

STUDY OF THE LEPTIN LEVEL AND SOME IRON STATUS IN IRON DEFICIENT ANEMIC PREGNANT WOMEN IN ERBIL PROVINCE ⁺

دراسة مستوى اللبتين وبعض مقاييس الحديد في مصول الحوامل اللاتي يعانين من فقر الدم النقص

الحديدي في محافظة أربيل

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Abstract :

Background:Leptin is a 16-KD protein hormone that synthesized by adipose tissues and placenta during pregnancy. The early indications that leptin might function in hematopoiesis arose from the cytokine characteristics of leptin and its receptor, the identification of leptin receptors in hematopoietic tissues.

Aim:The objective of the present study is to investigate the effect of iron deficiency anemia on the levels of serum leptin.

Subjects & Method:One hundred and twenty iron deficient, pregnant women at equal number of different gestation periods (40: 1st trimester, 40:2nd trimester, 40: 3rd trimester) were subjected to the study. Their ages were between 15-41 years. They were investigated at Maternity hospital in Arbil governorate from 1st January 2007 to 30th July 2007. Sixty healthy normal pregnant women at equal number of different gestation period were subjected to the study as a control group.

Hemoglobin concentration, red blood cell indices (MCV and MCH), serum ferritin, serum iron, serum TIBC and serum level of leptin were estimated from each subjected women.

Results:The mean values of serum leptin of anemic pregnant women were 20.18 ± 1.702 ng/ml, while the mean value of serum leptin of control (normal) pregnant women was 26.29 ± 3.309 ng/ml.

Statistical analysis revealed that Serum ferritin and serum iron levels were significantly ($P < 0.001$) decreased in iron deficient anemic pregnant women which reached 81.98 ± 6.869 μ g /dl and 21.36 ± 2.946 μ g/l respectively. Serum total iron Binding capacity (TIBC) increased, but not statistically significant . The mean values reached 422.8 ± 16.82 μ g /dl in iron deficient anemic pregnant women.

Conclusion: From the results of the study, we concluded that there were decreased in serum levels of leptin, iron and ferritin in pregnant anemic women, while total iron binding capacity increased.

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المستخلص:

اللبتين هو هرمون بروتيني يصنع من قبل الانسجة الدهنية وكذلك المشيمة خلال الحمل. هنالك مؤشرات سابقة تشير الى ان اللبتين يتوظف في تكوين الدم. تهدف الدراسة لبيان تاثير نقص الحديد على مستويات اللبتين في مصول الحوامل.

شملت الدراسة 120 من الحوامل التي يعانين من فقر الدم بثلاث فترات من الحمل (الاولى والثانية والثالثة) يتراوح اعمارهن ما بين 15-41 عاما مع ستون امرأة حامله سليمة لا يعانين من مرض واعتبرت كمجموعة سيطرة. أجريت الدراسة في وحدة الأمومة لمستشفى اربيل للفترة من الأول من كانون الثاني الى نهاية تموز 2007. أجريت فحوصات تركيز الهيموغلوبين، حجم متوسط حجم الكريات الحمر، متوسط تكوين الكرية الحمر ، فريتين المصل، حديد المصل ، سعة ارتباط الكلي للحديد ومستويات اللبتين في مصول الحوامل كافة. اظهرت النتائج الى ان معدل قيم مستويات اللبتين في مصول الحوامل اللاتي يعانين من فقر الدم النقص الحديدي قد بلغت 1.72 ± 20.18 ng/ml بينما كانت المستويات في مجاميع السيطرة 3.309 ± 26.29 ng/ml. بينت التحليل الاحصائي ان هناك نقصان معنوي ($p < 0.05$) في تراكيز الحديد والبروتين في الحوامل اللاتي يعانين من فقر الدم النقص الحديدي حيث نقصت الى 6.869 ± 81.98 µg /dl بالرغم من عدم وجود فروقات معنوية في مستوى سعة ارتباط الكلي للحديد ولكن قيمتها ازدادت حيث وصلت 16.82 ± 422.8 µg /dl. استنتجت الدراسة بان هناك نقصان في مستويات اللبتين والحديد والفريتين في الحوامل اللاتي يعانين من فقر الدم بسبب النقص الحديدي مع ازدياد الارتباط الحديدي الكلي..

Introduction:

Leptin is a 16-KD protein hormone, that synthesized by adipose tissues and placenta during pregnancy [1]. It is predominantly synthesized by adipocytes [2] to limit the intake of food, promote the break-down of fat, and increase energy expenditure [3-5].

Leptin, an adipokine with cytokine-like actions, in addition to its proliferative role in the liver, might also regulate the iron regulatory hormone (hepcidin-a 25 amino acid peptide) [6]

The early indications that leptin might function in hematopoiesis arose from the cytokine characteristics of leptin and its receptor (*Ob-R*), the identification of leptin receptors in hematopoietic tissues, and from the adipocyte-specific expression of the obese gene given that adipocytes are the most abundant stromal cell type in adult human bone marrow [7].

Thus in addition to serve as a localized energy reservoir, the possibility that leptin produced within the marrow might regulate hematopoiesis may be raised [8]. Leptin has also been shown to stimulate fetal and adult erythroid and myeloid development [9]. Cytokines and growth factors control the proliferation, survival, differentiation, and activity of immune cells [10].

Iron deficiency (ID) is the most common and widespread nutritional disorder in the world. Around 600-700 million people world wide have a marked (IDA) [11]. It can be estimated that most preschool children and pregnant women in non-industrialized countries, and at least 30-40% in industrialized countries, are iron deficient [12]. Nearly half of the pregnant women in the world were estimated to be anaemic: 52% in non-industrialized- as compared with 23% in industrialized-countries.

Because of the low sensitivity and specificity of Hb, its usefulness is greatly enhanced by combining it with a more specific index of iron status. A very useful coupling of

measurements is that of Hb with SF concentration. If both measurements are normal Hb as above and SF>16 µg/l, IDA is excluded; if both are low, IDA is likely. If the SF is low but the Hb is normal, the individual is at risk of ID, while it is generally recommended to add SF to the test better to distinguish IDA from anemia of other causes during pregnancy [13].

Since no research has been conducted so far on the effect of new hormone leptin on normal and iron deficient pregnant women with advancing gestational ages, in our region, the objective for the present study is to investigate the effect of iron deficiency anemia on the levels of serum leptin .

Patients and Methods:

One hundred and twenty, suspected iron deficient, pregnant women at equal number of different gestation periods (40: 1st trimester, 40:2nd trimester, 40: 3rd trimester), were subjected to the study. Their ages were between 15-41 years. They were investigated at Maternity hospital in Arbil governorate from 1st January 2007 to 30th July 2007.

Sixty healthy normal pregnant women at equal number of different gestation period were subjected to the study as a control group. Their ages were between 17-35 years.

Subjected pregnant women who had Hb concentration less than 11g/dl considered anemia [14,15].

Nine milliliter of venous blood were collected from each subjected women by vein puncture using a 10 ml disposable syringe and the blood was divided as follows: 2ml of blood in container-1 containing K-EDTA used for hematological investigations; hemoglobin concentration, packed cell volume, red blood cells count. Mean cell volume(MCV), and mean cell hemoglobin(MCH), were calculated as follow:

$MCV (fl)=PCV/RBCs \text{ count} \times 10$

$MCH(pg)=Hb/RBCs \text{ count} \times 10$

The remaining blood was transferred into container 2 (anticoagulant free)and centrifuged at 3000 rpm for 15 minutes, for serum was separation. Collected serum were divided into two containers as follows: one milliliter was stored at -40°C for later estimation of leptin by ELISA and the remainder was immediately used for estimation of serum ferritin, serum iron and total iron binding capacity by using BioMerieux kit.

Analysis of data was performed by using SPSS (Version 11.5). Results are expressed as mean \pm SE. P value < 0.05 was considered statistically significant

The Results:

Effect of IDA on the levels of serum leptin and some iron status at first trimesters of pregnancy.

The leptin and some iron status results are shown in Table-1 it is seen that the level of leptin was not changed significantly P <0.05. the mean values of serum leptin of anemic pregnant women were (20. 18 \pm 1.702) ng/ml, while the mean values of serum leptin of control (normal) pregnant women were (26.29 \pm 3.309)ng/ml.

SF was markedly decreased P< 0.001 in anemic pregnant women (21.36 \pm 2.946) µg/l, when compared with normal pregnant women at same gestational period (43.26 \pm 5.396) µg/l, (Figure, 1).

Statistical analysis revealed that SI was significantly decreased P<0.001 in iron deficient anemic pregnant women (81.98 \pm 6.869) µg /dl, compared with (155.1 \pm 6.574) µg /dl in normal pregnant women (Figure, 2).

Serum total iron Binding capacity (TIBC) was increased, but not statistically significant (Table 1). In iron deficient anemic pregnant women the mean TIBC level was (422.8 ± 16.82) $\mu\text{g}/\text{dl}$ to (369.2 ± 18.59) $\mu\text{g}/\text{dl}$ in normal pregnant women.

Effect of IDA on the levels of Leptin and some Iron statues at second trimester of pregnancy

As shown in Table, (2) there was no significant difference in the levels of serum leptin between iron deficiency anemic pregnant and normal pregnant in the same gestational period. IDA caused a significant decrease ($P < 0.001$) in SF level from 42.54 ± 7.057 $\mu\text{g}/\text{l}$ in normal pregnant women to 16.15 ± 2.129 $\mu\text{g}/\text{l}$ in iron deficient pregnant women (Figure 3).

Interestingly serum iron was severely decreased ($P < 0.001$) in anemic pregnant 58.65 ± 3.532 $\mu\text{g}/\text{dl}$ to 118.4 ± 8.263 $\mu\text{g}/\text{dl}$ in normal pregnant (Figure 4).

TIBC values were significantly ($P < 0.001$) increased in iron deficiency anemic women at second trimester TIBC which reached 509.0 ± 12.589 $\mu\text{g}/\text{dl}$ (Figure 5).

Table 1: Effect of IDA on the levels of leptin and some iron status at first trimester of pregnancy.

Parameters Treatments	LEPTIN ng/ml	FERRITIN $\mu\text{g}/\text{L}$	IRON $\mu\text{g}/\text{dL}$	TIBC $\mu\text{g}/\text{dL}$
Anemia	20.18 ± 1.702	21.36 ± 2.946	81.98 ± 6.869	422.8 ± 16.82
Control	26.29 ± 3.309	43.26 ± 5.396	155.1 ± 6.574	369.2 ± 18.59
P value	N.S	$P < 0.001$	$P < 0.001$	N.S

Table 2: Effect of IDA on the levels of leptin and some iron status at second trimester of pregnancy.

Parameters Treatments	LEPTIN ng/ml	FERRITIN $\mu\text{g}/\text{L}$	IRON $\mu\text{g}/\text{dL}$	TIBC $\mu\text{g}/\text{dL}$
Anemia	28.39 ± 1.330	8.34 ± 0.475	44.40 ± 1.965	588.3 ± 11.43
Control	18.38 ± 1.547	41.21 ± 8.433	111.8 ± 12.28	379.3 ± 22.33
P value	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$

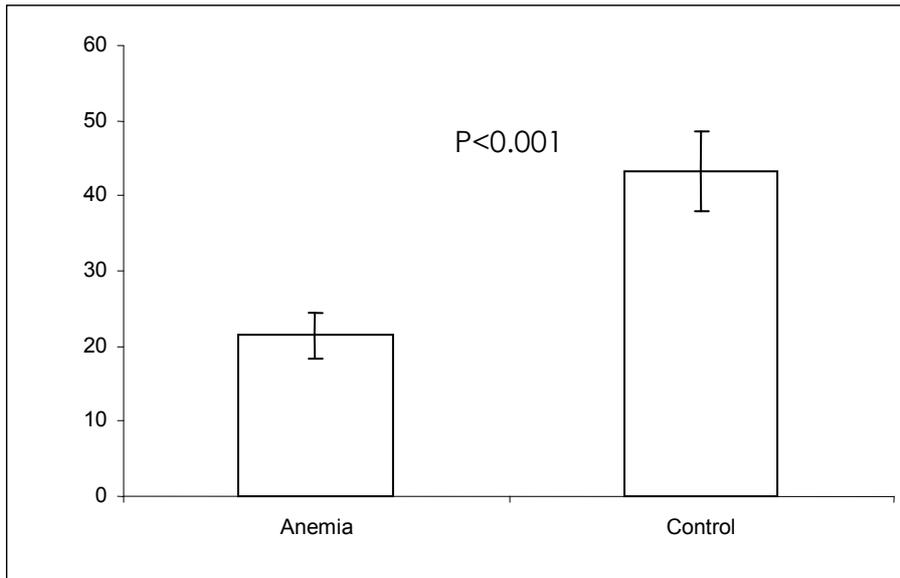


Figure (1): Effect of IDA on the levels of SF at first trimester of pregnancy.

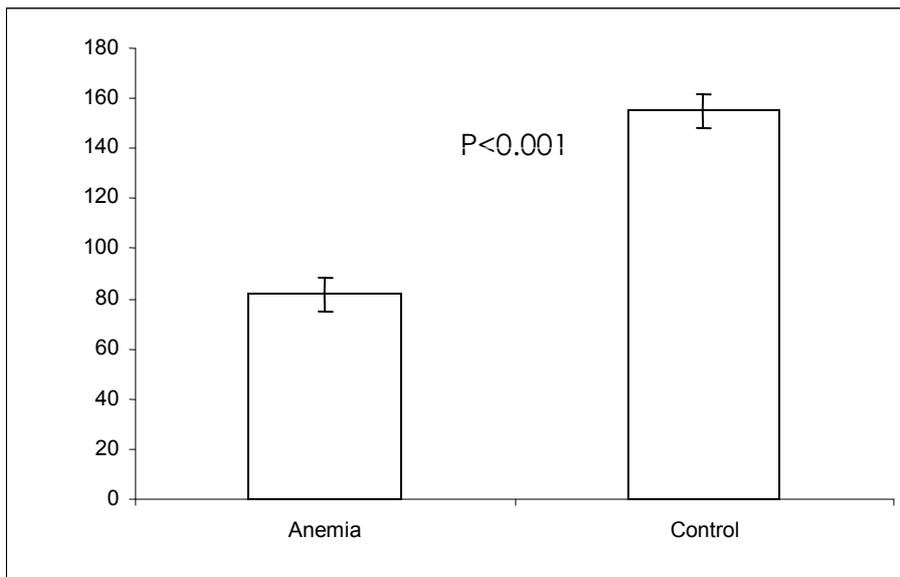


Figure (2): Effect of IDA on the levels of SI at first trimester of pregnancy.

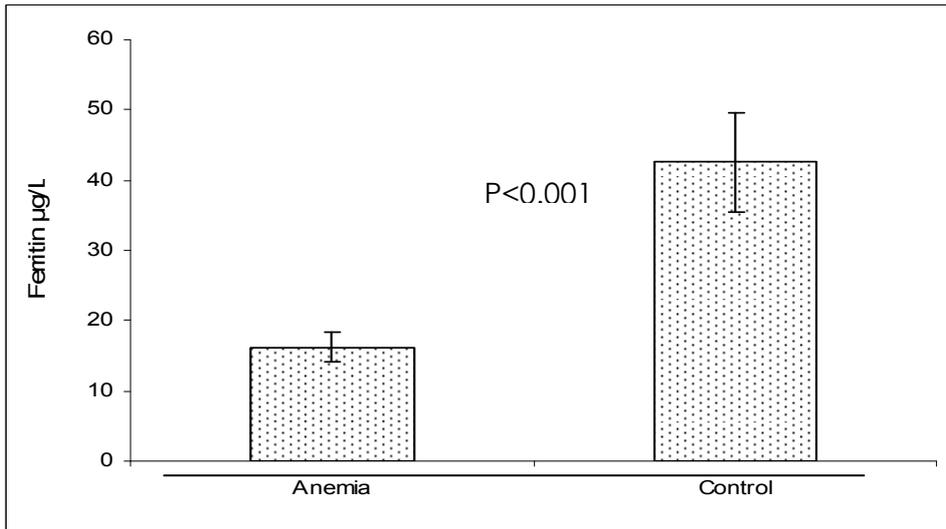


Figure (3): Effect of IDA on the levels of SF at second trimester of pregnancy.

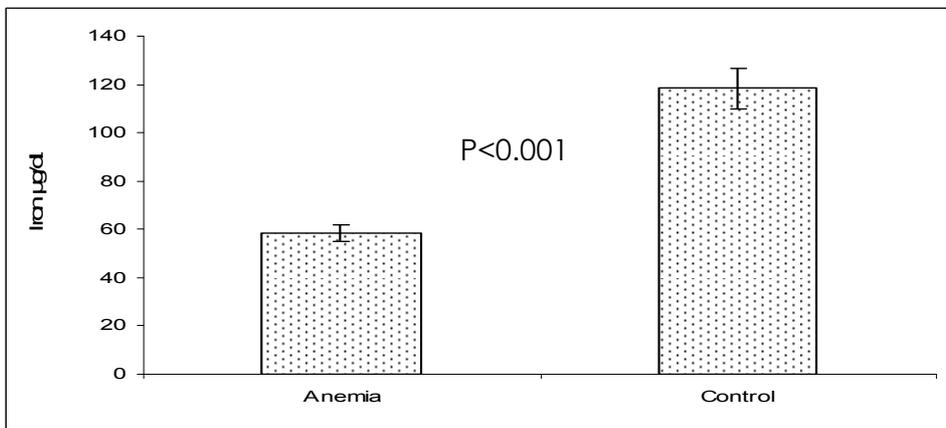


Figure (4): Effect of IDA on the levels of SI at second trimester of pregnancy.

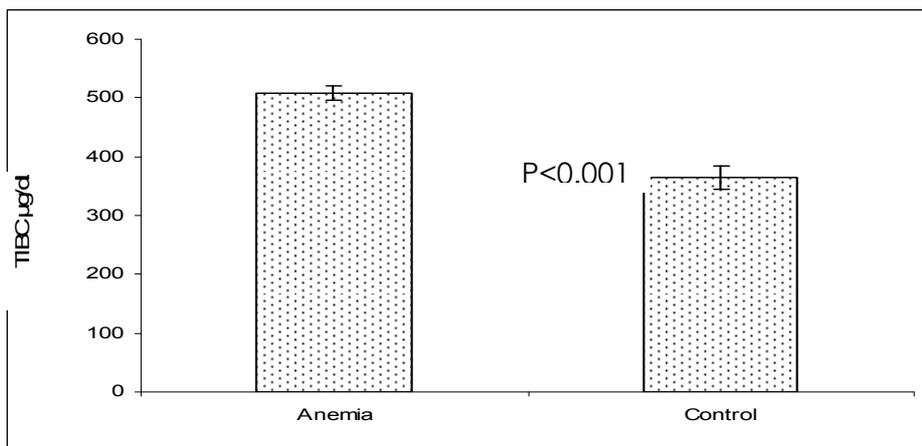


Figure (5): Effect of IDA on the levels of TIBC at second trimester of pregnancy.

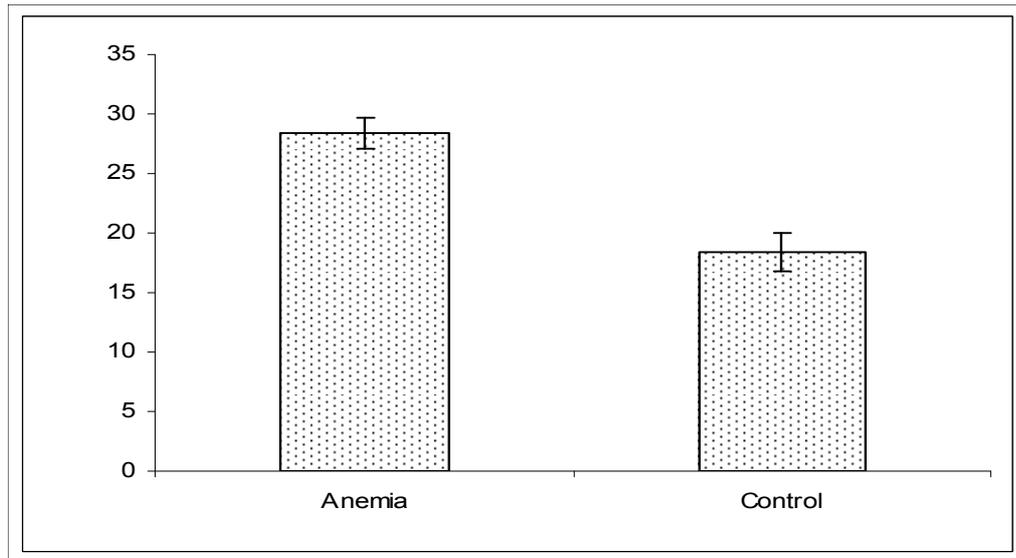


Figure (6): Effect of IDA on the levels of Leptin at third trimester of pregnancy.

Effect of IDA on the levels of Leptin and some Iron status at third trimester of pregnancy.

As shown in Table ,3 and Figure ,6 there was significant ($P<0.001$) increase in serum leptin level from 18.38 ± 1.547 ng/ml in normal pregnant women to 28.39 ± 1.330 ng/ ml in iron deficient pregnant women. Interestingly serum ferritin level was severely decreased ($P<0.001$) by iron deficiency interaction 8.34 ± 0.475 μ g/l in iron deficiency pregnant compared with 41.21 ± 8.433 μ g/l in control pregnant groups alone (Table 3 and Figure 7).

Serum iron level was also significantly lowered ($P<0.001$) from 111.8 ± 12.28 μ g/l in normal pregnant to 44.40 ± 1.965 μ g/dl in iron deficient pregnant. In addition, iron deficient interaction caused significant ($P<0.001$) increase in serum TIBC from 379.3 ± 22.33 μ g/dl in control pregnant to 588.3 ± 11.43 μ g/dl in iron deficient pregnant women (Table 3 and Figures 8 and 9).

Table 3: Effect of IDA on the levels of leptin and some iron status at third trimester of pregnancy.

Parameters Treatments	LEPTIN ng/ml	FERRITIN μ g/L	IRON μ g/dL	TIBC μ g/dL
Anemia	24.78±1.895	16.15±2.129	58.65±3.532	509.0±12.589
Control	30.41±2.632	42.54±7.057	118.4±8.263	364.3±19.715
P value	N.S	P<0.001	P<0.001	P<0.001

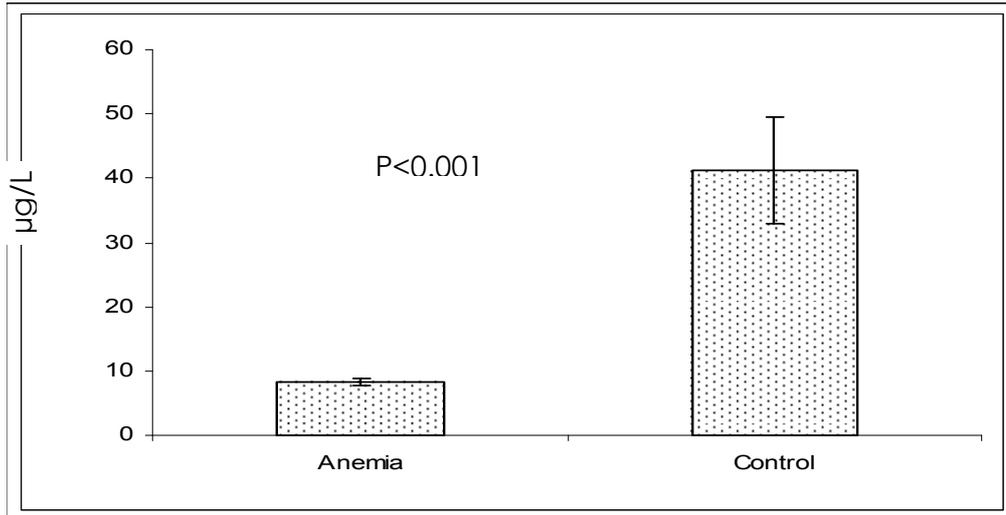


Figure (7): Effect of IDA on the levels of SF at third trimester of pregnancy.

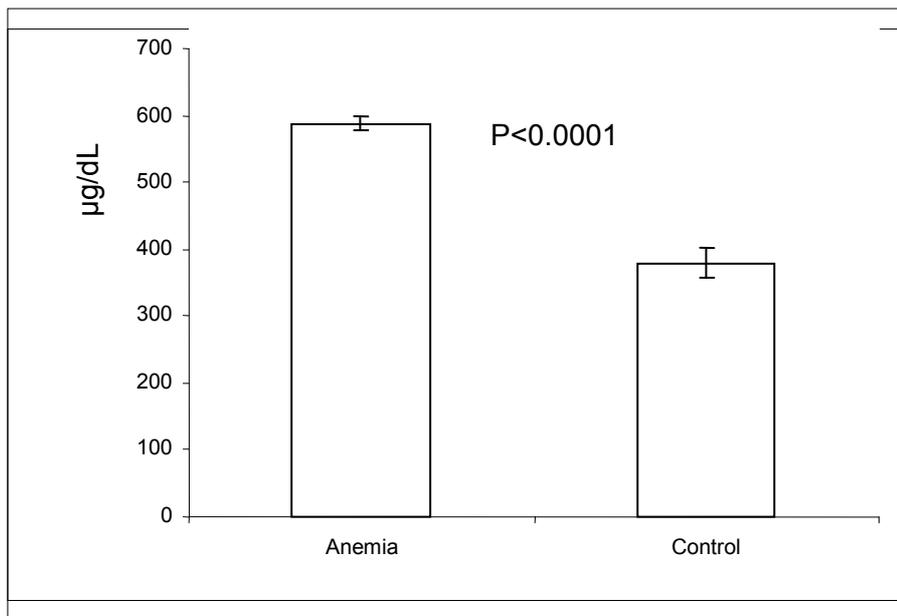


Figure (8): Effect of IDA on the levels of TIBC at third trimester of pregnancy.

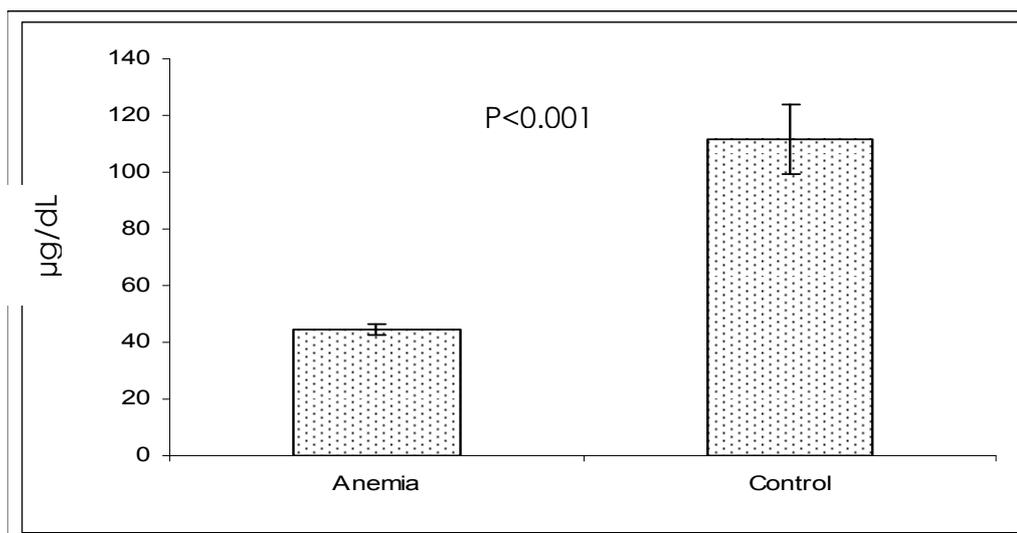


Figure (9): Effect of IDA on the levels of SI at third trimester of pregnancy.

Discussions:

In order to include the anemic pregnant women in the study, suspected women subjected to initial some hematological investigation: estimation of hemoglobin concentration and Pregnant women who had Hb concentration less than 11g/dl considered anemia [14,15] and further investigation such as mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) for morphologic classification of anemia.

The pronounced fall in the average plasma ferritin concentration to low levels in pregnancy indicates that maternal iron stores are utilized to meet fetal requirements [16] The results of our study agree with the findings of [17], which is clearly understood, in a study carried on 150 anemic women that mean serum ferritin concentrations were $< 30 \mu\text{g/l}$. On the other hand, Chandyo [18] concluded that the SF level was significantly lower in iron deficient pregnant women than that of normal pregnant women.

These results may be due to iron store of the body, which is used to increase the hemoglobin mass of the mother and its mass is directly proportional to the increased need for oxygen transport during pregnancy and is one of the important physiologic adaptations that occurs in pregnancy. [19]

The additional demands placed on maternal iron stores by the growing foetus, placenta and the increased maternal red cell mass through partially offset by cessation of menstruation and increased absorption of iron during pregnancy lead to an increased demand of iron [20]

Serum ferritin concentration is a sensitive index of the earliest stage of depletion of the body iron reserves. The changes in the median serum ferritin concentration correspond to known changes in the size of the body iron stores and iron deficiency characterized by a low serum ferritin in pregnancy, and a reduction in iron reserves great enough to impair erythropoiesis [16].

Transferrin is the iron transport protein, can be estimated as the total iron binding capacity (TIBC), this transferrin levels increases during pregnancy, reflecting an increase of 2.5 times in total circulating transferrin [21] While a rise in serum transferrin is a sign of iron deficiency, it is also believed to indicate increasing erythropoiesis. Transferrin synthesis in the liver increases under the influence of estrogen hormone and may be unrelated to other changes in iron metabolism [22,23]

In this study, we found that serum leptin level in IDA pregnant was higher significantly than normal pregnant. Our data are in agreement with the findings of Schwartz, [24] who demonstrated that hypoxia by IDA increases serum leptin production.

Leptin can directly regulate hepatic hepcidin expression. Increased production of hepcidin in the presence of leptin was predicted to result in decreased duodenal iron absorption enterocytes resulting in hypoferrremia [16,25,26] and impaired iron recycling from reticuloendothelial macrophages because of the inhibitory actions of hepcidin on ferroportin protein expression [27,28].

In conclusion, we have shown that there were decreased in serum levels of leptin, iron and ferritin in pregnant anemic women, while total iron binding capacity increased.

In addition, confirming similar studies, this study demonstrated that anemic pregnant women have higher levels of leptin. Considering this issue further, research into the pathophysiology of leptin and hematopoiesis might be needed for more information on this relationship and studies using synthetic hormone in animal and human can help to decrease problems especially hereditary types of anemia.

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