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Evaluation of Adipokines and Metabolic Hormones in Coronary Artery Disease Patients: Association with Inflammatory and Oxidative Stress Biomarkers

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Annotation: One of the common diseases affecting cardiovascular health is coronary artery disease, which is strongly associated with metabolic disorders, oxidative stress, and inflammation. This study aimed to evaluate the relationship between adipokines and metabolic hormones with markers of inflammation and oxidative stress. The study was conducted at Al-Sharqat General Hospital between January and March 2025, and included 60 patients with coronary artery disease and 30 individuals as a control group. The results showed a significant decrease in the levels of both adiponectin (ADPN) and ghrelin (GHRL) in the patient group compared to the healthy group. Conversely, the levels of leptin (LEP), C-reactive protein (CRP), and malondialdehyde (MDA) were elevated in the patient group compared to the control group. Correlation analysis revealed weak positive correlations between all variables, indicating an interconnected role of metabolic, inflammatory, and oxidative pathways in the development of the disease. The ROC curve analysis also showed strong diagnostic performance for all studied biomarkers, demonstrating their potential usefulness in diagnosing and monitoring the disease.

Keywords: Coronary Artery Disease; Adiponectin; Leptin; Ghrelin; C-reactive protein; Malondialdehyde.

Introduction

Coronary artery disease (CAD) is one of the most common cardiovascular disorders and remains a leading cause of death worldwide. The primary cause of this disease is the narrowing or blockage of the coronary arteries due to the buildup of fatty plaques, a process known as atherosclerosis. This reduces blood flow to the heart muscle, leading to myocardial ischemia [1]. The development of this disease is influenced by an interaction between genetic factors and environmental risk factors, including hypertension, dyslipidemia, smoking, and diabetes. Furthermore, obesity and physical inactivity significantly contribute to the increased risk of developing the disease [2]. The deposition of low-density lipoprotein (LDL) cholesterol within the artery wall triggers a chronic inflammatory response, which plays a pivotal role in plaque formation and progression [3]. Several studies have confirmed the central role of inflammation in the initiation and progression of the disease. Chronic low-grade inflammation is a significant and influential factor in all stages of the disease, from early plaque formation to the development of acute clinical events such as myocardial infarction. Inflammatory cytokines contribute to plaque instability, increasing the likelihood of plaque rupture and subsequent thrombus formation [4]. Furthermore, oxidative stress has been identified as a major factor in disease progression and progression. It stimulates the excessive production of reactive oxygen species, leading to lipid peroxidation and endothelial cell damage. The interaction between oxidative stress and inflammation increases the risk of vascular damage and exacerbates the disease [5].

Adiponectin is an adipokine secreted primarily by adipose tissue and plays a crucial role in regulating metabolic homeostasis, such as glucose and lipid metabolism. Low adiponectin levels have been linked to metabolic dysfunction and cardiovascular disease, reflecting its protective anti-inflammatory and anti-atherosclerotic properties [6]. Leptin and insulin are both metabolic hormones, crucial regulators of energy balance and metabolic processes. Dysregulation of these hormones leads to insulin resistance and endothelial dysfunction, both hallmarks of metabolic and cardiovascular diseases. This dysfunction promotes inflammatory responses and metabolic disturbances [7]. Metabolic disturbances are associated with chronic low-grade inflammation. Continuous activation of inflammatory pathways leads to the development of insulin resistance, impaired insulin signaling, and increased metabolic dysfunction. In adipose tissue, inflammation is strongly linked to disease progression, as is hormonal imbalance [8]. Oxidative stress also plays a key role in the development of metabolic diseases. This results in an imbalance between the production of reactive oxygen species and antioxidant defense mechanisms, leading to cell damage, lipid peroxidation, and endothelial dysfunction. This process is closely linked to both inflammation and metabolic disturbances [9]. Importantly, adiponectin exerts protective effects by regulating both inflammation and oxidative stress. It has been shown to enhance antioxidant mechanisms and suppress inflammatory signaling pathways, thereby reducing cell damage and improving metabolic function [10]. Overall, the interaction between adiponectin, metabolic hormones, inflammation, and oxidative stress represents a highly complex network that significantly contributes to the pathogenesis of metabolic and cardiovascular diseases [11].

Objectives of the Study

This study aims to:

1- To evaluate the levels of Adiponectin, Leptin, and Ghrelin in patients with Coronary Artery Disease and compare them with healthy individuals.

2- To measure inflammatory and oxidative stress markers, including C-reactive protein and Malondialdehyde, and determine the differences between the two groups.

3- To analyze the correlations between adipokines, metabolic hormones, and markers of inflammation and oxidative stress, as well as to evaluate their diagnostic performance.

2- Materials and Methods

2-1 Study Design and Participants:

This case-control study was conducted between January 2025 and March 2025. A total of 90 individuals were enrolled, including 60 patients diagnosed with Coronary Artery Disease and 30 apparently healthy subjects serving as a control group. Patients were recruited from the outpatient clinics of Al-Shirqat General Hospital, and the diagnosis was confirmed by specialist physicians based on established clinical criteria. Participants' ages ranged from 35 to 65 years, with matching between groups in terms of age and gender.

2-2 Inclusion and Exclusion Criteria:

Patients with confirmed coronary artery disease were included in the study. Individuals with diabetes mellitus, chronic kidney or liver diseases, autoimmune disorders, acute inflammatory conditions, or malignancies were excluded. In addition, smokers and those who had taken anti-inflammatory or antioxidant medications within the preceding three months were also excluded .

2-3 Sample Collection:

Blood samples were collected after an overnight fasting period of 8-12 hours. Approximately 5 mL of venous blood was drawn from each participant. The samples were allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 minutes to separate the serum. The obtained serum was aliquoted and stored at -32°C until biochemical analysis.

2-4 Biochemical Measurements:

Serum levels of Adiponectin, Leptin, and Ghrelin were determined using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions. The level of Malondialdehyde (MDA) was measured using the thiobarbituric acid reactive substances (TBARS) method as an indicator of lipid peroxidation. Serum C-reactive protein (CRP) concentrations were measured using a standard immunoturbidimetric method.

2-5 Statistical Analysis:

Data were analyzed using SPSS software (version XX). Results were expressed as mean ± standard deviation (Mean ± SD). Independent samples t-test was applied to compare differences between groups. Pearson correlation analysis was used to assess the relationships among variables. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the studied biomarkers. A p-value of less than 0.05 was considered statistically significant.

3- Results

The results showed a significant decrease in both adiponectin (APN) and ghrelin levels in the patient group compared to the healthy control group at a $p < 0.0001$, as shown in Table 1 and Figures 1 and 2. This is consistent with previous studies [12, 13]. Our results also showed a significant increase in leptin, C-reactive protein (CRP), and malondialdehyde (MDA) levels in the patient group compared to the control group at a $p < 0.0001$, as shown in Table 1 and Figures 3, 4, and 5. This aligns with the findings of previous studies [14, 15, 16]. Correlation analysis of all variables in the patient group revealed a weak positive correlation between all variables, as shown in Table 2.

Table 1. Comparison of the research parameters of patients group with control group:

Groups / **Parameters**	**Mean ± SD** Control	Patients	**P-value**
APN	**9.157±1.442**	**4.668±0.966**	**<0.0001****
Ghre	**624.000±45.151**	**424.600±45.265**	**<0.0001****
Leptin	**9.870±2.547**	**19.968±5.024**	**<0.0001****
CRP	**1.450±0.426**	**6.858±1.191**	**<0.0001****
MDA	**1.650±0.333**	**4.060±0.708**	**<0.0001****

*** P ≤ 0.05, ** P ≤ 0.01,**

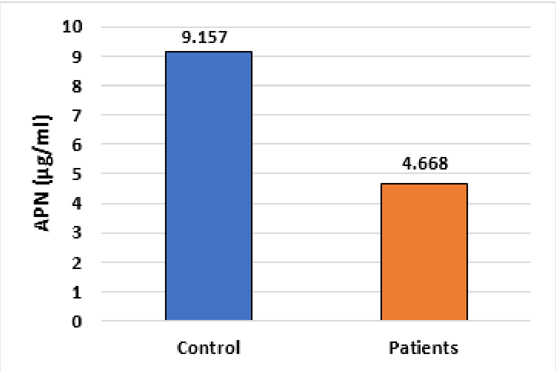

Figure 1 shows the APN level in the patient group Compared to the control group.

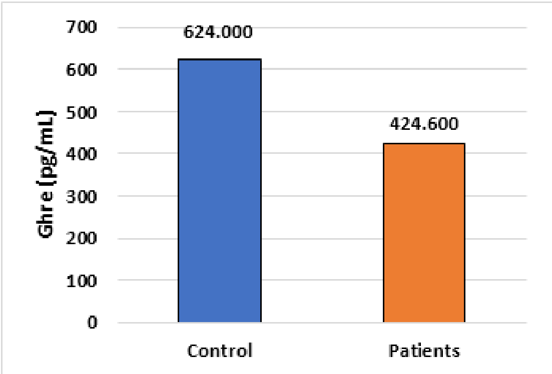

Figure 2 shows the Ghrelin level in the patient group Compared to the control group.

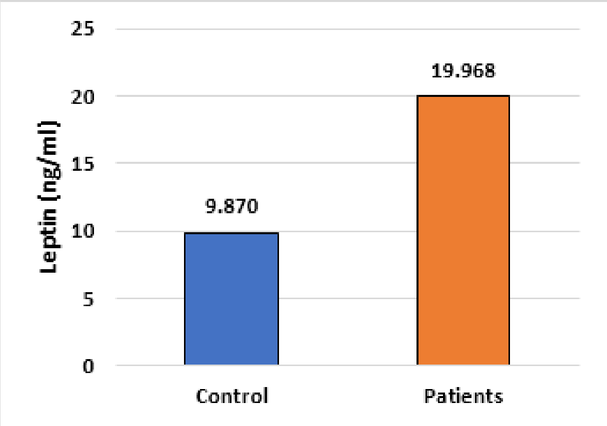

Figure 3 shows the Leptin level in the patient group Compared to the control group.

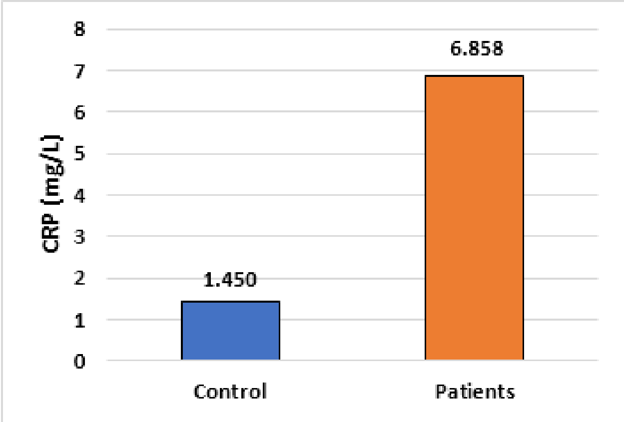

Figure 4 shows the CRP level in the patient group Compared to the control group

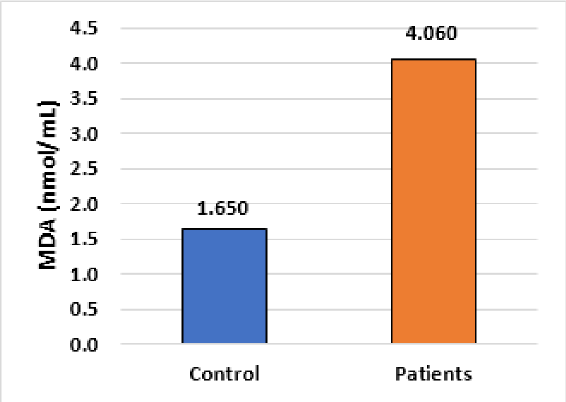

Figure 5 shows the MDA level in the patient group Compared to the control group.

Table 2. Shows the correlation between all parameters in the patient group.

		Leptin	APN	Ghre	CRP	MDA
Leptin	**r**	1				
	p					
	N	60				
APN	**r**	0.332**	1			
	p	0.010				
	N	60	60			
Ghre	**r**	0.363**	0.597**	1		
	p	0.004	0.000			
	N	60	60	60		
CRP	**r**	0.450**	0.615**	0.738**	1	
	p	0.000	0.000	0.000		
	N	60	60	60	60	
MDA	**r**	0.324*	0.512**	0.292*	0.525**	1
	p	0.011	0.000	0.024	0.000	
	N	60	60	60	60	60

****. Correlation is significant at the 0.01 level (2-tailed).**

***. Correlation is significant at the 0.05 level (2-tailed).**

r. Pearson correlation

p. Sig. (2-tailed)

N. number of samples

3-1 Results of ROC analysis of biochemical variables in patients and control group:

ROC analysis data are shown in Table 3

Table 3. ROC analysis of biochemical variables in patients and control group.

Parameters	Cut off	Sensitivity %	Specificity %	AUC	P-value
APN	**≤6.4**	**96.7**	**100.0**	**0.999**	**<0.001**
Leptin	**>14.1**	**90.0**	**90.7**	**0.979**	**<0.001**
Ghre	**≤510**	**100.0**	**100.0**	**1.000**	**<0.001**
CRP	**>2.3**	**100.0**	**100.0**	**1.000**	**<0.001**
MDA	**>2.3**	**100.0**	**100.0**	**1.000**	**<0.001**

The results of the ROC analysis, as shown in Table 3, revealed that the APN indicator possesses a high ability to detect both positive cases (high sensitivity 96.7%) and negative cases (high specificity 100.0%), with an AUC value of 0.999 at a statistically significant level (P<0.001). Furthermore, based on the high sensitivity, specificity, and AUC value of all variables shown in Table 3, all indicators are suitable as primary diagnostic tools for the majority of pathological conditions and for differentiating them from normal cases. Therefore, they can be relied upon in the diagnosis of coronary artery disease. This is illustrated in the following figures for all variables:

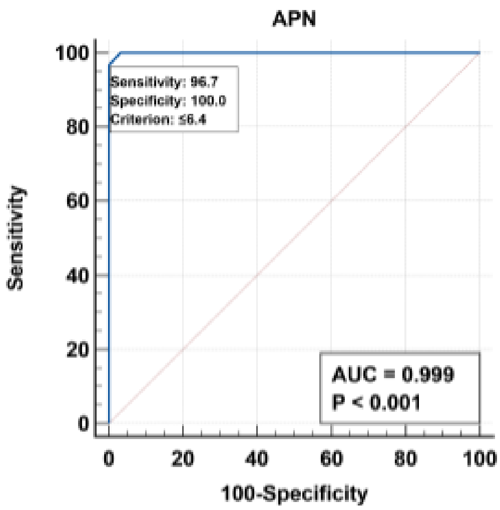

Figure 1 the ROC analysis of APN in the patient and control groups.

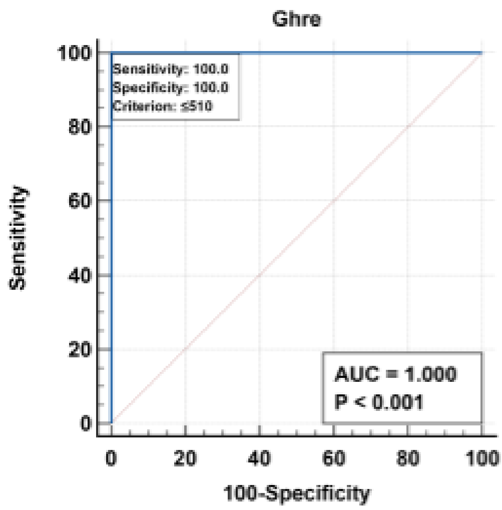

Figure 2 the ROC analysis of Ghrelin in the patient and control groups.

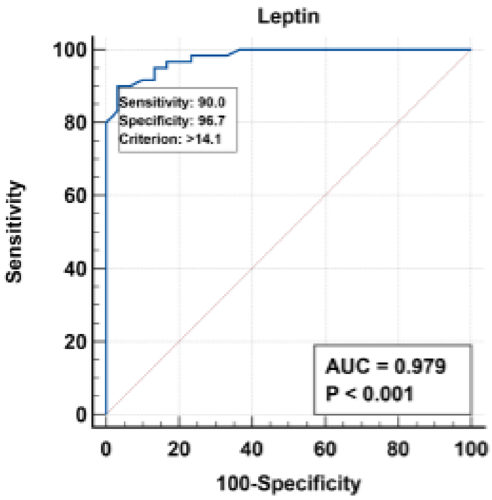

Figure 3 the ROC analysis of Leptin in the patient and control groups.

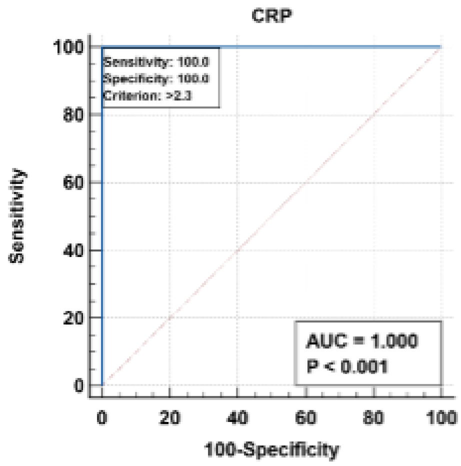

Figure 4 the ROC analysis of CRP in the patient and control groups.

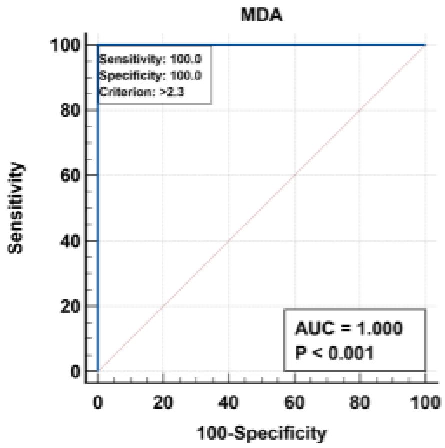

Figure 5 the ROC analysis of MDA in the patient and control groups.

4- discussion

The observed reduction in adiponectin levels among patients with Coronary Artery Disease may be attributed to the presence of chronic low-grade inflammation. Pro-inflammatory cytokines, such as TNF-a and IL-6, are known to suppress adiponectin secretion from adipose tissue. In addition, increased infiltration of immune cells into adipose depots further downregulates its expression, thereby promoting the progression of atherosclerosis [17]. Moreover, decreased adiponectin levels are closely linked to adipose tissue dysfunction, particularly in visceral fat. Under pathological conditions, adipose tissue shifts from a metabolically protective organ to a source of inflammatory mediators, resulting in reduced adiponectin production and increased cardiovascular risk [18]. According to previous studies, an inverse relationship has been found between adiponectin levels and coronary artery disease. Individuals with coronary artery disease have been found to have lower levels of adiponectin, supporting its protective role against the development and progression of atherosclerosis [19]. Furthermore, the concept of "adiponectin resistance" has been proposed, where impaired adiponectin receptor signaling reduces its biological effects despite its presence. This reduced response contributes to the loss of its anti-inflammatory and anti-atherosclerotic effects, leading to accelerated disease progression [20]. Regarding ghrelin levels, its anti-inflammatory function may be lost due to decreased circulating levels in coronary artery disease patients. Ghrelin has been shown to modulate immune responses and thus inhibit inflammation in blood vessels; therefore, its reduction may contribute to creating a pro-inflammatory environment that leads to atherosclerosis [21]. Moreover, ghrelin plays a protective role in maintaining endothelial integrity by reducing oxidative stress and limiting the production of reactive oxygen species. Therefore, decreased ghrelin levels may exacerbate oxidative damage and endothelial dysfunction, both of which are key factors in the development of coronary artery disease [22]. It is important to note that the concurrent decrease in both adiponectin and ghrelin levels plays a major role in inducing a broader metabolic dysfunction characterized by increased inflammation and oxidative stress. This combined dysfunction may create a pathological environment that accelerates the formation and instability of atherosclerotic plaques in affected patients [23].

Elevated leptin levels in coronary artery disease patients may be due to increased adipose tissue mass and a condition known as leptin resistance. As a result, leptin loses some of its regulatory function in energy homeostasis while maintaining its pro-inflammatory activity. This, in turn, leads to increased production of inflammatory factors and contributes to vascular inflammation and increased atherosclerosis [24]. Furthermore, leptin has been shown to directly affect vascular cells by promoting oxidative stress and stimulating smooth muscle cell proliferation. It also leads to increased endothelial dysfunction by increasing reactive oxygen species production, thereby accelerating plaque formation and instability [25]. Significantly elevated C-reactive protein (CRP) levels reflect a persistent systemic inflammatory response in these patients. CRP is synthesized in the liver in response to pro-inflammatory cytokines, particularly interleukin-6 (IL-6), and is widely recognized as a sensitive biomarker of inflammation. Increased cardiovascular risk and poor clinical outcomes are strongly associated with elevated CRP levels [26]. Furthermore, C-reactive protein (CRP) is not merely a negative marker; it may actively participate in the pathogenesis of atherosclerosis. It can contribute to endothelial dysfunction, promote monocyte polarization, and stimulate complement activation, thereby exacerbating vascular inflammation and lesion development [27]. Regarding oxidative stress markers, elevated levels of malondialdehyde (MDA) are associated with lipid peroxidation and cell damage in coronary artery disease patients. MDA is a known end product of unsaturated fatty acid oxidation and is used as a reliable indicator of oxidative stress status [28]. Excessive production of reactive oxygen species may contribute to elevated MDA levels, along with impaired antioxidant defense mechanisms. This dysfunction leads to oxidative modification of lipids and proteins, which plays a significant role in endothelial dysfunction and the development of atherosclerotic plaques [29]. In general, elevated levels of leptin, C-reactive protein, and MDA indicate a state of metabolic and inflammatory dysfunction accompanied by increased oxidative stress. These interconnected processes form a pathological triad that significantly contributes to the initiation and progression of coronary artery disease [30].

5- Conclusion

The results of this study revealed clear and significant differences in adipokine and metabolic hormone levels among coronary artery disease patients. Specifically, our results showed a marked decrease in both adiponectin and ghrelin levels, while conversely, leptin, C-reactive protein, and malondialdehyde concentrations were elevated compared to the control group. Furthermore, a weak positive correlation was identified among all studied variables, suggesting a complex interplay between metabolic disturbances, inflammation, and oxidative stress in disease progression. Additionally, receiver operating characteristic (ROC) curve analysis demonstrated high diagnostic accuracy for all measured parameters, supporting their potential utility as complementary biomarkers in the diagnosis and monitoring of coronary artery disease.

6- Recommendations

1- The possibility of relying on studied biomarkers, including adiponectin, leptin, ghrelin, C-reactive protein, and malondialdehyde, as indicators that enhance early clinical diagnosis and monitoring of coronary artery disease.

2- Conducting future studies with a larger number of samples and a longer time period is necessary to verify and determine the effective predictive role of these biomarkers in disease progression and complications.

Ongoing research into the interaction and relationship between inflammation, oxidative stress, and metabolic disorders in order to develop integrated therapeutic strategies targeting these pathways.

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