



The Role of Oxidative Damage in the Progression of Coronary Heart Disease: A Study of Biochemical Markers in Patients from Kirkuk City

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Abstract:

Cardiovascular diseases, particularly coronary heart disease (CHD), are among the most prevalent conditions associated with atherosclerosis, primarily affecting adults aged 40 years and older. Oxidative damage plays a crucial role in various pathological conditions, with reactive oxygen species (ROS) contributing significantly to CHD progression. This study included 60 CHD patients (30 males and 30 females) aged 40–69 years, all of whom were non-smokers, non-alcoholics, and free from comorbidities such as hypertension or diabetes. A control group of 30 healthy individuals (15 males and 15 females) aged 40–67 years was also included. Blood samples were collected from hospitals in Kirkuk for biochemical analysis.

The findings revealed a significant decrease ($P \leq 0.05$) in the levels of high-density lipoprotein (HDL), superoxide dismutase (SOD), vitamin E (VE), and total antioxidant capacity (TAC) in CHD patients compared to the control group. The measured values were 29.128 ± 2.001 mg/dL (HDL), 40.038 ± 7.245 U/mL (SOD), 26.136 ± 6.376 μ mol/L (VE), 216.19 ± 34.85 μ mol/L (TAC), whereas the control group exhibited 56.267 ± 8.890 mg/dL, 72.191 ± 2.729 U/mL, 39.251 ± 7.839 μ mol/L, and 422.66 ± 69.11 mg/mL, respectively. Additionally, gender showed a statistically significant effect ($P \leq 0.05$) on CHD risk, with

differences observed between male and female patients compared to the healthy group. Age also played a critical role, with significant variations ($P \leq 0.05$) across age groups, indicating an increased CHD risk with advancing age. Furthermore, body mass index (BMI) showed significant differences ($P \leq 0.05$) when comparing all biochemical variables between patients and the control group. The study highlights the significant role of oxidative stress and antioxidant depletion in CHD patients, with age, gender, and BMI contributing to disease progression. These findings emphasize the importance of early intervention strategies to manage oxidative stress and reduce CHD risk. The results revealed a significant decrease in antioxidants (SOD, vitamin E, TAC) and HDL levels in CAD patients compared to controls, confirming oxidative stress's role in disease progression. Age, gender, and BMI were linked to higher risk. These findings highlight the importance of early detection and risk factor management in heart disease prevention.

Keywords: Coronary heart disease, Oxidative stress, Antioxidants, Age-related risk, Biomarkers.

دور الضرر التأكسدي في تطور مرض الشريان التاجي: دراسة للعلامات البيوكيميائية لدى المرضى في مدينة كركوك

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الخلاصة:

تُعدُّ أمراض القلب والأوعية الدموية، ولا سيما مرض الشريان التاجي (CHD)، من بين أكثر الحالات شيوعاً المرتبطة بتصلب الشرايين، حيث تصيب بشكل أساسي البالغين الذين تبلغ أعمارهم ٤٠ عاماً فأكثر. يلعب الضرر التأكسدي دوراً حاسماً في العديد من الحالات المرضية، حيث تساهم أنواع الأوكسجين التفاعلية (ROS) بشكل كبير في تطور مرض الشريان التاجي. شملت هذه الدراسة ٦٠ مريضاً مصاباً بمرض الشريان التاجي (٣٠ ذكراً و٣٠ أنثى) تتراوح أعمارهم بين ٤٠ و٦٩ عاماً، وكان جميعهم من غير المدخنين، وغير المدمنين على الكحول، وخالين من الأمراض المصاحبة مثل ارتفاع ضغط الدم أو السكري. كما تم تضمين مجموعة ضابطة مكونة من ٣٠ فرداً سليماً (١٥ ذكراً و١٥ أنثى) تتراوح أعمارهم بين ٤٠ و٦٧ عاماً. تم جمع عينات الدم من المستشفيات في كركوك لإجراء التحليل البيوكيميائي. كشفت النتائج عن انخفاض معنوي ($P \leq 0.05$) في مستويات البروتين الدهني عالي الكثافة (HDL)، وإنزيم ديسموتاز الفائق (SOD)، وفيتامين E (VE)، والسعة الكلية لمضادات الأوكسدة (TAC) لدى مرضى الشريان التاجي مقارنة بالمجموعة الضابطة. حيث بلغت القيم المقاسة ٢٩,١٢٨ ± ٢,٠٠١ ملغم/ديسيلتر (HDL)، و٤٠,٠٣٨ ± ٧,٢٤٥ وحدة/مل (SOD)، و٢٦,١٣٦ ± ٦,٣٧٦ ميكرومول/لتر (VE)، و٢١٦,١٩ ± ٣٤,٨٥ ميكرومول/لتر (TAC)، بينما أظهرت المجموعة الضابطة قيماً بلغت ٥٦,٢٦٧ ± ٨,٨٩٠ ملغم/ديسيلتر، و٧٢,١٩١ ± ٢,٧٢٩ وحدة/مل، و٧,٨٣٩ ± ٣٩,٢٥١

ميكرومول/لتر، و ٤٢٢,٦٦ ± ٦٩,١١ ملغم/مل، على التوالي. علاوة على ذلك، أظهر الجنس تأثيرًا إحصائيًا معنويًا ($P \leq 0.05$) على خطر الإصابة بمرض الشريان التاجي، مع وجود اختلافات بين المرضى الذكور والإناث مقارنة بالمجموعة السليمة. كما لعب العمر دورًا حاسمًا، حيث لوحظت فروق معنوية ($P \leq 0.05$) بين الفئات العمرية المختلفة، مما يشير إلى زيادة خطر الإصابة بمرض الشريان التاجي مع التقدم في العمر. بالإضافة إلى ذلك، أظهر مؤشر كتلة الجسم (BMI) فروقًا معنوية ($P \leq 0.05$) عند مقارنة جميع المتغيرات البيوكيميائية بين المرضى والمجموعة الضابطة. تسلط هذه الدراسة الضوء على الدور المهم للإجهاد التأكسدي واستنزاف مضادات الأكسدة لدى مرضى الشريان التاجي، مع مساهمة العمر والجنس ومؤشر كتلة الجسم في تطور المرض. تؤكد هذه النتائج على أهمية استراتيجيات التدخل المبكر لإدارة الإجهاد التأكسدي وتقليل خطر الإصابة بمرض الشريان التاجي. كشفت النتائج عن انخفاض كبير في مستويات مضادات الأكسدة (SOD، وفيتامين E، TAC) ومستويات HDL لدى مرضى CAD مقارنة بالضوابط، مما يؤكد دور الإجهاد التأكسدي في تطور المرض. تم ربط العمر والجنس ومؤشر كتلة الجسم بزيادة المخاطر. تسلط هذه النتائج الضوء على أهمية الكشف المبكر وإدارة عوامل الخطر في الوقاية من أمراض القلب.

الكلمات المفتاحية: مرض الشريان التاجي، الإجهاد التأكسدي، مضادات الأكسدة، الخطر المرتبط بالعمر، المؤشرات البيوكيميائية.

1. Introduction:

Cardiovascular diseases are among the most common diseases affecting the general population, especially adults aged 40 years and above. According to 2012 statistics, approximately 17.1 million deaths worldwide were attributed to cardiovascular diseases, particularly coronary artery disease [1]. Atherosclerosis is the pathological process underlying these diseases, severely affecting all blood vessels, including cerebral, coronary, and peripheral arteries [2]. Atherosclerosis is considered an inflammatory and chronic condition driven by innate immunity [3, 4], resulting from the deposition of lipids in the inner walls of blood vessels. These deposits can grow to the point of obstructing blood flow, leading to the formation of plaques or clots, which can cause strokes or aneurysms in the abdominal blood vessels, gangrene in one of the extremities, cardiac arrhythmias, myocardial infarction, pulmonary embolism, and finally, sudden death [5]. In this context, oxidative stress plays a significant role. Oxidative stress refers to a state of imbalance resulting from the excessive production of reactive oxygen species (ROS) and other related oxidizing agents. This imbalance leads to tissue injury and cellular dysfunction, particularly under pathological conditions. The overproduction of ROS contributes to the development of cardiovascular diseases and atherosclerosis [6]. ROS, which are continuously formed as byproducts of cellular metabolism, are the most abundant free radicals in biological systems. At low concentrations, ROS are essential for various physiological processes, such as enhancing the immune system, eliminating inflammation, and regulating cell differentiation. However, when their production exceeds reasonable limits, ROS can attack biological molecules such as

proteins, fatty acids, and nucleic acids, leading to oxidative damage, impairment of cellular functions, and interference with normal metabolic processes [7, 8]. Lipids, including animal fats and plant oils, are important contributors to coronary heart disease. The accumulation of lipids in adipose tissues leads to dyslipidemia, which is a risk factor for atherosclerosis in coronary arteries [9, 10]. This condition contributes to the progressive development of cardiovascular diseases, as lipids accumulate in the walls of blood vessels and form plaques, further exacerbating oxidative stress. To combat oxidative damage, antioxidants are crucial. These substances help protect cells from oxidative damage that could lead to conditions such as Alzheimer's disease, cancer, and cardiovascular diseases. The antioxidant system includes both enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants, such as catalase (CAT), superoxide dismutase (SOD), and peroxidase, work to neutralize harmful free radicals. Non-enzymatic antioxidants include vitamins, minerals, and natural compounds like polyphenols, flavonoids, and carotenoids, which are found in fruits and vegetables and help reduce the risk of cardiovascular diseases [11-14]. Among the key antioxidants, Superoxide Dismutase (SOD) plays a vital role in the body by converting superoxide radicals into less harmful molecules, like hydrogen peroxide and oxygen. Vitamin E (VE) also acts as a potent antioxidant, maintaining the integrity of cell membranes and protecting against ROS-induced damage, particularly in blood vessels. Its concentration is closely linked to blood lipid levels, and it is naturally present in eight forms, with alpha-tocopherol being the most effective [1, 12, 15]. Several risk factors contribute to the development of coronary heart disease (CHD), including increased oxidation of molecules, inhibition of nitric oxide (a vasodilator), and direct cytotoxic effects on endothelial cells. These factors include obesity, age, gender, high blood pressure, dyslipidemia, diabetes, and smoking [1, 16, 17]. CHD is more common in men under the age of 55, with a higher prevalence than in women. Most heart attacks occur after the age of 65, and the incidence increases with age. Women before menopause rarely suffer from heart attacks, likely due to the protective effects of hormones that diminish after menopause [18,19]. Age groups under 45 for men and over 55 for women are considered risk factors for cardiovascular diseases [20]. Smoking is another significant risk factor for CHD, as nicotine increases the stickiness of blood platelets, making thrombus formation more likely. Reducing smoking rates can lead to improvements in blood pressure, HDL levels, and lipid profiles [19, 21].

2. Materials and methods:

2.1. Sample Collection

The study included 60 patient samples (30 males, 30 females) aged between 40 and 69 years, who were randomly selected. They were non-smokers, non-alcoholics, and free from other diseases such as hypertension or diabetes. Control samples included 30 individuals (15 males, 15 females) aged between 40 and 67 years who were free from coronary artery disease but may have had other non-cardiac health conditions. Blood samples were collected from both patients and healthy individuals in hospitals in Kirkuk. In the assessment of coronary artery disease (CAD), clinicians employ a multifaceted approach that includes the evaluation of medical history, physical examinations, and diagnostic tests. Initially, they investigate symptoms such as angina or dyspnea and analyze risk factors including hypertension or diabetes mellitus. Standard diagnostic procedures encompass an electrocardiogram (ECG) to identify arrhythmias, a stress test to observe cardiac function under exertion, and laboratory analyses to evaluate lipid levels and myocardial enzymes. Furthermore, imaging modalities like coronary angiography yield comprehensive visual representations of arterial obstructions. Prompt identification of CAD is crucial for effective management and the mitigation of potential complications.

2.2. Initial Processing of Blood Samples

Blood was drawn from the antecubital vein using a sterile syringe (5 ml) and transferred into EDTA-containing gel tubes to prevent clotting. The samples were left at 37°C for 10 minutes and then centrifuged at 4000 rpm for 10 minutes. The serum was separated and placed in clean, tightly sealed plastic tubes, which were stored at -86°C in a deep freezer until biochemical analysis was performed.

2.3. Estimation of Total Antioxidant Capacity (TAC) in Blood Serum

The FRAP (Ferric Reducing Antioxidant Power) method [22] was used to estimate TAC. This method is simple and effective for assessing antioxidant power. FRAP values were obtained by comparing the absorbance changes in the reaction mixture with those containing known concentrations of Fe (II) ions.

2.4. Estimation of Superoxide Dismutase (SOD) Level in Blood Serum

The level of SOD (Superoxide Dismutase) activity was estimated using the diagnostic kit (SOD Assay Kit-WST) prepared by the Japanese company Dojindo. The Nitro Blue Tetrazolium (NBT) method was used to determine SOD activity in the presence of the highly soluble salt Water-Soluble Tetrazolium (WST-1), which forms a water-soluble formazan dye upon reaction with the superoxide anion. SOD activity (U/mL) was measured colorimetrically at a wavelength of $\lambda = 450$ nm.

2.5. Estimation of Vitamin E Level in Blood Serum

The concentration of VE was estimated using the diagnostic kit (Human Vitamin E ELISA Kit) prepared by the company MyBioSource. The ELISA technique was used at ($\lambda=450$ nm).

2.6. Estimating high-density lipoprotein (HDL) concentration in serum

The enzymatic method was used to estimate high-density lipoprotein (HDL) concentration in serum using the Biolabo diagnostic kit [23] supplied by the French company Biolabo (HDL Kit). The principle of operation of this method is based on the quantitative sedimentation of chylomicrons and lipoproteins after adding phosphotungstic acid / $MgCl_2$), so that HDL remains in the filtrate alone after the centrifugation process.

2.7. Statistical analysis

The statistical analysis was performed using the Minitab 15 software, applying a significance level of ($p \leq 0.05$). I utilized my expertise in statistical planning to ensure the robustness of the analysis. Initially, I verified the assumptions of normality and homogeneity in the data. Once these conditions were met, the one-way analysis of variance (ANOVA) method was employed to compare the differences between the groups. This approach allowed for a thorough evaluation of whether any statistically significant differences existed among the groups. In addition to the ANOVA, I calculated key descriptive statistics, including the mean, standard deviation (SD), standard error, and significance level, to provide a comprehensive overview of the data distribution and the precision of the results.

3. Results and Discussion:

The concentrations of various parameters, including TAC, SOD, VE, and HDL, were measured in samples from patients with coronary artery disease and a control group. The study was organized into four main sections: The first section examined the total number of participants, consisting of 60 patients and 30 controls. The second section focused on gender distribution, with an equal percentage (50%) for each gender. The third section categorized participants into age groups: 40-49, 50-59, and 60-69 years and above. It was observed that 66.66% of both genders were aged 50 years or older. The mean age and standard deviation (SD) for the patients were calculated, with males having an average age of 56.0 ± 7.280 years, females having an average age of 58.430 ± 8.380 years, and controls of 52.233 ± 8.877 . The fourth classification was based on body mass Index (BMI, kg/m^2): BMI₁ (ages 18.5–24.9) had normal weight, BMI₂ (ages 25–29.9) were overweight, and BMI₃ (ages 30–39.9) were classified as obese. The (mean \pm SD) BMI values for these groups were (23.707 ± 1.555) for BMI₁, (26.962 ± 1.296) for BMI₂, and (33.110 ± 2.37) for BMI₃. Additionally, the (mean \pm

SD) BMI for the healthy control group was (22.437 ± 1.874). This study compared oxidative stress markers (TAC, SOD, VE) and HDL levels between CAD patients and controls, while analyzing demographic patterns. Key findings revealed: 1) Significant antioxidant depletion in patients, 2) Majority (66.7%) of participants were ≥50 years old, 3) Patients showed higher average age and BMI than controls, and 4) Obesity prevalence (BMI3 group) was notable among patients. These results highlight age and metabolic factors as critical contributors to CAD progression.

3.1. The measurement of the average concentrations of TAC, SOD, VE, and HDL in the serum of patients with coronary atherosclerosis and the healthy control group.

The results, as shown in Table 1 and Figure 1, showed a significant decrease at the probability level (P ≤ 0.05) in the levels of TAC, SOD, VE, HDL and concentrations in patients with coronary atherosclerosis. The results were (216.19 ± 34.85), (40.038 ± 7.245), (26.136 ± 6.376), and (29.128 ± 2.001), respectively, compared to the healthy control group, which had results (422.66 ± 69.11), (72.191 ± 2.729), (39.251 ± 7.839), and (56.267 ± 8.890), respectively.

Table 1: The concentrations level of TAC, SOD, VE, and HDL in the serum of patients with coronary atherosclerosis and the healthy control group.

Parameters (Units)	Patients (n=60) mean ± SD	Controls (n=30) mean ± SD
TAC (µmol/L)	216.19 ± 34.85	422.66 ± 69.11
SOD (U/mL)	40.038 ± 7.245	72.191 ± 2.729
VE (umol/L)	26.136 ± 6.376	39.251 ± 7.839
HDL (mg/dL)	29.128 ± 2.001	56.267 ± 8.890

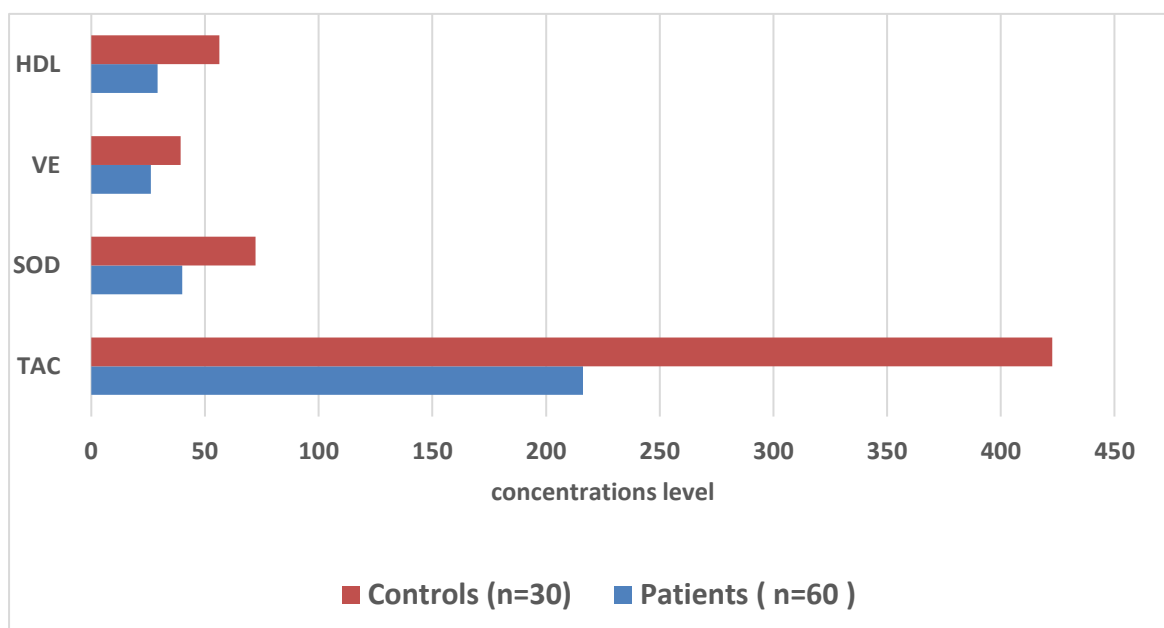


Figure 1: The concentrations level of TAC, SOD, VE, and HDL in the serum of patients with coronary atherosclerosis and the healthy control group.

The current results were consistent with the study of Karajibani, Mansour, et al [12] and Sözmen, Bülent, et al. [24] and Chikkanna Da, et al. [25] and Buczyński, A., et al. [26] where they observed a decrease in the levels of antioxidant concentrations (SOD TAC) and HDL. This is an indication that oxidative stress leads to the weakening and suppression of the antioxidant system in the body due to the increase in lipid peroxides (Malonaldehyde) which leads to a decrease in the activity of antioxidants SOD. This decrease can be explained by the effect of the increase in reactive oxygen species (ROS) derived from free radicals which inhibits the activity of SOD, because the lower the concentration of ROS, the greater the activity of SOD [24]. In light of these results, the most rational and scientifically supported recommendation for the general public is to use a balanced diet with an emphasis on fruits and vegetables rich in antioxidants and whole grains. The results of clinical trials in the secondary prevention of vitamin E have been encouraging, and studies have confirmed that vitamin E supplementation has an objective role in individuals with cardiovascular disease [27]. Contrary to the current study, there were no significant differences in plasma SOD in CHD patients compared to healthy controls. However, there was a consistent and significant difference in TAC and vitamin E levels in CHD patients compared to healthy controls [28]. Although (a) VE Tocopherol is an effective antioxidant and plays a protective role against CAD, its levels were observed to be higher in patients with CHD compared to healthy controls, which contradicts the antioxidant hypothesis. These results were inconsistent with the current study. One explanation for these conflicting results is that patients with CHD have been interested in managing their health through lifestyle modifications and taking therapeutic medications, in addition to their tendency to intentionally eat a healthy diet and take vitamins, especially VE. CHD patients may benefit from taking VE vitamin supplements on a regular basis after being diagnosed with coronary artery disease [29]. High levels of TC in the blood are considered among the most important risk factors for coronary artery disease (CHD), while high HDL cholesterol provides protection against these disorders [24]. Regarding beneficial treatments, statins remain the first-line treatment for dyslipidemia and have proven effective in lowering blood cholesterol levels and reducing the incidence of cardiovascular disease [30]. A significant decrease in antioxidant levels and an increase in blood lipids may be the cause of the suppression of the antioxidant system, lack of adherence to a healthy diet,

eating foods containing fats and red meat, not eating fruits and foods rich in vitamins, the patient's neglect of treatments, and a significant decrease in HDL levels.

3.2. Measurement of the Average Concentrations of TAC, SOD, VE HDL, and by Sex in the Serum of Male and Female Patients with Coronary Atherosclerosis and a Healthy Control Group.

The results showed a significant decrease ($P \leq 0.05$) in the levels of concentrations of (TAC, SOD, VE, and HDL) as shown in Table 2 and Figure 2, in male patients with coronary atherosclerosis. The results were $219.62 \pm 20.66 \mu\text{mol/L}$, $39.828 \pm 8.297 \text{ U/mL}$, $26.000 \pm 5.218 \mu\text{mol/L}$, $30.1421.387 \text{ mg/dL}$, respectively compared with the healthy group ($408.63 \pm 72.48 \mu\text{mol/L}$, $72.449 \pm 2.812 \text{ U/mL}$, $38.845 \pm 6.758 \mu\text{mol/L}$, $57.406 \pm 9.642 \text{ mg/dL}$), respectively. In female patients with coronary atherosclerosis, the concentrations of TAC, SOD, VE, and HDL significantly decreased, with values of $212.76 \pm 44.95 \text{ U/mL}$, $40.248 \pm 6.152 \text{ mg/dL}$, $26.271 \pm 4.527 \mu\text{mol/L}$, and $28.115 \pm 2.025 \mu\text{mol/L}$, , and, respectively, compared to the healthy control group. The results were statistically significant with $P > 0.05$, and the concentrations in the healthy group were $436.68 \pm 79.55 \mu\text{mol/L}$, $71.933 \pm 2.715 \text{ U/mL}$, $39.658 \pm 6.995 \mu\text{mol/L}$, and $55.127 \pm 8.244 \text{ mg/dL}$.

Table 2: The concentrations of TAC, SOD, VE HDL, and by Sex in the serum of male and female patients with coronary atherosclerosis and a healthy control group

Sex	Parameters(Units)	Patients (n=60) mean \pm SD	Controls (n=30) mean \pm SD
Male	TAC ($\mu\text{mol/L}$)	219.62 ± 20.66	408.63 ± 72.48
	SOD (U/mL)	39.828 ± 8.297	72.449 ± 2.812
	VE ($\mu\text{mol/L}$)	26.000 ± 5.218	38.845 ± 6.758
	HDL (mg/dL)	30.142 ± 1.387	57.406 ± 9.642
Female	TAC ($\mu\text{mol/L}$)	212.76 ± 44.95	436.68 ± 79.55
	SOD (U/mL)	40.248 ± 6.152	71.933 ± 2.715
	VE ($\mu\text{mol/L}$)	26.271 ± 4.527	39.658 ± 6.995
	HDL (mg/dL)	28.115 ± 2.025	55.127 ± 8.244

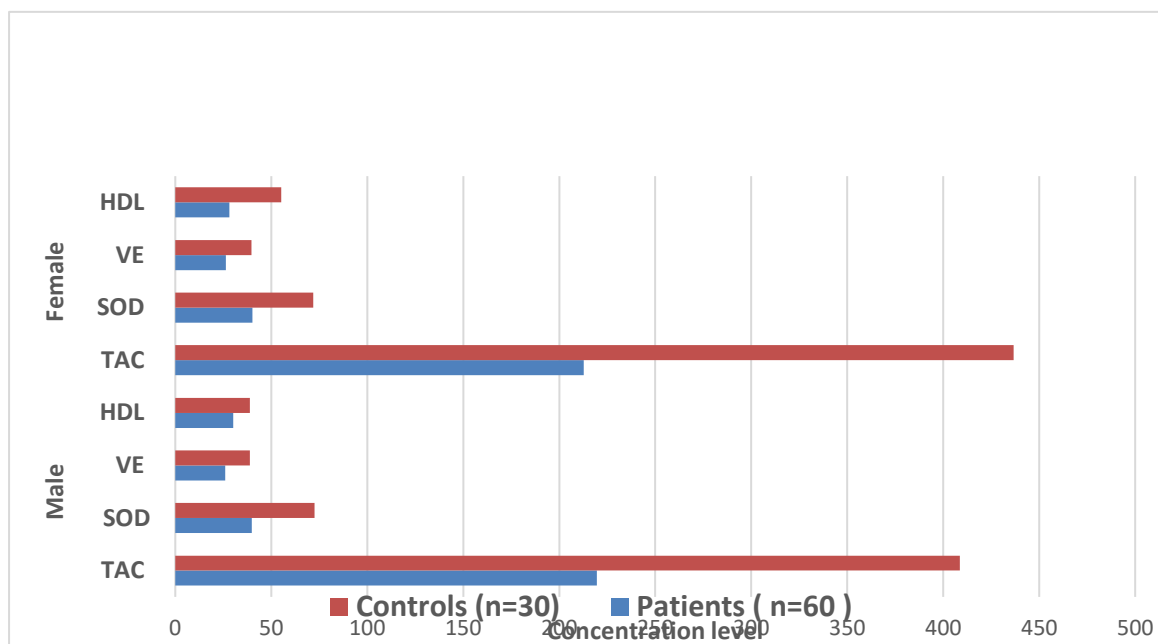


Figure 2: The concentrations level of TAC, SOD, VE HDL, and by Sex in the serum of male and female patients with coronary atherosclerosis and a healthy control group

When comparing only two groups of patients (males and females) with coronary atherosclerosis, no statistically significant differences were found at the probability level ($P > 0.05$). It was noted that TAC and HDL concentrations were higher in males than in females. SOD concentrations were higher in females than in males, and no significant changes in VE concentrations were observed between males and females. The researchers suggested that low levels of total antioxidants (TAC and HDL) may be involved in the development of atherosclerosis. There is some evidence that antioxidant therapy may be beneficial for the prevention of coronary heart disease (Souiden, Yosra, et al. [31]). Furthermore, a significant decrease in both SOD activity levels and total antioxidant TAC was found in patients with coronary atherosclerosis. This finding suggests that decreased levels of both SOD and TAC likely contributed to the development of coronary artery disease (CHD) stenosis in Tunisian men [32]. Free radicals play an important role in the body through various mechanisms, including androgenesis systems and essential metabolic processes such as oxidative phosphorylation and mitochondrial respiration, as well as environmental factors such as light, heat, and metals. The mechanisms underlying various coronary microvascular

dysfunctions are due to intima-reactive vasculature, low levels of endogenous estrogen, coagulation disorders, and abnormal inflammatory reactions [12]. A significant decrease in VE levels negatively impacts CHD patients due to a weakened system. They have antioxidant properties, as VE has an important role as an antioxidant due to its ability to stop the spread of oxidants produced during cellular metabolism and toxic chemicals. It also prevents the spread of lipid peroxidation in phospholipid membranes and protects membranes and arteries from ROS [33]. Studies have confirmed the increased consumption of fruits, green vegetables, vegetable oils (such as soybeans, corn, and sunflowers), whole grains, wheat germ, nuts, seeds, and leafy vegetables as antioxidants, as they affect the clinical outcomes of CHD patients. It has a broad ability to protect biological membranes and nucleic acids when exposed to attack by free radicals in cells [8, 34]. Researchers confirmed that CHD symptoms are delayed in women (Sutton-Tyrrell Kim et al.) [35] by 10 to 15 years compared to men due to the protective effect of ovarian hormones. The prevalence of carotid atherosclerosis is evident among premenopausal women and women 5-8 years after menopause, as they found a prevalence of plaques (deposits) of 25% among premenopausal women and 54% among postmenopausal women. Estrogen also has a regulating effect on a number of factors such as metabolism, lipids, inflammatory markers, and the coagulation system. It also enhances the direct vasodilatory effect through A and B receptors in the vascular wall. Furthermore, there are changes in lipid profiles around the time of menopause. The risk of CHD increases in women during the transition to menopause, and changes occur in the distribution of body fat, causing obesity as a result of the frequent accumulation of visceral fat after menopause, due to the imbalance. Hormonal [36], and the decrease in HDL levels after menopause is also affected by the lack of estrogen, which plays an important role in reducing harmful cholesterol levels and raising levels of HDL cholesterol [37]. Many studies have confirmed that raising HDL levels is a logical therapeutic goal and that any decrease in its concentration leads to an increase in cardiovascular diseases [5]. The hormone estrogen reduces HDL levels by reducing the activity of the triglyceride lipase enzyme in the liver, which breaks down HDL. Global studies have shown that the risk of atherosclerosis for both sexes is inversely related to HDL levels in the blood; the higher the HDL levels, the lower the cardiovascular risk factors. [38]. A low HDL concentration of less than 40 mg/dL in males and 50 mg/dL in females. It has been suggested that the difference in phenotypes between males and females may be determined by the action of sex hormones. In women, estrogen is the dominant sex hormone, and any decrease in its production before or after menopause alters lipid metabolism more favorably toward atherosclerosis by lowering HDL levels. It also has a

direct effect on endothelial cell function and vascular. We believe that men under the age of 45 are at greater risk of developing CHD than women of the same age. Since 66.66% of the study samples of both sexes were aged (50) years and above, where the average age of females (58.430 ± 8.380) was greater than the age of males (56.000 ± 7.280), this can be explained by the fact that women at this age lack the role of the estrogen hormone, which has an important role in the pre-menopausal stage in many physiological and metabolic processes of the body, and as a result. It was suggested to take nutritional supplements of vitamin E, as it is one of A powerful, essential fat-soluble antioxidant. It acts as an antioxidant, exclusively capturing free oxygen radicals, protecting lipids in cell membranes from oxidation, and preventing bad cholesterol from adhering to blood vessel walls

۳.۳. Measurement of TAC, SOD, VE, and HDL Concentrations by Age Group in the Serum of Patients with Coronary Atherosclerosis and Healthy Controls

Table 3 and Figure 3 showed a significant decrease at the probability level in TAC, SOD, VE, and HDL concentrations ($P \leq 0.05$) for patients with coronary atherosclerosis with age according to the three age groups compared to the age groups of the healthy group. We note that the levels of total antioxidants TAC decreased with age in patients with CHD, especially in the age group (50-59) years, which is greater than other age groups compared to healthy people, and its level increased in the age group (60-69), and this may be explained by the patient's prevention of the risk of contracting the disease, taking medications, and following a healthy diet rich in vitamins, while the levels of (SOD, HDL, VE) decreased gradually with age according to the age groups (40-49), (50-59), (60-69) years, respectively. Antioxidant concentrations (VE, SOD, TAC) gradually decreased with age. This indicates that oxidative stress in the cardiovascular system occurs when antioxidant capacity is insufficient to reduce ROS and other free radicals. Early observational studies focused on dietary antioxidants, such as beta-carotene-tocopherol and ascorbic acid, and demonstrated an inverse association between the intake of these antioxidants and cardiovascular disease [39]. SOD is an antioxidant enzyme that plays a vital role in the body, converting superoxide radicals to H_2O_2 and oxygen, eliminating free oxygen radicals that contribute to endothelial dysfunction in patients with coronary artery disease (CHD). SOD is also active in other tissues. After the conversion of superoxide radicals to H_2O_2 , the final product, catalase then converts H_2O_2 to water and oxygen [12,7]. Vitamin E acts as an antioxidant. It has anti-inflammatory activity and regulates the expression of proteins involved in the absorption, transport, and degradation of tocopherols, as well as the absorption, storage, and export of lipids such as cholesterol. It

plays an important role in combating atherosclerosis due to the oxidation of lipids accumulated within the blood vessels. Macrophages resulting from foam cells contribute to the formation of atheroma in arterial walls. Oxidative stress plays a crucial role in this process, leading to endothelial injury and plaque formation [40]. Studies have shown that with aging, lipid peroxidation is directly linked to systemic oxidative stress. Two important components of oxidative stress with aging are the decline in the abundance of dietary antioxidants and the accumulation of oxidation products of biological structures [41]. The present study focuses on key oxidative stress parameters, including TAC, SOD, VE, and HDL, across different age groups. Previous research suggests that oxidative stress markers tend to increase with age due to metabolic changes and reduced antioxidant defenses [42]. The findings of Towfighi et al. support this, as their study analyzed oxidative stress parameters in middle-aged CHD patients (35–54 years) by gender [20]. Since 66.66% of the current study samples for both sexes were 50 years old and above, the average age of females (58.43 ± 8.38) was higher than that of males (56.00 ± 0.28). This aligns with studies indicating that oxidative stress-related changes become more pronounced with aging [43], particularly in postmenopausal women, where decreased estrogen levels may contribute to alterations in antioxidant status.[44]. We believe that the main risk factors for cardiovascular disease are the increase in males under 45 years and females over 55 years. Engaging in physical exercise, maintaining a healthy diet, managing body weight, and taking appropriate medications can help mitigate oxidative stress and reduce potential risk factors associated with aging.

Table 3: The concentration level of TAC, SOD, VE, and HDL Concentrations by Age Group in the Serum of Patients with Coronary Atherosclerosis and Healthy Controls

Parameters (Units)	Ages (years)	Patients (n=60) mean ± SD	Controls (n=30) mean ± SD
TAC (µmol/L)	(40 - 49) years	219.10 ± 31.98	448.35 ± 71.99
	(50 - 59) years	181.10 ± 28.31	381.57 ± 21.99
	(60 - 69) years	203.48 ± 38.64	369.28 ± 16.94
SOD (U/mL)	(40 - 49) years	44.763 ± 7.822	71.510 ± 3.201
	(50 - 59) years	34.765 ± 9.186	70.782 ± 3.246
	(60 - 69) years	31.033 ± 8.261	69.616 ± 3.243

VE (umol/L)	(40 - 49) years	28.067 ± 5.644	40.946 ± 4.773
	(50 - 59) years	27.979 ± 6.920	39.067 ± 5.059
	(60 - 69) years	25.312 ± 4.872	37.820 ± 4.028
HDL (mg/dL)	(40 - 49) years	29.052 ± 1.265	56.673 ± 5.950
	(50 - 59) years	28.330 ± 2.888	54.613 ± 4.453
	(60 - 69) years	27.735 ± 1.593	53.750 ± 5.609

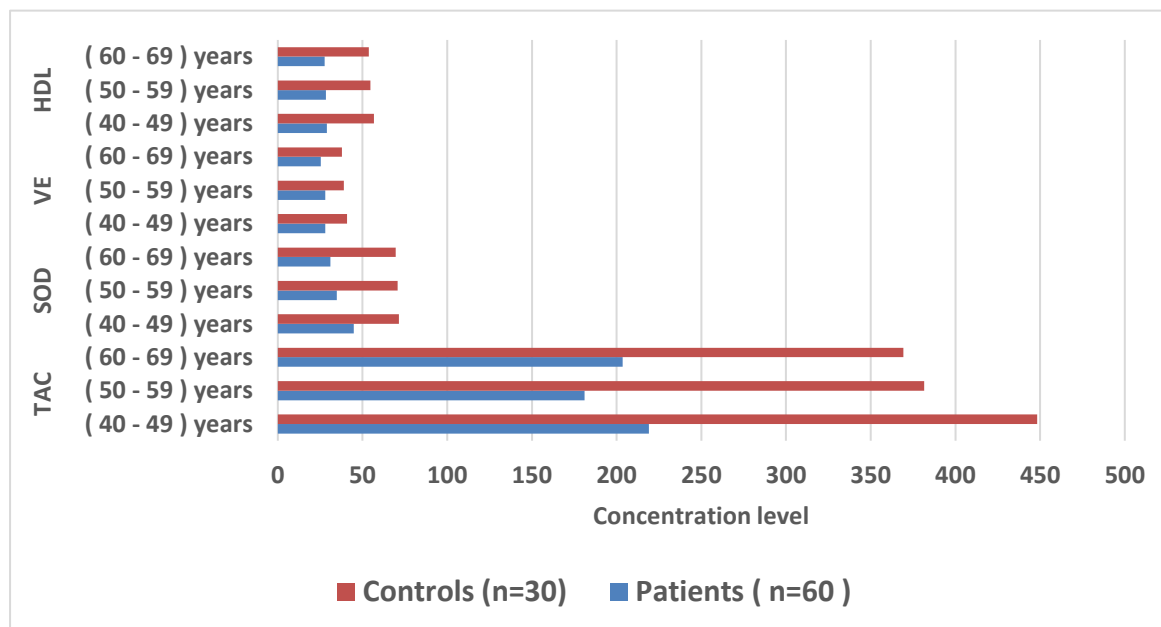


Figure 3: The concentration level of TAC, SOD, VE, and HDL Concentrations by Age Group in the Serum of Patients with Coronary Atherosclerosis and Healthy Controls

3.4. Measurement of TAC, SOD, VE , and HDL Concentrations in Blood Serum of Patients with Coronary Atherosclerosis and a Healthy Group Based on Body Mass Index (BMI).

The results, as shown in Table 4 below, showed that the body mass index (BMI) plays an important and influential role on antioxidants in coronary heart disease, as the concentrations of (TAC SOD, VE, HDL,) decreased significantly at the probability level ($P > 0.05$) with an increase in BMI (BMI_1 , BMI_2) in patients with coronary atherosclerosis when compared with the BMI control group of healthy people. The three BMI groups did not show any significant differences between the groups of patients with coronary atherosclerosis.

Increased BMI is considered a marker of obesity and is one of the risk factors for the development of oxidative stress associated with several diseases, including atherosclerosis, in terms of the increase in oxidation products and the decrease in antioxidant levels [45]. The results of the current study showed an inverse relationship between antioxidants (V.E, SODAC) and blood lipids in coronary heart disease, with increased BMI (obesity) in patients compared to healthy people. This study was consistent with HirakawaYoichiro et al. [9], and Kushi, Lawrence H. et al. with a study [46] explained that obesity is a risk factor for CHD and

confirmed that patients who have one or more risk factors, such as high blood pressure, diabetes, and smoking, are more likely to die than other patients who do not have risk factors. They also noted that physical activity, the use of medications, or attention to health awareness reduce risk factors, and that body mass indexes and high waist-to-hip ratios were associated with the risk of cardiovascular disease [47]. The World Health Organization confirmed that 23% of the global burden of coronary artery disease (CHD) is attributable to overweight/obesity, with increased CHD mortality rates [9]. Postmenopausal women in otherwise healthy obese women have been associated with decreased antioxidant levels due to progressive loss of estrogen, increased body weight, and central obesity. 35.9% of postmenopausal women were overweight, 25% were obese, and 60.9% were morbidly obese. TAC levels were significantly lower in obese women than in overweight women, and serum log TAC levels were inversely associated with BMI [48]. Body weight increases in women during the first years of menopause due to altered body fat distribution, with central obesity occurring more frequently and visceral fat becoming more prevalent after menopause, with escalating comorbid risk factors and components of metabolic syndrome in women compared to men [49]. This study aligns with the large-scale international study by Hirakawa, Yoichiro et al. [9], which investigated the impact of body mass index (BMI) on the relationship between lipid variables and the risk of coronary artery disease. Their findings demonstrated that the risk of disease... Regardless of BMI, the association between lipid variables and coronary artery disease remained significant, highlighting the complex interplay between metabolic factors and cardiovascular health. The World Health Organization confirmed in 2002 that more than half of global obesity cases are attributed to dyslipidemia [9]. In recent years, numerous studies have demonstrated a strong association between obesity and oxidative stress and inflammation due to high levels of reactive oxygen species (ROS) and impaired antioxidant defenses, with increased inflammation resulting from excess fat accumulation leading to overweight and obesity [50].

Table 4: Measurement of TAC, SOD, VE , HDL, and Concentrations in Blood Serum of Patients with Coronary Atherosclerosis and a Healthy Group Based on Body Mass Index (BMI).

Parameters (Units)	BMI (Kg / m ²) (n=90) mean ± SD			
	Controls (n=30) mean ± SD	Patients (n=60) mean ± SD		
	BMI Controls (n=30)	BMI ₁ (n=20)	BMI ₂ (n=20)	BMI ₃ (n=20)
	22.437±1.874	23.707±1.555	26.962±1.296	33.110±2.726
TAC (µmol/L)	422.66 ± 69.11	223.127 ± 32.15	217.95 ± 37.00	212.21 ± 29.17

SOD (U/mL)	72.191 ± 2.729	44.566 ± 8.166	37.025 ± 10.617	32.503 ± 9.171
VE (umol/L)	39.251 ± 7.839	27.351 ± 5.854	25.068 ± 6.067	24.967 ± 7.121
HDL (mg/dL)	52.267 ± 8.890	29.831 ± 2.046	29.740 ± 1.684	28.762 ± 3.189

4. CONCLUSION

This study highlights the significant impact of oxidative stress and antioxidant depletion in the development and progression of coronary heart disease (CHD). The findings revealed a notable decrease in the levels of HDL, vitamin E (VE), superoxide dismutase (SOD), and total antioxidant capacity (TAC) in CHD patients compared to the control group. These reductions suggest that oxidative damage plays a crucial role in CHD pathophysiology, contributing to disease severity and progression. Additionally, the study demonstrated that gender significantly affects CHD risk, with both male and female patients exhibiting distinct biochemical differences compared to healthy individuals. Age was also found to be a key determinant, as older individuals showed more pronounced biochemical changes, further supporting the notion that advancing age is a major risk factor for CHD. Moreover, body mass index (BMI) was strongly associated with oxidative stress markers, indicating that individuals with higher BMI are more susceptible to CHD due to increased oxidative burden and metabolic alterations. The observed reductions in antioxidant levels and enzymatic defense mechanisms suggest an imbalance between oxidative stress and the body's ability to neutralize reactive oxygen species (ROS). This imbalance may accelerate the progression of atherosclerosis and other CHD-related complications. Therefore, these findings emphasize the necessity of adopting early intervention strategies, such as lifestyle modifications, dietary supplementation with antioxidants, and weight management, to mitigate oxidative damage and reduce CHD risk. In conclusion, this study provides valuable insights into the biochemical alterations associated with CHD, reinforcing the importance of oxidative stress as a central factor in disease progression. Future research should focus on exploring potential therapeutic strategies aimed at enhancing antioxidant defenses and minimizing oxidative damage to improve cardiovascular health and patient outcomes. In summary, this research offers significant insights into the biochemical changes linked to coronary heart disease (CHD), emphasizing the critical role of oxidative stress in the advancement of the condition. Nonetheless, the conclusion currently lacks clarity regarding the practical implications of these findings for the diagnosis or prevention of coronary artery disease. A more definitive statement encapsulating the clinical implications and importance of the results is necessary to

effectively communicate the relevance of this study. Subsequent investigations should focus on specific explorations of diagnostic indicators and preventive strategies informed by oxidative stress assessments. Additionally, it is crucial to recognize the limitations inherent in this study, including sample size, demographic diversity, or external variables that may influence the applicability of the results. Addressing these limitations in future research is essential for enhancing the credibility and relevance of the outcomes.

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