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Energy Level and Oxidative Stress Status in Cardiovascular Disease

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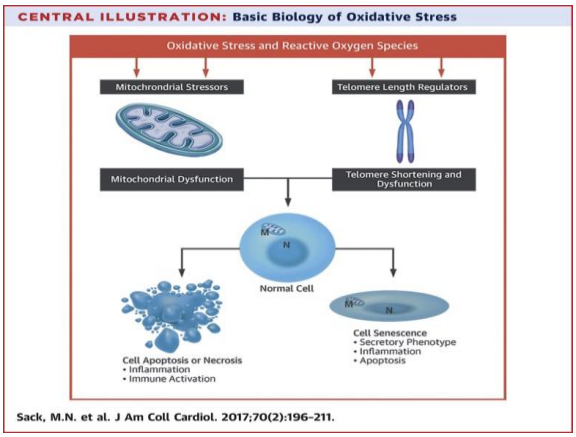
ABSTRACT

The mitochondrial metabolism is the primary source of energy upon which the heart draws to fulfill its function of pumping blood throughout the body to supply the organs with oxygen. Cardiovascular disease (often referred to as CVD) is the leading cause of death because of the "vascular aging," phenomena which comprises all age-associated changes in arteries, cardiovascular disease is a primary contributor to morbidity and death in the elderly. This disease is caused by a complex interaction of a wide range of risk factors and pathogenic pathways. Deregulation of autophagy, endoplasmic reticulum (ER) stress, and activation of apoptosis are some cell abnormalities that contribute to the CVD pathogenesis. Other cell abnormalities include metabolic abnormalities, excessive production of reactive species (ROS), energy deficit, and endoplasmic reticulum (ER) stress. One of the conceivable ways that mitochondria can be implicated in cellular damage is by an excessive production of reactive oxygen and nitrogen species (ROS and RNS). The presence of abnormally high levels of oxidative and nitrosoxidative stress within the circulatory system is a necessary component in the progression of cardiovascular disease. The objective of this study was to measure ATP levels, MDA, catalase, and lipid profile. All of these parameters were determined by using an enzyme-linked immunosorbent assay (ELIZA). The findings of this study showed that there is a connection between cardiovascular disease and oxidative stress, as well as those factors (ATP, MDA, catalase, and lipid profile) that influence on the cardiovascular system.

GRAPHICAL ABSTRACT



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Introduction

Cardiovascular disease is a primary contributor to morbidity and death in the elderly. This correlation is strongly tied to the fact that CVD has a close relationship with age. Because aged vessels are more susceptible to atherosclerotic lesions, vascular injury, impaired angiogenesis, and calcification, it is evident that the aging endothelium is increasingly unable to regulate all of its tasks. This manifests as a significant impairment of endothelium-dependent relaxation (endothelial dysfunction) in elderly people [1]. The most important factor in the development of endothelial dysfunction is oxidative stress, which connect with etiology of cardiovascular disease (CVD) [2]. An increase in the ROS generation by mitochondria is another factor that contributes to the oxidative stress generated by social isolation (there is evidence that oxidative stress is likely to be a key molecular mechanism linking the chronic psychosocial stress to the cardiovascular disease). The mitochondrial respiratory chain is a significant contributor of reactive oxygen species (ROS), which are neutralized by glutathione and other naturally occurring antioxidant systems. The mitochondria inability to produce enough antioxidants causes a disruption in the ATP production and oxidative damage. Catalase, glutathione peroxidase, and superoxide dismutase are antioxidant enzymes with their activities inhibited when people are socially isolated for long periods of time [3]. There are many diseases cardiovascular, among which is coronary artery disease (CAD), atherosclerosis is the most common cause of (CAD) characterized by a persistent inflammatory condition. Ischemia, either acute or chronic, is the hallmark of (CAD), this is the leading cause of death in the developed world. Ischemia is caused by an inadequate delivery of oxygen to the myocardium. Mitchondria play a significant part in the atherosclerosis development and its associated pathology. The malfunction of mitochondria leads to an increase in the formation of reactive oxygen species (ROS), which oxidize cellular proteins, lipids, and DNA [4]. This study will discuss some of the biochemical parameters that play a role in CVD leading to a disease like atherosclerosis. These parameters include ATP, MDA, catalase, and lipid profile. The energy source is adenosine triphosphate (ATP) that can be used and stored [5]. Malondialdehyde (MDA) is one of the byproducts that result from the oxidation of polyunsaturated fatty acids in the cells. The malondialdehyde quantity is generally regarded as a measure of oxidative stress [6]. Oxidative stress is brought on by high-intensity exercise because it causes the body to create free radicals. Measurements of superoxide dismutase and malondialdehyde levels can be used to detect the presence of oxidative stress [7]. MDA with three carbon atoms and two aldehyde groups is one of the byproducts of the oxidation of unsaturated fatty acids (lipid peroxidation). It is one of the markers for the existence of the oxidation process in the body's tissues [8]. Hydrogen peroxide can be detoxified into water by a number of enzymes, among which catalase, a tetramericheme protein, has different functions depending on the amount of hydrogen peroxide present: in the case of a high concentration, catalytic detoxification activity is the most significant, whereas in the case of a low concentration, peroxidase activity is the main function, with the peroxidation of various substrates such as alcohol functions or ascorbic acid [9]. A crucial enzyme called catalase employs the non-radical ROS hydrogen peroxide as a substrate. This enzyme is in charge of neutralizing hydrogen peroxide through its breakdown, hence preserving an ideal level of the molecule in the cell that is also necessary for cellular signaling processes. The enzyme's participation in numerous illnesses and infections, both directly and indirectly, provides evidence of its significance. The function of catalase was linked to the pathogenesis and development of oxidative stress-related illnesses [10]. Lipids are very vital for all the animals, incorporating human, and comprise one of the most important kinds of energy storage in the body [11]. A lipid profile that is not ideal has been identified as a significant risk factor in the CVD onset and progression. A high level of total cholesterol (TC), low-density lipoprotein cholesterol (LDLC), triglycerides (TG), and the lower levels of high-density lipoprotein cholesterol (HDLC) have all been shown to be

associated with an increased risk of cardiovascular disease (CVD) in a number of epidemiological studies [12]. An increase in the production of active oxygen types that causes an increase in total cholesterol or a drop in the HDL-C level in the blood may be to blame for the decline in HDL-C levels. LDL-C is a well-known important carrier of cholesterol from the liver to perivascular tissues [8]. It frequently has connections to dyslipidemia and arterial hypertension (high serum TG and low serum HDL-C vs. high serum TC and LDL-C) [13]. Increased LDL levels, endothelial cell activity, or oxidative stress-related increases in MDA levels could all be contributing factors [14]. The aim of this study was to examine the effect of some parameters through reactive species generation which may lead to the cardiovascular diseases. This can be achieved by measuring (ATP) and (MDA) as result of increment of reactive species, measuring catalase as antioxidant enzyme, measuring lipid profile, ROC analysis for ATP, MDA, and catalase.

Materials and methods

This study was conducted at Ibn Al-Nafis Hospital in (January 2021 to March 2021). The study included 80 volunteers between the ages of 40-69 years. After receiving the patients' consent and the appropriate institutional review board's ethical blessing and they were divided into two groups 30 controls, and 50 cardiovascular disease patients. Serum was collected from 10 mL of venous blood, after centrifugation. The enzyme-linked immune sorbent assay (ELAZA) technique was used to estimate ATP, MDA, catalase, lipid profile levels, and calculating body mass index. This technique works by coupling an antibody or antigen to an enzyme used in the assay. Statistical Analysis System (SAS, 2012) was utilized to find the effects of various factors on study parameters. A significant comparison was made between two means by using T-test. By Chi-square test, a big variation between the percentage (0.05 and 0.01 probability) was revealed in this study (Excel, 2010).

Results and Discussion

Body mass index (BMI) is a simple calculation based on height and weight that is frequently used to categorize humans as overweight or obese. It is explained by determining the ratio of a person's body weight in kilograms to their height in meters (kg/m^2) [15].

The result of BMI was presented in Table 1. The results show mean±SE of CVD group and the control group of BMI [(29.05 ±0.67) (23.08 ±0.43)], respectively, where the result indicates a significant difference between the two studied groups ($P \leq 0.05$).

Obesity and high levels of body fat are associated to the raised levels of a number of risk factors for cardiovascular disease, according to the findings of the current analysis, which indicated a link with (CVD). In adults regardless their gender, a positive link was found between the two different indices of adiposity and the risk factors of cardiovascular disease. In addition, it appears that BMI was a superior indicator for predicting various risk factors associated with cardiovascular disease than PBF in samples [16]. According to the findings of several studies, the differences in BMI are associated with an increased risk of cardiovascular disease (Adams, 2020) [17].

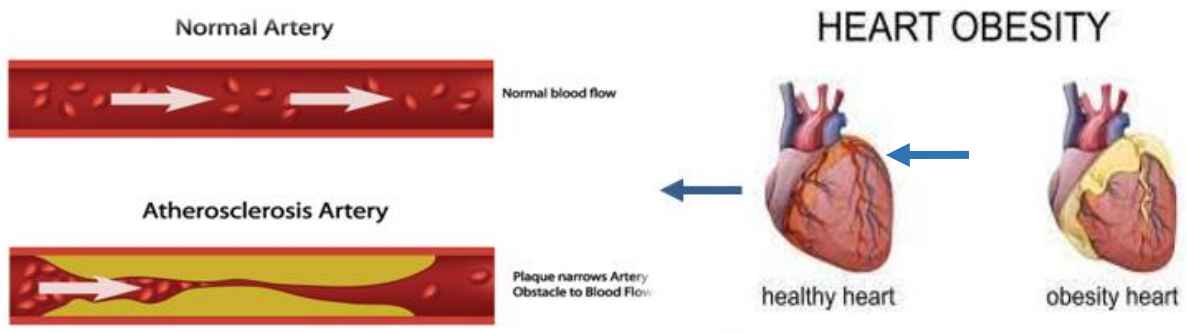

Figure 1: Heart obesity

The results of ATP were presented as mean ±SE in cardiovascular disease and control [(17.41 ±0.76), (89.07 ±7.13)], respectively, as presented in Table 1. In this study, ATP appeared in a high concentration at the beginning of the disease. The ATP result showed a significant variance (P>0.05). The ATP synthesis in mitochondria needs the presence of the ubiquitous cofactor NAD+. According to the findings of several studies, the available amount of NAD+ is a limiting factor for the energy synthesis in mitochondria. This study demonstrates that CAD affects the hearts. Compared with the findings of the earlier studies, the measured ATP levels were rather low (Ait-Aissa K, 2019) [18].

The MDA results were presented as mean ±SE in cardiovascular patients and control [(185.60 ±11.02) (75.81 ±3.92)], respectively, as listed in Table 1. In this study, MDA appeared in a high concentration at the beginning of the disease. The MDA result showed a significant variance (P>0.05) in the CVD group.

The presented data suggest that individuals with ACS have MDA levels that are noticeably greater than those of healthy controls, which play a crucial role in the antioxidant defense, was much higher in. the control group than in patients with acute coronary syndrome (ACS). According to these findings, patients with STEMI and NSTEMI had high levels of oxidative stress and inadequate levels of antioxidant defense (AladağN 2021) [19].

The catalase results were presented as mean ±SE in CVD and control group [(169.87 ±7.38) (289.96 ±7.86)], respectively, as indicated in Table 1. In this study, catalase appeared in a high concentration at the beginning of the disease. The catalase result showed a significant variance (P>0.05).

According to the findings of this study, the H_2O_2 accumulation in WAT (White adipocytes) as a result of the catalase deletion causes both adipogenesis and lipogenesis. It would appear that an increase in the level of oxidative stress caused by a lack of catalase promotes the preadipocytes development into adipocytes. In terms of lipogenesis, greater oxidative stress in WAT caused by increased H_2O_2 leads to decreased mitochondrial biogenesis and function, which in turn results in increased lipid synthesis rather than increased lipid oxidation. “A lack of catalase causes NOX4 (Nox4 is a protective reactive oxygen species generating vascular NADPH oxidase) to become active, which leads to an elevated level of oxidative stress" (Shin SK, 2020) [20].

Catalase dysfunction or deficiency has been hypothesized to have a role in the development of a number of age-related degenerative disorders, such as type 2 diabetes, high blood pressure, anemia, vitiligo, and Alzheimer's disease. In addition, it has been found that catalase is a crucial enzyme involved in mutagenesis, inflammatory conditions, and the apoptosis inhibition. All of these illnesses have been linked to the oxidative stress disorders. During the apoptosis suppression, catalase plays a role in preventing apoptosis from occurrence [10].

The results of lipid profile, where presented as mean ±SE to cardiovascular disease and control (cholesterol) [(224.45 ±13.66) (123.72 ±4.98)], respectively (Triglyceride) [(333.78 ±14.96) (182.09 ±4.63)], respectively (HDL) [(29.53 ±1.28) (67.18 ±3.34)], respectively, (LDL) [(125.14 ±13.64) (35.46 ±4.94)], respectively, as presented in Table 2. The result of lipid profile showed a significant difference between the two studied groups (P>0.05). The HDL-C levels and the TC/HDL-C and TG/HDL-C ratios were linked to all-cause mortality and the risk of hospitalization for CHD and stroke in samples with at least one significant cardiovascular risk factor, whereas LDL-C was linked to stroke but not to CHD. Mortality from all causes was correlated with HDL-C levels and the ratios of TC/HDL-C and TG/HDL-C. The HDL-C levels, the ratios of total cholesterol to HDL-C, and total fat to HDL-C were related with an increased risk of all-cause death and hospitalization. A sensitivity analysis performed with patients, who had not been using lipid-lowering medication at the beginning of the research, confirmed these findings (Orozco-Beltran D, 2018) [21].

Table 1: Statistical distribution of some biochemical parameters (ATP, MDA, and catalase) serum of cardiovascular patients and control

Parameters	Group	Mean±SE	P-value
BMI (kg/m^2)	Patients	29.05 ±0.67	0.0001
	Control	23.08 ±0.43	
ATP (ng/mL)	Patients	17.41 ±0.76	0.0001
	Control	89.07 ±7.13	
MDA (mmol/mL)	Patients	185.60 ±11.02	0.0001
	Control	75.81 ±3.92	
Catalase (pg/mL)	Patients	169.87 ±7.38	0.0001
	Control	289.96 ±7.86	

Table 2: Statistical distribution of lipid profile serum of cardiovascular patients and control

Parameters	Group	Mean±SE	P-value
Cholesterol (mg/dl)	Patients	224.45 ±13.66	0.0001
	Control	123.72 ±4.98	
Triglyceride (mg/dl)	Patients	333.78 ±14.96	0.0001
	Control	182.09 ±4.63	
HDL (mg/dl)	Patients	29.53 ±1.28	0.0001
	Control	67.18 ±3.34	
LDL (mg/dl)	Patients	128.17 ±13.29	0.0001
	Control	20.12 ±4.55	

ROC analysis

The ROC analysis, which is an abbreviation of Receiver Operating Characteristic curve, is a graph explaining the identification capability of double classifier as the discernment threshold varies [22]. The ROC curve is utilized to discriminate between the patients and control groups. There is a difference .in the parameters between the two groups, as. demonstrated by Tables 3, 4, and 5. The result of the ROC analysis between the patient and control groups were. ATP = 0.969, MDA=0.89, and catalase = 0.94.

ROC test for ATP markers showed perfect cut-off value with 96% sensitivity and 97% specificity indicating that ATP considered as a good diagnostic marker with cut-off value 29.4 the subjects under this level considered as patients.

The ROC test for catalase markers showed a good cut-off value with 84% sensitivity and 100% specificity indicating catalase as a good diagnostic marker with cut-off value 216 the subjects under this level are considered as a patient.

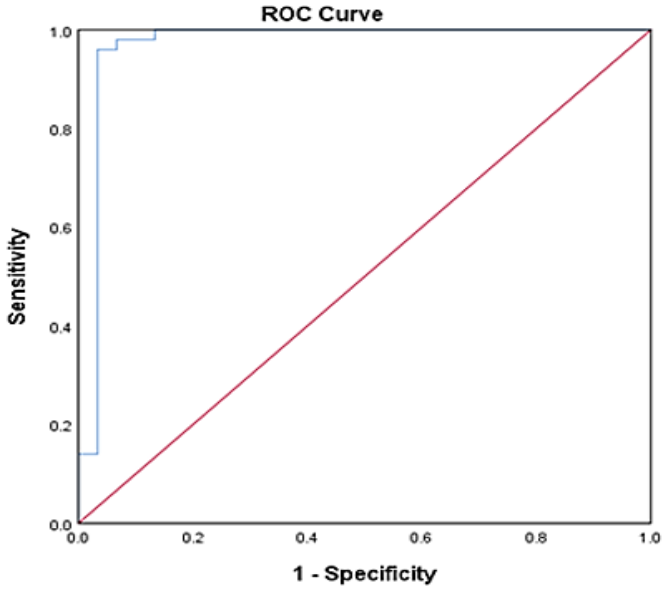

Figure 2: ROC curve analysis of ATP, in patients and control group

Table 3: ROC curve analysis of test ATP for patients and control groups

Test Result Variable(s)	Area	Sensitivity	Specificity	Cut off value	Asymptotic 95% Confidence Interval	
					Lower Bound	Upper Bound
ATP	0.969	96%	97%	29.4	0.913	1.000

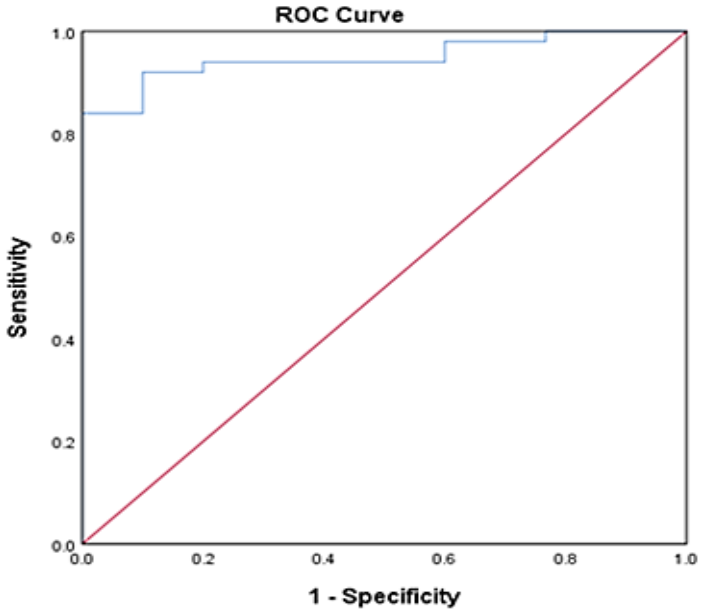

Figure 3: ROC curve analysis of catalase in patients and control group

Table 4: ROC curve analysis of test catalase for patients and control groups

Test Result Variable(s)	Area	Sensitivity	Specificity	Cut-off value	Asymptotic 95% Confidence Interval	
					Lower Bound	Upper Bound
Catalase	94%	84%	100%	216.3	0.9٠	99

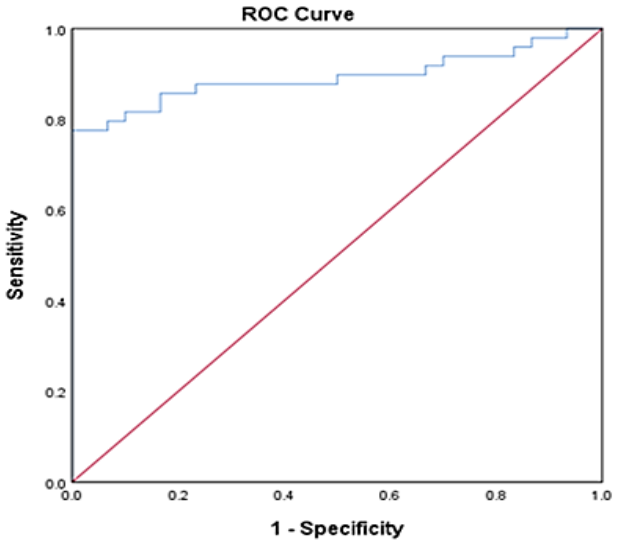

Figure 4: ROC curve analysis of MDA in patients and control group

Table 5: ROC curve analysis of test MAD for patients and control groups

Test Result Variable(s)	Area	Sensitivity	Specificity	Cut-off value	Asymptotic 95% Confidence Interval	
					Lower Bound	Upper Bound
MDA	89.3%	77.6%	100%	114.6	0.82	96

Conclusion

The result of ATP and oxidative stress status demonstrate a significant change between two groups (cardiovascular disease and control), it is appeared that the level of ATP in disease was high compared with control. Malondialdehyde levels in patient group show a significant relationship. The catalase levels of the patients group have a significant activity when it comes to oxidative stress; this enzyme is quite important. There is a substantial association between the patients' group and the values of lipid profile.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

There are no conflicts of interest in this study.

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