



## Tikrit Journal of Pure Science

ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)

Journal Homepage: <http://tjps.tu.edu.iq/index.php/j>



### Study of the correlations between serum iron and Hecpidin with some biochemical variables in hyperlipidemia of elderly males and females in Salah Al Deen Province

Khalida Khalil Abdullah<sup>1</sup>, Saleh Mohammed Rahim<sup>2</sup>

<sup>1</sup> Department Of Biology , College of Education , Samara University , Samara , Iraq

<sup>2</sup> Department Of Biology , College of Science , Kirkuk University , Kirkuk , Iraq

DOI: <http://dx.doi.org/10.25130/tjps.25.2020.023>

#### ARTICLE INFO.

##### Article history:

-Received: 1 / 12 / 2019

-Accepted: 27 / 1 / 2020

-Available online: / / 2020

**Keywords:** correlations, iron, hepcidine, cholesterol, triglycerides

##### Corresponding Author:

**Name:** Khalida Khalil Abdullah

**E-mail:** [kha.ab3@gmail.com](mailto:kha.ab3@gmail.com)

**Tel:**

#### ABSTRACT

The present research was designed to investigate the role of the relationship between Iron and hepcidin hormone with some biochemical variables in patients with hyperlipidemia in both males and females elderly in Salah al-Din governorate. The study included 40 individuals distributed into two groups. The first group was the control group, which included 20 human males and females and the second group included 20 patients (10 males and 10 females) whose ages ranged between (60-79) years. Blood was collected to estimate the hepcidine hormone, iron, cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins, and very low-density lipoproteins. The results showed a significant increase in ( $P \geq 0.05$ ) in the concentration of iron and hepcidin hormone, cholesterol, triglycerides, low-density lipoproteins and very low-density lipoproteins while showed a significant decrease in ( $P \geq 0.05$ ) in the concentration high-density lipoproteins in patients Males and females hyperlipidemia compared to the control group. The results also indicated a direct correlation relationship between iron and hepcidine hormone and studied variables cholesterol, triglycerides, low-density lipoproteins and very low-density lipoproteins in patients compared to the control group. It is concluded through the results that iron and the hepcidin hormone may have an important role in the development of cardiovascular diseases in hypertensive patients in elderly both males and females.

#### Introduction

Cardiovascular disease is the leading cause of death in many countries and among its causes is a high level of blood lipids in Hyperlipidemia, predominantly low-density lipoproteins, cholesterol, triglycerides and low in high -density lipoproteins. The High concentrations of circulating cholesterol especially low-density lipoproteins cholesterol are associated with an increased risk of cardiovascular and atherosclerosis. In 1981, an iron hypothesis was presented that indicates that iron depletion protects against heart disease [1] and it suggest that high levels of iron stores in The body promotes cardiovascular disease by stimulating the oxidation of cholesterol and low density lipoprotein. Epidemiological studies have shown later that not the total body load of iron, but its distribution between visceral cells on the one

hand, such as hepatic cells, and on the other hand in phagocytic cells as defined by the hepcidin hormone in the serum, which leads to the link between atherosclerosis and the risk of cardiovascular disease. hepcidin regulates the iron balance in the body's systems by controlling its release from the intestinal cells in the duodenum responsible for the absorption of food, phagocytic cells and hepatocytes [2 ]. The increase in the hormone causes an increase in the entry of iron into the bloodstream, thereby increasing its absorption by the macrophage cells transporting it. It has also been assumed that this hormone disrupts the movement of iron from phagocytic cells and promotes their conversion to foam cells and eventually sclerosis events. So research suggests that iron and the hepcidin hormone have a role in

atherosclerosis and related cardiovascular disease in the case of lipid disorder [3,4]. The current study aimed to show the relationship between serum iron and hepcidine hormone levels and hyperlipidemia among patients

### Materials and methods

Samples were collected from for (20) patients as well as the selection of a random group belonging to (20) healthy people were represented by the control group, and the study samples were divided into two groups: Group I: Control Group: included (20) people (male and female) Group II: Hyperlipidaemia patients (20) males and females aged (60-79) years were selected based on the diagnosis of doctors and clinical examinations. A blood sample (10ml) of brachial vein for each person was collected by means of a medical syringe for the tests under study, which included the measurement of the concentrations of total cholesterol, triglycerides and high-density lipoproteins using the number of ready-made masses from the French company BIOLABO, which depends on the color method and the results obtained from them. Concentrations of low-density lipoproteins and very low-density cholesterol. Hepcidine was measured by using an immunoassay method known as Enzyme-linked Immuno Sorbent Assay (ELISA) using the American ELISA Reader ELISA type BioTek Elx800 and a set of Hepcidine HITSEN Kit (ELISA) from Biotech Cusabio. Supplied with the kit. The results of this study were analyzed using T test. The mean averages of the coefficients were compared with ( $P < 0.05$ ) and the correlation coefficient was found to find the correlation between hepcidine and some variables studied in this study by applying the statistical program Minitab.

### Resultes

The results of the current study indicated, as shown in Table (1) that there was a significant increase ( $P \leq 0.05$ ) in the concentration of the hepcidine hormone, as its concentration reached ( $199.37 \pm 16.8$  pg / ml) in the group of males hyperlipidemia patients compared to the control group whose concentration was ( $120.36 \pm 2.86$  pg / ml) and the concentration of the hepcidin 10ormone in the group of patients with hyperlipidemia was females ( $235.80 \pm 17.03$ pg / ml) compared to the control group, whose concentration was ( $128.25 \pm 8.95$ pg / ml).

The results of the study also showed that there was a significant increase ( $P \leq 0.05$ ) in the iron concentration, as its concentration ( $146.30 \pm 10.49$   $\mu\text{mol} / \text{l}$ ) in the group of male hyperlipidemia patients compared to the control group whose concentration was ( $91.13 \pm 6.15$   $\mu\text{mol} / \text{l}$ ). Iron in the group of female hyperlipidemia patients ( $154.00 \pm 23.12$   $\mu\text{mol} / \text{l}$ ) compared to the control group whose concentration was ( $80.07 \pm 6.99$   $\mu\text{mol} / \text{l}$ ) The study also showed a significant increase ( $P \leq 0.05$ ) in the concentration of total cholesterol, triglycerides, Low-density lipoproteins and very low-density lipoproteins in hyperlipidemia patients compared to the control group, while the protein concentration decreased significantly. High-density lipoprotein in a group of males and females patients.

The linear correlation coefficient analysis test showed, as shown in Table (2) that there is a positive relationship at the level of significance ( $P \leq 0.05$ ) between the serum iron level and the hepcidine hormone with total cholesterol, triglycerides, low-density lipoproteins, very low-density lipoproteins, and a negative relationship at Significant level ( $P \leq 0.05$ ) between the iron level and the hepcidine hormone with high-density lipoproteins.

**Table 1: Hepcidine Concentrations and Some Biochemical Variables in Hyperlipidemic and Healthy Patients**

Clinical variables	Males patients hyperlipidemia	N 10	Healthy controls Males	Female patients hyperlipidemia	N 10	Healthy controls Female
Hepcidin pg/ml	$199.37 \pm 16.8^a$		$120.36 \pm 2.86^b$	$235.80 \pm 17.03^a$		$128.25 \pm 8.95^b$
Iron $\mu\text{mol/l}$	$146.30 \pm 10.49^a$		$91.13 \pm 6.15^b$	$154.00 \pm 23.12^a$		$80.07 \pm 6.99^b$
Cholesterol mg/dl	$279.50 \pm 29.15^a$		$168.13 \pm 16.18^b$	$276.70 \pm 25.27^a$		$166.93 \pm 15.52^b$
T.G mg/dl	$266.00 \pm 77.91^a$		$125.67 \pm 15.24^b$	$243.10 \pm 29.36^a$		$119.80 \pm 20.31^b$
HDL- C mg/dl	$31.500 \pm 1.900^b$		$45.067 \pm 4.743^a$	$33.700 \pm 2.946^b$		$47.867 \pm 5.854^a$
LDL-C mg/dl	$194.80 \pm 20.23^a$		$98.07 \pm 16.65^b$	$194.50 \pm 30.54^a$		$94.33 \pm 18.31^b$
VLDL-C mg/dl	$53.200 \pm 15.519^a$		$25.000 \pm 3.071^b$	$48.600 \pm 5.777^a$		$24.067 \pm 4.026^b$

-The values represent the mean  $\pm$  standard deviation

- The lower case letters indicate significant differences ( $P \leq 0.05$ )

\* Comparison of horizontal averages

**Table 2: Iron correlations with some biochemical variables (hepcidine, total cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins, and very low-density lipoproteins) in patients with males and females hyperlipidemia.**

Clinical variables	Iron	
	R value for female patient group Aged (60-79)Years	R value for male patient group Aged (60-79)Years
Hepcidin pg/ml	0.452	0.028
Cholesterol	0.372	0.529
T.G	0.045	0.484
HDL	- 0.086	- 0.438
LDL	0.310	0.430
VLDL	0.048	0.486

## Discussion

The results of the current research shown in Table (1) showed high total cholesterol, low-density lipoproteins, triglycerides and very low-density lipoproteins, and decrease in high-density lipoproteins for cholesterol in males, the reason is due to the male hormone testosterone, which works to increase the effectiveness Hepatic lipase and low efficacy of lipoprotein Lipase which increases HDL-c breakdown and high level of cholesterol and increased blood lipid level (TG), (LDL-c), (VLDL-c) that have an effect directly in the incidence of heart disease [5] and the increase in TC and LDL-c and VLDL-c in the age group (60-79) years is due to a decrease in testosterone levels and this hormonal change is usually associated with hyperlipidemia and a number of clinical conditions such as stroke and arterial disease, and that low levels of this hormone lead to a loss of beneficial effects that have an effect on the lining of the blood vessels, many studies indicated that Testosterone significantly improves blood flow through the coronary arteries throughout The body works by relaxing the coronary arteries by activating potassium channels and inhibiting the Venus Calcium [6]. In females, the cause of increase in total cholesterol, triglycerides, low-density lipoproteins, very low-density lipoproteins and decrease in high-density lipoproteins is related to the decrease or discontinuation of the female hormone estrogen, which leads to an increase in the level of cholesterol and an increase in view of vascular diseases and cardiovascular and this is what we observe after menopause leads to the occurrence of obesity, joint pain and osteoporosis because this hormone has a role in the protection and prevention of heart disease before menopause [7].

The high level of iron in the age group (60-79) years shows the effectiveness of the body through its excretion to increase the concentration of iron in the body and that minerals, including iron, begin to accumulate in the various tissues and cells of the body throughout the life of a person and is a cause of premature aging, because aging cells Often it is characterized by the presence of high iron in it, which reaches ten times what is present in the cells in the youth stage. When cells get old and age they work to collect iron within their tissues. In the case of iron

overload, the hepcidin hormone produced mainly from the liver can increase and prevent blocking See the iron cell [8] heibcidin regulates ferroportin (protein that releases cellular iron) Without this hormone iron would have increased more in the serum in the sense that heibcidin dominated the iron concentration in the plasma by preventing the absorption of iron from food, isolate or reserve iron in cells [9]. The high level of hepcidine reduces the absorption of food iron and also reduces the release of iron from large macrophages, which reduces the amount of iron available in the serum [10, 11]. Thus, the increase of hepcidine in the serum may increase the entry of iron into the bloodstream and thus increase its absorption by the phagocytic cells transporting it. The hormone may disrupt the movement of iron from the phagocytic cells and enhance their conversion to the foaming cells and eventually sclerosis events. Therefore, recent research suggests that iron and the hepcidin hormone have a role in atherosclerosis and related cardiovascular diseases in the case of fat disturbance [3,4] that high iron causes free radicals to be produced through their association with oxygen molecules during Fenton reactions and thus generated hydroxyl radicals and oxygen are highly oxidizing and have a harmful effect on cellular components such as DNA, proteins and fats through the oxidation of polyunsaturated fatty acids due to oxidative stress and thus decrease antioxidant defense systems in hyperlipidemic patients and cause the development of sclerotic lesions For arteries by keeping low-density lipoprotein cholesterol by oxidizing it and turning it into colloidal cells [4] It was also noted from the study results that the age group (60-79) years was the level of the hepcidine hormone in women slightly higher than in males and for the same age group and the reason may be attributed In that, the males have a fixed percentage over the age of the condition in which the patient is without patients with diseases related to iron deficiency while in females he rises depending on the menstrual period in the females as an increase in the concentration of hepcidine is observed at the interruption of the menstrual period in females i.e. it is ascending As the females progress in the world Over and above, this result is consistent with what has been found [12] in their study of the

gender differences in the case of iron and the expression of hepcidine in mice where a decrease in the average concentration of the content of hepcidine secreted from the liver was observed in male mice compared to females as the distribution of iron differs in male and female mice. This difference in the distribution of iron is associated with the different levels of hepcidine. [13] and [4] indicated the association of hepcidine levels with the presence of atherosclerotic plaques in a postmenopausal women study. High serum hepcidine concentrations are associated with increased iron and less iron, and hepcidine secretion increases in cases of inflammation and increased iron. It has also been assumed that increased hepcidine may be responsible for arteriosclerosis caused by iron and may be involved in the mechanism that links inflammation to vascular disease. It was found [14] that vascular damage is associated with iron stores in patients exposed to iron accumulation, and that increased iron is associated with the intensity of vascular damage, which indicates that the activation of macrophages by iron may be a cause of vascular damage in the live body, and this is consistent with [15] and [16] indicated our results to the causal role of the potential relationship of hepcidin in atherosclerosis, and may indicate that the iron status are causally linked to atherosclerosis. This indicates that an increased hepcidin level increases the risk of atherosclerosis. This is in line with the mechanism reached [1] and [3] in that hepcidine is effective in cardiovascular deaths and pathophysiology of atherosclerosis, and contrary to what it came to [17] which did not notice any relationship between hepcidine and atherosclerosis.

The current study also found, as shown in Table (2), that there is a direct correlation between the level of

### References

[1] Galesloot, T. E.; Geurts - Moespot, A. J.; den Heijer, M.; Sweep, F. C.; Fleming, R. E.; Kiemeneij, L. A., and Swinkels, D. W. (2013). Associations of common variants in HFE and TMPRSS6 with iron parameters are independent of serum hepcidin in a general population: a replication study. *J of medical genetics*, **50(9)**, 593-598.

[2] Roy, C.N; Mak, H.H; Akpan, I; Losyev, G; Zurakowski, D; Andrews, N.C.(2007). Hepcidin antimicrobial peptide transgenic mice exhibit features of the anemia of inflammation. *Blood*.**109**:4038–4044.

[3] Yayar, Ö.; Eser, B. and Kılıç, H. (2018). Relation between high serum hepcidin - 25 level and subclinical atherosclerosis and cardiovascular mortality in hemodialysis patients. *Anatolian journal of cardiology*, **19 (2)**, 117.

[4] Valenti, L.; Dongiovanni, P.; Motta, B. M.; Swinkels, D. W.; Bonara, P.; Rametta, R. and Fargion, S. (2011). Serum hepcidin and macrophage iron correlate with MCP-1 release and vascular damage in patients with metabolic syndrome

the hepcidin hormon and iron for male patients, and the reason for this is that the hepcidin hormon has a major role in the balance of iron in the body, as low levels of iron lead to a reduction in the production of hepcidine while High levels of iron lead to an increase in its production [18]. As the function of hepcidine lies by preventing the flow of iron into the plasma by preventing its absorption from the duodenum, and preventing the release of iron from macrophages, this is done by the hormone hepcidine that inhibits the ferroportin iron transporter receptors [19] The results of the study showed that there is a positive relationship between the level of iron in the blood serum and the level of cholesterol and triglycerides and low-density lipoproteins for both sexes of patients. It is evident that the high level of iron increases with age and with an increase in the level of blood fat as the high levels of iron stores in the body It enhances cardiovascular diseases by stimulating the oxidation of LDL cholesterol and consequently atherosclerosis. Research suggests that iron and the hepcidin hormone have a role in atherosclerosis and related cardiovascular disease in the case of fat disorder [3,4] in When the results of the study showed that there is a negative relationship between iron and high-density lipoproteins, that is, the higher the concentration of the iron level, the higher the high-density lipoproteins. The high-density lipoproteins help the body get rid of cholesterol and prevent its deposition in the arterial walls, as it carries cholesterol in the blood and transports it From different parts of the body to the liver [20] thus helping to avoid atherosclerosis by preventing the smooth muscle cells of the blood vessels from taking LDL-c. In addition, it works as an anti-inflammatory and has anti-oxidant properties [21].

alterations. *Arteriosclerosis, thrombosis, and vascular biology*, **31(3)**, 683-690.

[5] Hicham, B.; Claudia, N. M.; Abdelouahed, K. (2012). Health benefits of high-density lipoprotein in preventing cardiovascular disease. *J of Clinical lipidology* , **6, (6)** : 524-533 .

[6] Alvarez, E.; Cairraño, E.; Morgado, M.; Morais, C and Verde I.( 2010). Testosterone and cholesterol vasodilation of rat aorta involves L-type calcium channel inhibition. *Advances in Pharmacological Sciences*.

[7] David, G. G.; Asha, J.; Dolores, S. (2012). Greenspan's Basic and clinical Endocrinology . *Yale J Biol. Med.* **85(4)** : 559-570.

[8] Nemeth, E.; and Ganz, T. (2006). Regulation of iron metabolism by hepcidin. *Annu. Rev. Nutr.*, **26**, 323-342.

[9] Ronald Hoffman, E.J.B.; Leslie, E. Silberstein; Helen, E. Heslop; Jeffrey, I. Weitz and John Anastasi, (2013). *Hematology: Basic Principles and Practice*. 6 ed., Philadelphia, PA Elsevier Health Sciences

- [10] Díaz, V.; Peinado, A. B.; Barba-Moreno, L.; Altamura, S.; Butragueño, J.; González-Gross, M. and Gassmann, (2015). Elevated hepcidin serum level in response to inflammatory and iron signals in exercising athletes is independent of moderate supplementation with vitamin C and E. *Physiological reports*, **3(8)**, e12475
- [11] Gassmann, M. and Muckenthaler, M. U. (2015). Adaptation of iron requirement to hypoxic conditions at high altitude. *J of Applied Physiology*, **119(12)**, 1432-1440.
- [12] Kong, WN; NiuQM; GeL; Zheng N; Yan SF; Chen WB; Chang Yz; Zhao. SE(2014). Sex differences in iron status and hepcidin expression in rats. **160(2):**258-67
- [13] Kuragano, T.; Itoh, K.; Shimonaka, Y.; Kida, A., Furuta, M.; Kitamura, R. and Nonoguchi, H. (2011). Hepcidin as well as TNF- $\alpha$  are significant predictors of arterial stiffness in patients on maintenance hemodialysis. *Nephrology Dialysis Transplantation*, **26(8)**, 2663-2667.
- [14] Engberink, M.F; Povel, C.M; Durga J; Swinkels, D.W; de Kort, W.L, Schouten, E.G; Verhoef, P; Geleijnse, J.M.(2010). Hemochromatosis (HFE) genotype and atherosclerosis: increased susceptibility to iron-induced vascular damage in C282Y carriers *Atherosclerosis*. **211**:520–525.
- [15] Pigeon, C.; Ilyin, G.; Courselaud, B.; Leroyer, P.; Turlin, B.; Brissot, P. and Loréal, O. (2001). A new mouse liver-specific gene, encoding a protein homologous to human antimicrobial peptide hepcidin, is overexpressed during iron overload. *J of biological chemistry*, **276(11)**, 7811-7819.
- [16] Nemeth, E.; Valore, E. V.; Territo, M.; Schiller, G.; Lichtenstein, A.; and Ganz, T. (2003). Hepcidin, a putative mediator of anemia of inflammation, is a type II acute-phase protein. *Blood*, **101(7)**, 2461-2463
- [17] Pechlaner, R.; Kiechl, S.; Mayr, M.; Santer, P.; Weger, S.; Haschka, D., and Weiss, G. (2016). Correlates of serum hepcidin levels and its association with cardiovascular disease in an elderly general population. *Clinical Chemistry and Laboratory Medicine (CCLM)*, **54(1)**, 151-161.
- [18] Zoller, H; KOCH RO; Theurl I; Obrist P; Pietrangelo A; MontosiG; Haile DJ; Vogel W and Weiss G;(2001) Expression of the duodenal iron transporters divalent- metal transporter 1 and ferroportin I in iron deficiency and iron overload. *Gastroenterology* ; **120**: 1412- 1419.
- [19] Girelli, D.; Nemeth, E.; and Swinkels, D. W. (2016). Hepcidin in the diagnosis of iron disorders. *Blood*, **127(23)**, 2809-2813.
- [20] Edlow, J. A.; Panagos, P. D.; Godwin, S. A.; Thomas, T. L., and Decker, W. W. (2009). Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache. *J of Emergency Nursing*, **35(3)**, e43-e71.
- [21] Ridgway, N. and McLeod, R. (2016). *Biochemistry of lipids, lipoproteins and membranes*. Elsevier. .330, 331, 361, 437, 438, 524, 525.

## دراسة العلاقات الترابطية بين حديد مصل الدم وهرمون الهبسيدين مع بعض المتغيرات الكيموحيوية

### لدى مرضى فرط الدهون من الذكور والاناث كبار السن في محافظة صلاح الدين

خالدة خليل عبدالله<sup>1</sup> ، صالح محمد رحيم<sup>2</sup>

<sup>1</sup>قسم علوم الحياة ، كلية التربية ، جامعة سامراء ، سامراء ، العراق

<sup>2</sup>قسم علوم الحياة ، كلية العلوم ، جامعة كركوك ، كركوك ، العراق

#### الملخص

صمم البحث الحالي بهدف التحري عن دور العلاقة بين الحديد وهرمون الهبسيدين مع بعض المتغيرات الكيموحيوية لدى المرضى المصابين بفرط الدهون من الذكور والاناث كبار السن في محافظة صلاح الدين، شملت الدراسة 40 فردا وزعت إلى مجموعتين المجموعة الأولى مجموعة السيطرة ضمت (20) شخصا (ذكورا وإناثا) والمجموعة الثانية ضمت 20 من المرضى (10 ذكورا و10 إناث) تراوحت اعمارهم بين (60-79) سنة. تم جمع الدم لتقدير هرمون الهبسيدين والحديد والكوليسترول والدهون الثلاثية والبروتينات الدهنية عالية الكثافة والبروتينات الدهنية واطئة الكثافة والبروتينات الدهنية واطئة الكثافة جدا، وقد بينت النتائج ارتفاع معنوي ( $P \leq 0.05$ ) في تركيز الحديد وهرمون الهبسيدين والكوليسترول والدهون الثلاثية والبروتينات الدهنية واطئة الكثافة والبروتينات الدهنية واطئة الكثافة جدا بينما بينت النتائج انخفاض معنوي ( $P \leq 0.05$ ) في البروتينات الدهنية عالية الكثافة في مرضى فرط الدهون من الذكور والاناث بالمقارنة مع مجموعة السيطرة كما اشارت النتائج ايضا الى وجود علاقة ارتباط طردية بين الحديد وهرمون الهبسيدين والمتغيرات المدروسة لدى المرضى بالمقارنة مع مجموعة السيطرة يستنتج من خلال النتائج بأنه قد يكون للحديد ولهرمون الهبسيدين دورا مهما في تطور الامراض القلبية الوعائية لدى مرضى فرط الدهون كبار السن من الذكور والاناث.