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Evaluation of the Level of Sirtuin7 and Some Biochemical Parameters in Patients with Cardiovascular Disease

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Abstract

The regulatory protein SIR7 Homolog 7 is known as sirtuin7 and is one of the seven most important sirtuins found in mammals, it is located primarily in the nucleus and is released from the nucleus into the nucleoplasm in response to stress. This study evaluated the relationship between low levels of sirtuin7 in the blood and cardiovascular disease in addition to studying the effect of gender on the level of sirtuin7 and the measured biochemical variables. Blood samples were collected from 45 patients with cardiovascular disease and 45 blood from healthy people as a control group. The following Clinical examinations was performed for both cardiovascular patients and control group: Sirtuin7 enzyme (SIRT7), tumour necrosis factor alpha (TNF-α), lipoxygenase enzyme (LOX), superoxide dismutase (SOD), albumin, glutathione peroxidase (GPx), glutathione (GSH) and malondialdehyde (MDA), in addition to studying the effect of sex on all of these examinations. Recorded results that low levels of the enzyme sirtuin7 in blood serum (2.6885 ± .88859) occurred in patients with cardiovascular disease compared to control group (13.5435 ± 2.19009). A significant difference was recorded at the probability level ($p \leq 0.01$) in the levels

of Sittuin7, tumour necrosis factor-α, lipoxygenase enzyme, lipoxygenase enzyme, superoxide dismutase.

Keywords: Sirtuin7 Enzyme, Cardiovascular Patients, Effect of Sex.

Introduction

The enzyme sirtuin7 is the least studied and well-known of the seven sirtuins found in mammals, but some studies have shown that it participates in many cellular processes and that its biological function has gradually become clear in health and disease. Sirtuin 7 consists of 400 amino acids that act as a class III histone deacetylase in humans. It is expressed in various organs and tissues of the body. Its highest expression is found in hyperplastic tissues such as the spleen and liver, and its lowest expression is found in skeletal muscles, the brain, and the heart [1]. The sirtuin7 enzyme is located primarily in the nucleus [2] and is released from the nucleus to Nucleoplasm in response to stress [3]. It acts as a dynamic nuclear master regulator of mitochondrial function through its ability to deacetylate GABPB1 and stimulate the formation of the GABP complex [4]. The GABP complex is a master regulator of mitochondrial biogenesis, which is the process of forming new mitochondria inside cells, as this complex activates nuclear-encoded genes involved in biogenesis. For mitochondria [5]. Cardiovascular disease (CVD) is a group of disorders and problems that affect the cardiovascular system and is considered the first and main cause of death around the world [6]. Mitochondrial dysfunction contributes to cardiovascular diseases [7], as mitochondria are the main sources for the production of reactive oxygen species (ROS) in cells [8] Excessive ROS promotes increased oxidative stress [9] Oxidative stress occurs when the rate of ROS production is higher than the capabilities of antioxidants and is an important risk factor for cardiovascular disease [10].

Aim of the Study

This research aims to conduct a biochemical study of cardiovascular patients and study the effect of gender on all measured variables.

Materials and Working Methods

The current study was conducted by taking 45 blood samples from cardiovascular patients who were diagnosed by specialized doctors and 45 blood samples from healthy people as a control group. Both groups were male and female.

Preparation of Blood Serum

Blood samples were collected from patients with cardiovascular diseases (10ml), then the serum samples were separated and divided into four parts in small dry plastic tubes and kept in covered tubes at a temperature of (-20°C) until it is used in measuring the specified variables in the research.

Measurement of Some Biochemical Variables in Blood Serum

The level of sirtuin7 and TNF-α were assessed by ELISA. This ELISA kit uses the Sandwich-ELISA method [11] and [12] respectively. The effectiveness of the lipoxygenase enzyme in blood serum was determined based on the method followed by the researchers in the research [13]. The level of albumin in blood serum was determined using the bromocresol green method, in which ready-made standard analysis tools from the French company BIOLABO were used [14]. The activity of the superoxide dismutase enzyme was estimated according to a modified method ((modified nitro tetrazolium photochemical method (NBT))) [15]. Glutathione peroxide (GPx) was estimated according to the method used in the research [16]. The concentration of glutathione in blood serum was estimated based on a modified method based on the use of (Ellman's Reagent) [17] . The level of malondialdehyde

concentration in blood serum was estimated according to the method used by the researcher in the research [18].

Statistical Analysis

The data collected from the study was analysed using a t-test, which is a type of statistics used to determine whether there is a significant difference between the averages of the two groups.

Results and Discussion

The study, as shown in Table (1), included measuring 8 variables in patients with cardiovascular disease and comparing them to healthy people. The results showed a significant decrease in the level of sirtuin7 concentration at the probability level ($p \leq 0.01$) in the serum of patients with cardiovascular disease compared to its concentration level in healthy people. The results also showed a significant increase in the level of tumours necrosis factor alpha (TNF-α) concentration and a significant increase in the activity of the lipoxygenase enzyme in the serum of patients with cardiovascular diseases compared with healthy people at a probability level ($p \leq 0.01$). The results also indicated a significant decrease in the levels of antioxidants (albumin, SOD, GPx, GSH) at the probability level ($p \leq 0.01$) in both male and female patient groups compared to healthy people for both groups. a probability level ($p \leq 0.01$) in the serum of patients with cardiovascular diseases compared to its concentration in healthy subjects.

The results also indicated a significant increase in the level of Malondialdehyde at a probability level ($p \leq 0.01$) in the serum of patients with cardiovascular diseases compared to its concentration in healthy subjects.

Table (1): Levels of biochemical variables measured in the blood serum of people with cardiovascular disease compared to the control group.

Biochemical variable	Patient group (No.45)	Control group (No.45)
	Mean ± Std .Deviation	Mean ± Std .Deviation
Sirtuin7 (ng / ml)	2.6885 ± .88859 **	13.5435 ± 2.19009
Tumor necrosis factor-α(pg / ml)	325.57 ± 46.88302 **	7.6453 ± 1.43800
Lipoxygenase (U / L)	129.39 ± 69.87575 **	52.5016 ± 5.19309
Albumin (g / dl)	31.2545 ± 6.94866 **	54.3705 ± 4.53965
Superoxide dismutase (U / L)	2.3567 ± .64348 **	4.0283 ± 1.00445
Glutathione peroxidase (U / L)	73.1519 ± 12.89980 **	122.15 ± 21.27557
Glutathione (µmol / L)	10.1639 ± 1.93200 **	0.5360 ± 7.37368
Malondialdehyde (µmol / L)	2.5445 ± .63196 **	.1739 ± .13924

**It means that there is a significant difference at the probability level ($p \leq 0.01$).

Effect of Sex

The impact of sex on all the biochemical variables measured was studied in both the patient group and the control group, as well as the effect of sex on the group of cardiovascular patients and the control group. The results shown in Tables (2) and (3) indicate a significant decrease in the probability level ($p \leq 0.01$) in the concentration level of sirtuin7 in the blood serum of both male and female patient groups compared to their respective control groups.

Moreover, the results in Table (4) indicate that the level of sirtuin7 in female patients with cardiovascular disease was lower than that in males with the same condition. Additionally, the results pointed to the role of sex in cardiovascular disease, as lower levels of sirtuin7 were observed in both the patient and control groups of females compared to their male counterparts. Previous studies have suggested that this decrease may be due to fluctuations in estrogen and progesterone hormone levels in females. where Estrogen and progesterone possess antioxidant properties and can protect cells from oxidative damage [19]. SIRT7 is involved in regulating pathways responding to oxidative stress by deacetylating key genes involved in DNA repair and antioxidant defense. Therefore, a decrease in estrogen and progesterone hormone

levels may weaken cellular antioxidants, leading to increased oxidative stress [20]and this reduced regulation of SIRT7 expression in females patients with cardiovascular diseases more form than in males.

As indicated by the results in the tables, there was a significant increase in the level of tumour necrosis factor-alpha (TNF-α) concentration at the probability level ($p \leq 0.01$) in both male and female patient serum groups compared to the control group for both sexes. In females, the level in both patient and control groups was higher than in males. According to a previous study, this increase is attributed to the influence of hormonal fluctuations associated with the menstrual cycle, pregnancy, and menopause on immune responses and the production of inflammatory cytokines. It has been established that estragon and progesterone, in particular, modulate the immune system and may contribute to the elevation of TNF-alpha levels in females during these stages [21] . The results indicated a significant elevation in the level of lipoxygenase concentration at the probability level ($p \leq 0.01$) in both male and female patient groups compared to the control group of both sexes. It was noted that its level in the patient and control groups for females was higher than its level in the patient and control groups for males. This elevation is also attributed to hormonal fluctuations, especially estrogen and progesterone, which can influence the expression of enzymes involved in lipid metabolism, including LOX. Estrogen has been shown to regulate LOX expression in certain tissues, thus differences in hormone levels across the menstrual cycle, pregnancy, and menopause may contribute to differences in LOX levels between females and males [22] . Given that LOX enzymes participate in inflammation and immune responses, and because females generally exhibit stronger immune responses compared to males, partly due to differences in levels of sex hormones, higher levels of immune activity in females may lead to increased production of LOX enzymes [23].

The results in Tables (2) and (3) also indicated a significant decrease in the levels of antioxidants (albumin, SOD, GPx, and GSH) at the probability level ($p \leq 0.01$) in both male and female patient groups compared to their respective control groups. This decrease is attributed to oxidative stress, which occurs due to an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defences. where Oxidative stress can lead to the depletion of antioxidant enzymes, and ROS can directly damage these enzymes, thereby reducing their activity and levels [24]. Aging is also associated with a decrease in the activity of antioxidant enzymes, due to decreased synthesis or increased oxidation with advancing age [25]. It was observed that the concentrations of antioxidant enzymes (GPx, SOD) in the patient and control groups for females were lower than their concentrations in the patient and control groups for males. This decrease in females is attributed to the change in estrogen hormone levels in females at different life stages, as estrogen hormone has been shown to enhance the activity of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) through various mechanisms. Therefore, a decrease in estrogen levels with age will result in a decrease in the activity of antioxidant enzymes [26]. While levels of (albumin and GSH) were lower in males compared to females, and this decrease is attributed to oxidative stress, which causes a reduction in antioxidant levels versus an increase in inflammation. A previous study revealed that males generally experience more oxidative stress than females, a phenomenon observed in both mice and humans. Additionally, gender differences exist in the production of reactive oxygen species; according to previous study also, females have a larger antioxidant system compared to males. Thus, women possess an antioxidant advantage linked to estragon, albeit diminishing with age [27].

The results indicated also to a significant increase in the level of malondialdehyde concentration at the probability level ($p \leq 0.01$) in the serum of male and female

patients compared to the control group for both genders. It was observed that the level in the patient and control groups for males was higher than that in the patient and control groups for females. This increase is attributed to oxidative stress, increased free radicals, and lipid peroxidation process [28] and [29] respectively.

Table (2): Levels of biochemical variables measured in the blood serum of males with cardiovascular disease compared with healthy males.

Biochemical variable	Patient group (Males) (No:23)	Control group (Males) (No:23)
	Mean ± Std.Deviation	Mean ± Std.Deviation
Sirtuin7 (ng / ml)	3.5251 ± .22337 **	15.5831 ± .61300
Tumor necrosis factor-α(pg / ml)	280.57 ± 4.10597 **	6.5139 ± .97507
Lipoxygenase (U / L)	61.8824 ± 3.33660 **	47.6765 ± 1.69422
Albumin (g / dl)	31.2207 ± 8.08689 **	52.7496 ± 4.24549
Superoxide dismutase (U / L)	2.8842 ± .34340 **	4.9455 ± .36833
Glutathione peroxidase (U / L)	85.1312 ± 3.68762 **	140.81 ± 3.30872
Glutathione (µmol / L)	9.5181 ± 1.47871 **	42.9222 ± 4.98800
Malondialdehyde (µmol / L)	2.6243 ± .59136 **	.1754 ± .10747

**It means that there is a significant difference at the probability level ($p \leq 0.01$) .

N.S It means there is no significant difference.

Table (3): Levels of biochemical variables measured in the blood serum of females with cardiovascular disease compared with healthy females.

Biochemical variable	Patient group (No:22) (Females)	Control group (No:22) (Females)
	Mean ± Std.Deviation	Mean ± Std.Deviation
Sirtuin7 (ng / ml)	1.8139 ± .18499 **	11.4113 ± .58062
Tumor necrosis factor-α(pg / ml)	372.60 ± 7.25328 **	8.8281 ± .68480
Lipoxygenase (U / L)	199.96 ± 3.23098 **	57.5461 ± 1.15733
Albumin (g / dl)	31.2897 ± 5.71416 **	56.0652 ± 4.29078
Superoxide dismutase (U / L)	1.8052 ± .34731 **	3.0693 ± .29482
Glutathione peroxidase (U / L)	60.6281 ± 3.59557 **	102.65 ± 12.54344
Glutathione (µmol / L)	10.8391 ± 2.14375 **	38.0413 ± 8.66600
Malondialdehyde (µmol / L)	2.4610 ± .67540 **	.1724 ± .16887

**It means that there is a significant difference at the probability level ($p \leq 0.01$).

N.S It means there is no significant difference.

Table (4): Levels of biochemical variables measured in the serum of females with cardiovascular disease compared with males with cardiovascular disease.

Biochemical variable	Patient group (No: 23) (Males)	Patient group (No:22) (Females)
	Mean ± Std.Deviation	Mean ± Std.Deviation
Sirtuin7 (ng / ml)	3.5251 ± .22337 **	1.8139 ± .18499
Tumor necrosis factor-α(pg / ml)	280.57 ± 4.10597 **	372.60 ± 7.25328
Lipoxygenase (U / L)	61.8824 ± 3.33660 **	199.96 ± 3.23098
Albumin (g / dl)	31.2207 ± 8.08689 N.S	31.2897 ± 5.71416
Superoxide dismutase (U / L)	2.8842 ± .34340 **	1.8052 ± .34731
Glutathione peroxidase (U / L)	85.1312 ± 3.68762 **	60.6281 ± 3.59557
Glutathione (µmol / L)	9.5181 ± 1.47871 **	10.8391 ± 2.14375
Malondialdehyde (µmol / L)	2.6243 ± .59136 N.S	2.4610 ± .67540

**It means that there is a significant difference at the probability level ($p \leq 0.01$) .

N.S It means there is no significant difference .

Conclusion

There was a significant decrease in the level of the concentration of the enzyme sirtuin7 in patients with cardiovascular disease compared to control, while there was a significant increase in the level of tumour necrosis factor-alpha, the enzyme lipoxygenase, and malondialdehyde in patients with cardiovascular disease compared to control, while there was a significant decrease in the level of concentrations of Antioxidants (SOD, GPx, GSH) in cardiovascular patients compared to control group , but there was no significant difference in albumin levels . But with regard to the effect on sex , there were clear results that showed a significant effect on the levels of each of the clinical examinations that was conducted , as it was recorded that the level of sirtuin7 decreased significantly with the rates of cardiovascular disease in females compared to male patients, while it was found that the concentrations of each of the factors Alpha-necrosis and the

lipoxygenase enzyme were higher in female cardiovascular patients compared to male patients. As for the antioxidant enzymes (SOD, GPx), a significant decrease was recorded in female cardiovascular patients compared to male patients, while there was a significant decrease in the antioxidants albumin and glutathione in female patients. Patients compared to cardiovascular diseases for males compared to female patients. Finally, there was a significant increase in malondialdehyde in cardiovascular patients compared to female patients.

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