The Role of Irisin and Some Immunological And Biochemical Parameters in Hypertensive Patients in Salah Al-Din Governorate

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ABSTRACT

Study Design: Cross sectional

Background: High blood pressure is the largest single contributor to the global burden of disease and is increasing annually, affecting an estimated 1.39 billion people worldwide and causing 10.4 million premature deaths annually. It usually has no symptoms, but can cause serious problems such as: Stroke, heart failure, and studies must be conducted on how to prevent and control high blood pressure.

Objective: This study aims to evaluate the level of the hormone irisin in patients with high blood pressure and its relationship to interleukin 2, interleukin 1 beta, and interleukin 17, and also to study the level of lipids in patients with high blood pressure and evaluate the level of risk of their blood pressure.

Methods: Research methods: This study was conducted in Saladin Governorate, the city of Tikrit in Iraq, where 90 samples were collected from males and females, blood was drawn from them in the morning while they were fasting, and they were divided into two groups. The first group was (50) male and female patients suffering from high blood pressure, which is essentially pathological and not hereditary. They were newly diagnosed as a result of their unhealthy lifestyle. For example, they eat a large amount of fat that has taken away from their weight, and they do not suffer from other chronic diseases. They exercise infrequently and have never had surgery. The second group is the control group (40 male and female individuals). Five milliliters of blood was drawn intravenously from hypertensive patients and healthy controls, and samples were collected from Salah al-Din General Hospital and some external medical laboratories. The ages of the patients ranged between (20-50) years. Interleukin 2 and interleukin 1 beta were measured and their relationship with high blood pressure was measured using measuring tools. A ready-made kit from the American company SUNLON based on ELISA technology using the Huma Reader device

Result: The results of immunological parameters showed a significant increase in the levels of interleukins (IL-17, IL-2, IL-1 beta), which was statistically significant ($P \leq 0.01$) among individuals suffering from high blood pressure compared to the control group. It also indicates a higher level of the hormone irisin compared to people. In healthy subjects, lipid levels (cholesterol, triglycerides, LDL, and VLDL) were elevated and statistically significant ($P \leq 0.01$) among individuals with hypertension compared to the control group. At the same time, there was a statistically significant decrease in HDL ($P \leq 0.01$) among individuals with hypertension who suffer from high blood pressure compared with the control group.

Conclusion: : This study aimed to provide important results regarding the levels of the hormone irisin in the blood of hypertensive patients and its association with interleukins (1 beta, 2, 17) and some lipid biochemistry in hypertensive patients. Explain whether there is a relationship between them in terms of the immune response in patients with high blood pressure.
Keywords: high blood pressure patients in Salah al-Din Governorate, interleukin-2, interleukin-1 beta, interleukin-17, the hormone irisin, cholesterol, triglycerides, HDL, LDL, VLDL

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INTRODUCTION

Hypertension, sometimes referred to as high blood pressure (HBP), is a common medical condition, and is a serious global public health issue[1], It is hard to diagnose and treat, which increases the risk of serious side effects damage, and other cardiovascular diseases (CVDs). The global population with high blood pressure has climbed by 90% in the last several decades. By the year 2025, hypertension is expected to impact 1.56 billion individuals worldwide, up from its position as the top cause of death in 2010. Over the past few decades,[2] increased with age, adults with blood pressure at age 55 have a 90% risk of developing high blood pressure over his or her lifetime. We must take into account the consequences of this disease: 35% of myocardial infarction cases, 49% of heart failure cases, and 24% of premature deaths are caused by high blood pressure [3]

Hypertension is characterized by persistently high blood pressure (BP) in the systemic arteries. BP is commonly expressed as the ratio of systolic BP (that is, the pressure that the blood exerts on the arterial walls when the heart contracts) and diastolic BP (the pressure when the heart relaxes). The BP thresholds that define hypertension depend on the measurement method. as systolic blood pressure (SBP) values of 130 mm Hg or more and/or diastolic blood pressure (DBP) of more than 80 mm Hg. High blood pressure is one of the most common chronic medical conditions characterized by a persistent rise in arterial pressure. The definition and categories of high blood pressure have evolved over the years, but there is consensus that persistent blood pressure readings of 140/90 mm Hg or more should be treated with the usual therapeutic goal of 130/80 mm Hg or less.[4]

Low-grade inflammation is a major contributor to hypertension, and it appears that both the innate and adaptive immune systems have a role in the development and maintenance of hypertension. Hypertension is linked to immune cell infiltration in the heart, kidneys, and vasculature, as well as elevated vascular cytokine levels brought on by vascular inflammation. The mechanisms behind inflammation and immune system activation in hypertension are yet unclear. Hypertension, the most common chronic cardiovascular disease, is associated with a number of clinical disorders.[5]

Sampling:

The study was conducted in which (90) samples were collected from males and females in the morning, while they were fasting, and they were divided into two groups. The first group was (50) male and female patients who suffer from high blood pressure that is essentially pathological, newly diagnosed as a result of their unhealthy lifestyle, for example, they eat a large amount of fat and also take a percentage of their weight, and they do not suffer from other chronic diseases. They exercise infrequently and have never undergone surgery. The second group is the control group (40 individuals, male and female). Five milliliters of blood was drawn intravenously from hypertensive patients and healthy controls, and samples were collected from Salah al-Din General Hospital and some external medical laboratories. The ages of the patients ranged between (20-50) years. Interleukin 2 and interleukin 1 beta were measured and their relationship with high blood pressure was measured using measuring tools. A ready-made kit from the American company SUNLON based on ELISA technology using the Huma Reader device.

Ethical consent:

Following the acquisition of institutional ethical approval and written informed consent from each patient, they were able to participate in the current study. This research has been approved by the Central Scientific Research Ethics Committee at Tikrit University.

The inclusion criteria:

These were derived from the above characteristics. They are a group of people with high blood pressure who were consented by these patients who agreed to participate in this study.

Statistical analysis

In this study, the results of physiological and immunological blood pressure and ELISA tests were subjected to statistical analysis using the Minitab-17 statistical program. One-way analysis of variance (ANOVA) was used, and Duncan-test multiple comparisons test was used at the (0.01) probability level to compare significant differences between the means of the current study groups. Descriptive statistics were used to extract the mean and standard error.
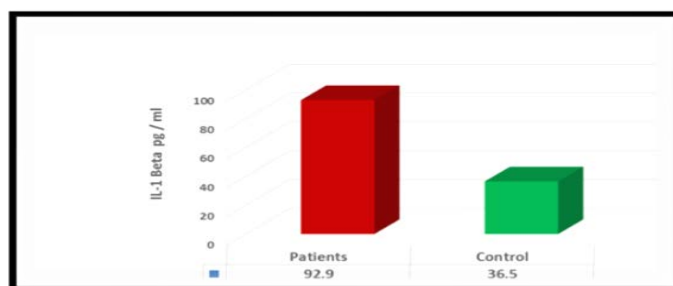

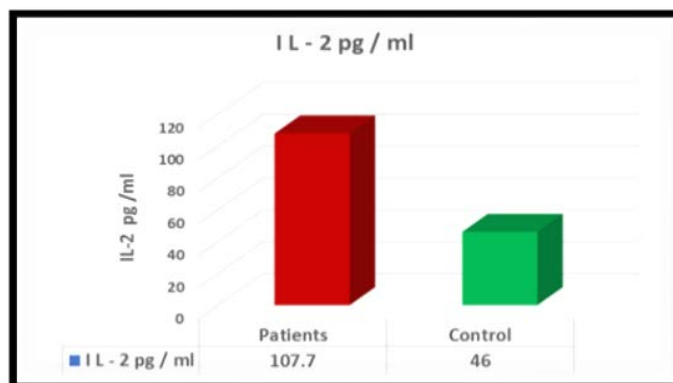**Figure 1.** Assessment Serum (Level of IL-1β pg/ml) in studied groups

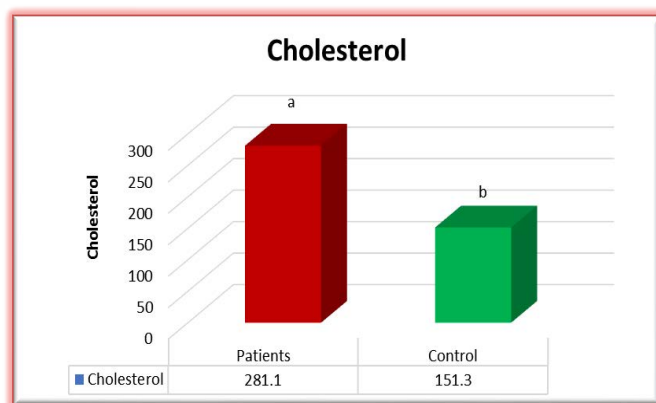**Figure 2.** Assessment Serum IL-2 (p g/ml) in Studied Groups
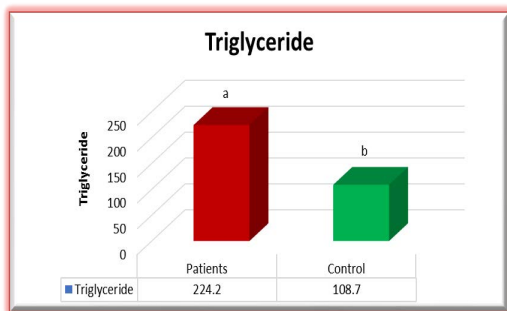

Figure 3. Cholesterol

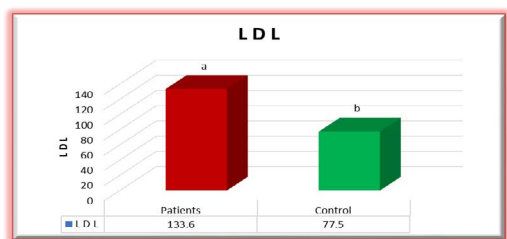**Figure 4.** Triglyceride
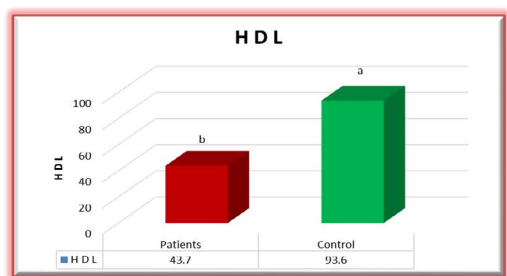
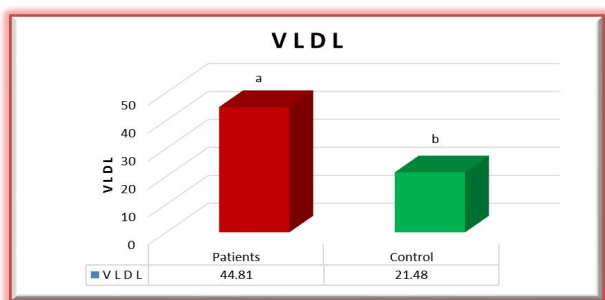**Figure 5.** HDL

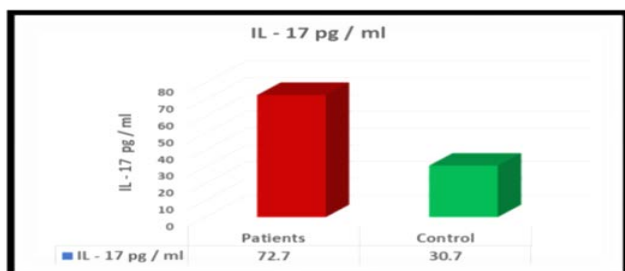**Figure 6.** LDL

Figure 7. VLDL

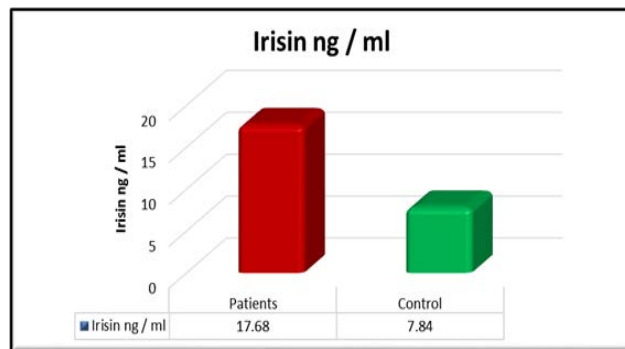**Figure 8.** Assessment of total irisin in studied groups.

Figure 9. Assessment of total irisin in studied groups.

The results of the study in Table 1 showed that there was a significant increase in the level (P ≥0.01) of immunological activity of interleukin-2, interleukin- 1 beta, and interleukin- 17 in people with high blood pressure compared to the control group. interleukin -2, The results of the analysis performed, , reveal a statistically significant increase in Irisin levels (P ≤0.01) among individuals with hypertension compared to individuals in the control group.

The results of the study in Table No. 1 showed a significant increase in the level (P ≤0.01) of cholesterol, triglycerides, and LDL. Still, they showed a statistically significant decrease in HDL at the level of (P ≤ 0.01) in people with high blood pressure compared to the control group.

The results of the study showed a [Figure (5), (6), (7), (8), (9)] significant increase in the level (P ≤ 0.01) of (cholesterol, triglycerides, and LDL). Still, they showed a statistically significant decrease in (HDL) at the level of (P ≤ 0.01) in people with high blood pressure compared to the control group.

The value of cholesterol in patients with high blood pressure was (281.1 ± 18.1) mg/dl compared to the control group, which was (151.3 ± 17.5) mg/dl. The value of triglycerides in patients with high blood pressure was (224.2 ± 20.0) mg/dl compared to the control group, which was (108.7 ± 18.9) mg/dl, Low-density lipoprotein (LDL) was the value of patients with high blood pressure (133.6 ±17.7) mg/dl compared to the control group (77.5± 15.8) mg/dl. VLDL showed in patients with high blood pressure (44.81±7.97) mg/dl compared to the control group (21.48 ± 3.63) mg/dl. However, it showed a statistically significant decrease in high-density lipoprotein (HDL) at the level (P ≤ 0.01) in people who suffer from high blood pressure reached (43.7±5.6) mg/dl compared to the control group (93.6± 9.7) mg/dl.

The results of the study showed a [Figure (1), (2), (3), (4)] significant increase in the concentration of interleukins in the serum of individuals diagnosed with high blood pressure, compared to the control group. The results showed an increase in the level of interleukin 2 in patients with high blood pressure, reaching (107.7±12.7) pg/ml, and the level of IL-2 was (46.0±10.9) pg/ml in the control group, with a statistically significant (P ≥0.01) and the strength of the significant difference between (T-test = 9.25**).

Interleukin-1 beta

The results showed an increase in the level of interleukin-1 beta in patients with high blood pressure, reaching (92.9±12.8) pg/ml compared to healthy people who do not suffer from high blood pressure, which is (36±6.52) pg/ml, with statistical significance (P ≥ 0.01 and the strength of the significant difference between (T-test =6.76**).

IL-17

The results showed an increase in the level of IL-17 in patients with high blood pressure up to (72.7±10.3) pg/ml compared to healthy controls (30.7±5.71) pg/ml, with a statistically significant (P ≥0.01) and the strength of the significant difference between (T test =6.09**).

I R I S I N

The results of the analysis performed, reveal a statistically significant increase in the levels of irisin (P ≥ 0.01) and the strength of the significant difference between (T-test = 6.05**) in individuals with high blood pressure. (17.68 ± 3.12) compared to individuals in the control group (7.84 ± 1.25) ng/m.

Table 1. Value of immune variables and the hormone irisin in patients with high blood pressure compared with the control group.

IL-1β	Cases	N	Mean	Std. deviation	T test	P-value
	Control	40	36.5	±6.52	6.76**	0.01
	Patients	50	92.9	±12.8		
IL-17	Control	40	30.7	±5.71	6.09**	0.01
	Patients	50	72.7	±10.3		
IL-2	Control	40	46.0	±10.9	9.25**	0.01
	Patients	50	107.7	±12.7		
IRISIN	Control	40	7,84	±1.25	6.05**	0.01
	Patients	50	17.68	±3.12		
P.Cholesterol			281.1	18.1	12.81**	0.01
C.Cholesterol			151.3	17.5		
P.Triglyceride			224.2	20.0	15.88**	0.01
C.Triglyceride		50	108.7	18.9		
P.HDL			43.7	5.6	13.10**	0.01
C.HDL		40	93.6	9.7		
P.LDL			133.6	17.7	15.87**	0.01
C.LDL			77.5	15.8		
P.VLDL			44.81	7.97	16.24**	0.01
C.VLDL			21.48	3.63		

The value represents the mean ± standard deviation
N=Number of samples
P= Patients
C= Control group

Exclusion criteria

Patients who did not show any signs that they were suffering from any disease or relationship to high blood pressure. Participants in the study were very few, with consent denied in some cases.

Study enrollment procedures:

The data collected for this study encompassed socio- demographic characteristics of the subjects, specifically their age and smoking status, as documented in their medical record

DISCUSSION

Interleukin-2 (IL-2) is a cytokine that stimulates the production of interleukin 2 (IL-2) by T cells[6]. It plays an important role in controlling the immune *system*.[7] As a cytokine signaling molecule, it is the protein responsible for regulating the activity of blood cells. White blood cells, specifically white blood cells involved in the immune system. Function, primarily lymphocytes.[8] The immune system through differentiation and balance between pro- and anti-inflammatory T cells·[7]

A study showed that interleukin 2 contributes to increasing the immune response to some diseases associated with high blood pressure, including ischemic heart disease, which is affected by high blood pressure, where T cells and CD4T helper T cells are stimulated..[9]

In a study that confirms the nature of its physiological basis, especially interleukin 2, there is a study that shows a relationship between the CD4T helper cell and an important role in the pathophysiological mechanisms underlying high blood pressure resulting from T cells.[10]

Increasing the interleukin 2 level in Nigeria's Bayelsa State among hypertensive individuals. Helper T cells, natural killer T cells, dendritic cells, lymphoid tissue stimulators, and T cells manufacture it·[11]
The exact role that IL-2 plays in hypertension remains unknown in several studies. The cytokine IL-2, which is generated by T cells that have been activated, is essential for preserving immune tolerance. But IL-2 production raises the risk of high blood pressure. In contrast to those with hypertension, regulatory T cells survive and proliferate.[12]

It is synthesized by helper T cells, macrophages, dendritic cells, natural killer T cells, lymphoid tissue stimulator, and T cells. Interleukin 17 (IL-17) is a cytokine that promotes inflammation. The production of multiple cytokines is stimulated by IL-17, ultimately leading to the recruitment of monocytes and neutrophils to the site of inflammation.[13]

Which are produced by a subset of CD4 T cells called Th17cells. Recent research has demonstrated the role of interleukin 17 in patients with high blood pressure and autoimmune diseases associated with high blood pressure, in addition to high levels of interleukin 17.[14]

In this study, it was stated that immune cells are activated by salt in high blood pressure, causing damage to end-organs that the immune system reacts to internal injury, such as high blood pressure. Activation of adaptive immunity participates in the differentiation of CD4 T cells into Th17 cells in order to control high blood pressure.[15]

The roles of FNDC5/irisin have a significant impact on blood vessels, skeletal muscle, articular cartilage, fat, liver, and nerves. The myogenic factor secreted during exercise, irisin, is essential for controlling fat browning, promoting liver metabolism, and maintaining musculoskeletal homeostasis. Potential mechanisms and signaling pathways of irisin action in pathological and skeletal muscle tissues ·[16]

Through a study, a method was found to prevent cardiovascular diseases. The term "exercise simulation" refers to a new therapeutic approach that aims to simulate or enhance the benefits of physical exercise in order to prevent and treat diseases. This approach is based on the beneficial effects of exercise through specific pathways and cellular processes·[17]

A study found that when an increase in the level of excess blood occurs so that the body is unable to drain it or an imbalance in energy occurs, it generates the hormone irisin, which is present in adipose tissue linked to the muscles. This hormone also plays a role in the metabolic immune response, as these fats are one of the reasons for generating an increase in blood pressure. blood pressure·[18]

Research results indicate that irisin levels were greater in individuals with high blood pressure compared to control subjects with normal blood pressure.

However, it is unclear whether the hypertension in our study is a consequence or a cause of high irisin levels. Since hypertension is a well-known condition associated with oxidative stress and systemic inflammation, previous research has shown that lowering reactive oxygen species and inflammation levels may partially help control hypertension[19-20]. Previous research has shown a relationship between irisin levels and the inflammatory factor [21-22]

One of the researchers in this study believes that there is a positive relationship between cholesterol and fatty acids that are formed through an unhealthy dietary pattern, which leads to the development of high blood pressure and increases the risk with increased fat storage.[23]

A study found that there were abnormally high levels of low-density fats and low-density proteins, as well as high cholesterol and triglycerides, noting a decrease in the levels of high-density fats and proteins compared to a normal group.[24]

Confirming the results that appeared in the study currently, there is a relationship between TC,LDL,VLDL abnormally high blood pressure complications affecting the complications of high blood pressure.[25]

In one recent study, it was found that lipid disorders increase high blood pressure, as it was found that lipid disorders consist of high values of cholesterol and triglycerides, high levels of fat LDL , and HDL blood pressure. Fats are metabolized, which leads to an imbalance in the levels of fats and lipoproteins in the blood, leading to high blood pressure. This study has proven that hyperlipidemia has an effect.[26]

The immune system believes that high blood pressure is linked to hyperlipidemia, or the accumulation of fats within the body, as a study found that the accumulation of high accumulated cholesterol inside the arteries promotes endothelial dysfunction and activation, where the production of cytokines leads to inflammation .[27]

Hypercholesterolemia leads to cholesterol accumulation in macrophages and other immune cells, which promotes inflammatory responses, including increased Toll-like receptor (TLR) signaling, inflammasome activation, and production of monocytes and neutrophils in the bone marrow and spleen. At the cellular level, activation of TLR signaling leads to decreased cholesterol efflux, leading to more cholesterol accumulation and amplification of inflammatory responses. Although cholesterol accumulation by promoting inflammatory responses has an important role in therapeutic interventions.[28]

The "cholesterol hypothesis" found that high blood cholesterol is one of the main risk factors, while lowering cholesterol levels can reduce the risk of hypertensive disease. Whereas dyslipidemia (i.e. hypercholesterolemia or hyperlipidemia) is defined as a defect in fat metabolism characterized by increased circulating levels of blood total cholesterol, LDL cholesterol, and triglycerides, high levels of LDL cholesterol and low HDL cholesterol have been associated with cardiovascular risk.[29]

Therefore, there is a study that states that high cholesterol, triglycerides, and low-density fat are low in high-density fat. We evaluate in this study the extent of the risk of developing cardiovascular diseases, of which high blood pressure is one of those diseases.[30]

CONCLUSION:

This study aimed to provide important results regarding the levels of the hormone irisin in the blood of hypertensive patients and its association with interleukins (1 beta, 2, 17) and some lipid biochemistry in hypertensive patients. Explain whether there is a relationship between them in terms of the immune response in patients with high blood pressure.

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