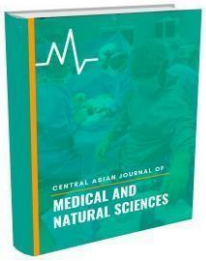

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Article

Evaluation of Copeptin, Osteopoietin, Renin and Some Physiological Parameters in Patients with Heart Diseases in Samarra City.

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Abstract: The research aimed to evaluate the levels of copeptin, osteopontin, renin, lipid profile, urea, and creatinine in patients with heart disease in Samarra City. Conducted between March and September 2024, the study involved 50 male and female patients with heart diseases, including atherosclerosis, heart failure, and angina pectoris, alongside a control group of 20 healthy individuals aged 59-75. Blood samples were analyzed using ELISA and various biochemical assays. Results revealed significantly higher levels of copeptin, osteopontin, and renin in heart disease patients compared to the control group. Additionally, elevated triglycerides, urea, and creatinine levels were observed. These findings indicate a correlation between elevated hormonal and physiological parameters and heart disease progression.

Keywords: Heart Disease, Renin, Copeptin, Lipid Profile, Osteopontin

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1. Introduction

Heart disease is a serious disease that threatens human life and is the leading cause of death in the United States of America [1]. Studies show that by 2030, the number of deaths is expected to rise to 23.6 million people in the United States of America due to cardiovascular diseases. Ischemic Heart Disease (IHD) is among the most prevalent illnesses in developed nations, which develops into atherosclerosis, which leads to a group of different diseases from the less severe, represented by angina pectoris, to more serious forms, including: acute myocardial infarction, chronic ischemia that leads to sudden cardiac death [2].

Atherosclerosis results from increased thickness and roughness of the inner lining of the artery wall with gradual deposition of some substances such as cholesterol, fatty acids, lipoproteins, calcium, complex carbohydrates, fibers and blood, thus reducing blood flow within the affected part of the arteries, which results in a decrease in the amount of blood passing through the artery as a result of increased thickness of the inner lining and narrowing of its course, thus reducing the blood that reaches the heart muscle carrying food and oxygen [3]. If the blockage in the arteries is partial, the patient suffers from angina, and in the case of complete blockage of the artery, the patient suffers from a heart attack, and if the blockage continues for 5-10 minutes, this area of the heart muscle affected by the complete blockage dies, leading to a heart attack that stops breathing or what is called myocardial infarction (MI [4].

Osteopontin:

It is a versatile glycoprotein that has significant roles in various pathophysiological processes. Persistent elevations in OPN are clinically linked to an increased risk of significant circulatory harm, making it a robust predictor of circulatory disease regardless of conventional predisposing factors [5]. It is regarded as both a predictive and indicative indicator for various diseases [6].

Renin:

A protein enzyme primarily sourced from the kidney, with its expression and secretion by The juxtaglomerular apparatus (JGA) is regulated by renal baroreceptors and the concentration of sodium chloride (NaCl). Renin is produced and kept as a dormant precursor known as pro-renin within the juxtaglomerular cells (JG), These are smooth muscle cells found in the walls of the afferent arteriole, situated in the distal section of the thick ascending limb of the loop of Henle. [7] When blood vessel pressure falls, internal reactions in the kidneys themselves cause many pro-renin molecules to cleavage in the juxtaglomerular cells, releasing renin. The majority of it enters the bloodstream and exits the kidneys to flow throughout the body, while a small portion stays in the renal fluids to trigger various functions within them. [8] Renin works to raise arterial pressure[9].

Copeptin:

Copeptin, a peptide hormone of 39 amino acids, It is released from the rear lobe of the hypophysis at the same time as AVP. Copeptin is an alternative marker of arginine vasopressin and is useful in assessing fluid and osmotic status in various diseases. In comparison to AVP, copeptin is more constant in plasma and serum, allowing it to be easily measured in blood [10]. Once released, it presists constant for various days and its concentrations raise swiftly in various situations like circulatory disease, brain attack, and shock. Once released, it remains steady for several days, but its levels can rise rapidly in conditions like cardiovascular disease, stroke, and shock [11].

2. Materials and Methods

Blood samples of 10 ml each were collected from the brachial vein using a medical syringe. Each sample was placed into test tubes and centrifuged at 3500 revolutions per minute for fifteen minutes to separate the serum. The resulting serum was then transferred to new plastic sample tubes, with all relevant information recorded on them, and stored at -20°C. The following tests were conducted:

Determination of total serum cholesterol level:

The concentration of cholesterol in the blood serum was measured according to the instructions in the leaflet attached to the ready-made kit and based on the Enzymatic method using the analysis kit manufactured by the French company Biolabo [12].

Determination of serum triglycerides and VLDL-C level:

Triglycerides are decomposed into glycerol and free fatty acids in the presence of the enzyme Lipase-LPL Lipoprotein, then glycerol is converted into a colored complex in the presence of glycerol kinase-Gk and glycerol 3-phosphoryl oxidase (GPO) with para-chlorophenol (PCP) P-Chlorophenol and 4-amino antipyrine to a pink complex Quinoneimin [12].

Thus, the concentration of VLDL-C can be calculated using the following equation [13].

VLDL-C conc. (mg/dl) = TG/5

Determination of serum (HDL-C) level:

lipoproteins, and chylomicrons. HDL-C is then acquired from the overlying liquid resulting from the spinning of the solution to be estimated using the ready-made cholesterol kit .[14]

Assessment of Serum Urea levels:

The concentration of serum urea was determined using a colorimetric method with a pre-prepared analysis kit from the French company Biomerieux [12].

Assessment of Serum Creatinine level:

The concentration of serum creatinine was measured using the BIOLABO kit from France [12] .

Determine the level of Copeptin, Osteopontin and Renin

In the Serum of Blood

Osteopontin, renin and copeptin hormones They were analyzed using an immunological technique called Enzyme-Linked Immunosorbent Assay (ELISA) with a BioTek ELx800 Reader, provided by the Chinese company SUNLONG. The tests was conducted following the instructions supplied in the kit's manual. The experimental samples were categorized into 4 groups. The 1st group comprised twenty five men patients with heart disease. The study samples were organized into four groups. The first group included twenty five male patients with heart disease. The third group consisted of ten healthy males as the control group. The fourth group contained ten healthy females as the control group. The statistical analysis of the results was carried out using the ANOVA test, and Duncan's multiple range test was employed to identify significant differences, with significance set at ($P \leq 0.05$) [15].

3. Results

Table (1) The lipid profile levels in the blood serum of male and female individuals suffering from heart disease.

Group / Parameters	Cholesterol mg/dl	T. G mg/dl	HDL-c mg/dl	LDL-c mg/dl	VLDL-c mg/dl
Control Male	168.13±16.18^{b}	125.67±15.24 ^{b}	45.067±4.743 ^{a}	98.07±16.65 ^{b}	25.134 ±2.071 ^{b}
Patients Male	279.50±29.15^{a}	266.00±77.91 ^{a}	31.500±1.900 ^{b}	194.80±20.23 ^{a}	53.200±3.519 ^{a}
Control Female	166.93±15.52^{b}	119.80±20.31 ^{b}	47.867±5.854 ^{a}	94.33±18.31 ^{b}	23.96 ±4.026 ^{b}
Patients Female	276.70±25.27^{a}	243.10±29.36 ^{a}	33.700±2.946 ^{b}	194.50±30.54 ^{a}	48.62±5.777 ^{a}

Table (2) The level of Osteopontin, Renin ,Copeptin hormones , Urea, Creatinine In the blood serum of male and female patients with heart disease.

Group / Parameters	Osteopontin ng/ml	Renin pg/ml	Copeptin pg/ml	Urea mmol/L	Cr mg/dl
Control Male	6.123 ±1.336b	219.14±5.75[b]	40.57±6.64[c]	28.333±3.155[b]	0.633±0.2350[b]
Patient Male	8.927 ±0.307a	369.20±12.15[a]	251.30 ±24.09 [a]	60.800±9.355[a]	1.360±0.1713[a]
Control Female	7.246 ±0.336b	240.12±7.33[b]	38.39±11.73[c]	26.867±4.764[b]	0.624±0.1125[b]
Patients Female	.015 ±0.307a9	393.48±11.99[a]	119.76±11.71 [b]	57.500±7.962[a]	1.2800±0.2394[a]

* Quantites are expressed as mean mean ± standard deviation

* Different lowercase letters (vertical) indicate significant differences (P≥ 0.05)

4. Discussion

The rise in total cholesterol, low-density lipoprotein cholesterol, triglycerides, and very low-density lipoprotein cholesterol, along with a decrease in high-density lipoprotein cholesterol, in the male study group is due to the decrease in the male hormone testosterone, which increases the activity of the hepatic lipase enzyme and the reduction in the activity of the lipoprotein lipase enzyme, This leads to increased breakdown of HDL-c, resulting in higher cholesterol levels and greater amounts of fats in the blood (TG, LDL-c, VLDL-c), which directly impacts the risk of heart disease [16].

This hormonal alteration is typically linked to a range of clinical conditions, including stroke and arterial diseases. A reduction in this hormone's levels results in the loss of its beneficial effects on the blood vessel lining. Many studies have indicated that the hormone testosterone significantly enhances blood flow through the coronary arteries to various body parts by relaxing these arteries through the activation of potassium channels and inhibition of calcium channels [17].

The increase in the above-mentioned variables in the female patient group is due to the decrease or cessation of the female hormone estrogen, which leads to an increase in cholesterol levels and increased exposure to vascular and heart diseases. This is what we notice after menopause, leading to obesity, joint pain, and bone necrosis because this hormone plays a role in protecting and preventing heart diseases before menopause [18]. The increase in the concentration of triglycerides may be due to the increased intake of foods rich in fats, resulting in an increase in the production of emulsifying particles (Chylomicrons) in the intestines. When they are decomposed, they trigger the release of fatty acids, leading to an increased influx of fatty acids into liver cells, which in turn raises the release of triglycerides in VLDL [19].

The breakdown of triglycerides from adipose tissue, muscle, and plasma results in the release of fatty acids into the mitochondria of skeletal muscles, where they undergo oxidation to supply the energy required for essential activities. A small portion of the total energy during vital activities comes from triglycerides in plasma due to the slow hydrolysis of fatty acids, which can lead to the accumulation of these triglycerides on blood vessel walls and their subsequent hardening [20]. High triglycerides or hypertriglyceridemia and low concentrations of high-density lipoprotein (HDL-c) are the most common in patients suffering from coronary artery disease [21].

The high level of low-density lipoprotein (LDL-c) concentration is due to the increase in fat consumption, When the amount of dietary cholesterol reaching the liver cells increases, it stimulates the activity of LDL-c receptors, causing LDL-c molecules to accumulate in higher concentrations in the blood, as most of the low-density lipoproteins are removed by binding to their receptors. However, in the case of high concentration in the plasma and due to the small size of their particles, some of them penetrate some tissues

such as the walls of the arteries, causing damage and arteriosclerosis because (LDL-c) is the primary transporter of cholesterol from the liver to peripheral tissues [22].

It also causes the arteries around the heart to narrow, leading to coronary artery disease, which avoids the sufficient amount of oxygen from reaching the heart, indicating an increase in the chances of heart attacks [23]. Which is considered a risk factor for the development of heart disease [24]. When LDL cholesterol molecules undergo oxidation, they become chemically modified, and when they are oxidized, LDL cholesterol molecules become smaller, as LDL cholesterol molecules Small LDL can easily enter the artery wall and deposit on it. LDL cholesterol particles are the main component of the deposited cholesterol layer, and can block the heart arteries and expose the person to a heart attack [25].

Low levels of HDL-c in hyperlipidemia patients may lead to an increased risk of atherosclerosis due to the important role played by HDL-c in transporting cholesterol from the body's tissue cells to the liver, thus reducing blood cholesterol. Thus, the concentration of HDL-c is negatively related to cardiovascular diseases, as it is considered that HDL-c can absorb cholesterol crystals that have begun to deposit in the arterial walls, thus helping to avoid atherosclerosis, in addition to acting as an anti-inflammatory and having antioxidant properties [26].

Elevated levels of osteopontin may indicate vascular damage due to hypertension. Chronic elevations in OPN are clinically linked to a higher risk of significant cardiovascular damage and are a strong indicator of heart disease, regardless of conventional risk factors. OPN expression levels are consistently elevated in many diseases involving chronic inflammation, such as self-immune conditions, wound healing, diverse cancers, and heart diseases. Several factors enhance OPN expression, such as oxidized oxygen species, angiotensin II, high glucose levels, and low oxygen tension, "Each of these factors plays a role in persistent vascular inflammation. When this inflammation is not resolved, it leads to prolonged, chronic OPN expression. Recently, OPN has garnered significant interest as a biomarker for various diseases [5].

The increase in renin hormone levels in both male and female heart disease patients is attributed to a strong link between the development of arterial plaque, Resulting from elevated blood fats and the stimulation of the renin-angiotensin system. This relationship plays a significant role in the onset of cardiovascular diseases, significantly contributing to many deaths due to its issues. Renin aids in the conversion of proteins into angiotensin I, Subsequently, another enzyme in the bloodstream transforms it into angiotensin II. Angiotensin II leads to the narrowing of blood vessels, leading to high blood pressure and heart failure [27].

Renin raises blood pressure and causes heart disease by three mechanisms. Granular cells within the afferent artery release the hormone renin within the bloodstream. This hormone facilitates the conversion of angiotensinogen (AGT), a protein produced by the liver, into angiotensin I. Angiotensin I is subsequently converted into angiotensin II by the angiotensin-converting enzyme (ACE), which is found on the surface of the endothelial cells lining the lung's blood vessels. Angiotensin II also stimulates the adrenal cortex to secrete aldosterone, which stimulates the epithelial cells in the distal tubule and collecting duct of the kidney to increase sodium reabsorption and exchange it for potassium. This process helps maintain electrochemical and water balance, resulting in higher blood volume and elevated blood pressure. Finally, the renin-angiotensin system influences the central nervous system to increase water consumption by triggering thirst and to maintain blood volume by decreasing urine output through the secretion of vasopressin from the posterior pituitary gland [28].

Several studies have shown that even when plasma renin activity is normal, AngII is crucial in the progression of hypertensive diseases, such as heart failure [29].

The reason for the rise in copeptin in heart patients is due to the arterial distention resulting from the decrease in cardiac output, which leads to the activation of arterial pressure receptors located in the aortic arches and carotid sinus, which in turn stimulates the hypothalamus to synthesize and secrete vasopressin (antidiuretic hormone) as a means of maintaining fluid balance within the body within normal limits because its secretion is

initially beneficial. The increase in plasma fats, especially cholesterol, hypercholesterolemia, accelerates the development and appearance of kidney dysfunction, and after a period of time, this dysfunction may lead to many disorders, including heart disease and cardiovascular diseases [30].

AVP is released into the bloodstream and binds to its receptors, which are the V1 receptors that mediate arterial vasoconstriction and are present in high concentrations on vascular smooth muscle cells, leading to their contraction and thus narrowing of the blood vessels as a result of a rise in inside the cell calcium by the G protein within a mechanism that includes inositol triphosphate and diacylglycerol, leading to high blood pressure and may lead to vascular and heart diseases, and the V2 receptors that mediate the antidiuretic impact in the kidneys, which are primarily located on the cells of the kidney's collecting tubules, where it works to increase the permeability of the cells to water by elevating intracellular cyclic adenosine monophosphate (cAMP) via the Gs signaling pathway. This rise in cAMP affects the water balance because copeptin has an essential role in the water balance within the body by regulating the amounts of excess water [31].

Elevated copeptin is initially beneficial, but as cardiac output continues to decline, arterial distention continues, and vasopressin and copeptin continue to be secreted, several things happen. At the kidney level, it stimulates sodium and water retention, which in turn increases body fluid volume and causes edema. At the cardiovascular level, copeptin raises peripheral resistance, leading to higher arterial blood pressure. This additional strain on the heart causes it to work harder to overcome the increased resistance as heart disease advances. Consequently, this elevated pressure triggers further secretion of copeptin [32].

High levels of copeptin are associated with heart disease, and this is consistent with the researcher's study [33]. As for the high levels of urea and creatinine in patients, it is attributed to the glomerular damage that occurred due to the increase in fats in the patient groups, this resulted in fibrosis of the kidney's interstitial tissues, atrophy of the tubules, and reduced renal perfusion, which in turn leads to higher concentrations of both urea and creatinine [34].

5. Conclusion

The study concluded that patients with heart diseases in Samarra City exhibited significantly elevated levels of copeptin, osteopontin, and renin, along with abnormal lipid profiles and increased urea and creatinine concentrations. These findings suggest that these biomarkers, particularly copeptin and osteopontin, may serve as important indicators of heart disease severity and progression. The elevated lipid and creatinine levels further highlight the risk of cardiovascular complications in affected individuals. Monitoring these physiological parameters could improve early diagnosis and treatment outcomes for heart disease patients.

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