepcidin and iron homeostasis. *Biochim Biophys Acta*. 2012; 1823: 1434-1443.
18. Manolov V., Marinov B., Velizarova M., *et al.* Anemia in pregnancy and serum hepcidin levels. *International Journal of Advanced Research*. 2015; 3 (1): 758-761.
19. Amat B., Sant-Rayn P., Momodou W., *et al.* Serum Hepcidin Concentrations Decline during Pregnancy and May Identify Iron Deficiency: Analysis of a Longitudinal Pregnancy Cohort in The Gambia. *The Journal of Nutrition. Nutrition and Disease*. 2017; 1131-1137.
20. Albendary E. and AL-Shehaa M. A Comparative Study between Serum Hepcidin Level, Iron Status and Iron Deficiency Anemia among Recently Diagnosed Gestational Diabetes Mellitus in Qassim Area KSA. *Tanta Medical Sciences Journal*. 2011; 6 (3): 107-116.