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The most important causes of oxidative stress and its impact on cardiovascular diseases

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Abstract

The increase in oxidative stress that contributes to CVD is one of the most common causative factors aggravated symptoms resulting in serious harm. This study was aimed to investigate different biomarkers of oxidative stress in patients with CVD and the biochemical parameters related to these disorders. Participants Methods The research included 56 participants aged between 30 and 65 years, with 28 patients in each group, to be treated as follows: the first group consisted of patients diagnosed with CVD (Group I) and the second was considered healthy (control Group II). Thus, in this study, we demonstrate that oxidative stress and inflammation are intimately connected with CVD. The mitochondrial processes that mediate this relationship will also be presented, as well as the different strategies to circumvent redox/inflammatory biological effects. With regards to each individual from the three groups, these indicators and parameters malondialdehyde (MDA), 8-hydroxydeoxyguanosine (8-OHdG), albumin, uric acid, urea and creatinine.

Keywords

Oxidative Stress,
Cardiovascular,
Albumin,
Uric Acid,
Urea, and Creatinine,
Biochemical Parameters

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1. Introduction

Cardiovascular diseases (CVDs) remain a globally relevant issue, even after many attempts to reduce both their occurrences and effects on human health [1]. Coronary heart disease (CHD), the most prevalent type of cardiovascular disease (CVD) [2], Research shows that oxidative stress is one of the main causes of the development of CVDs [3]. Excessive oxidative stress predominantly injures endothelial cells (EC) in blood vessels, leading to dysfunction/inflammation. Also, other blood vessel cells are involved, adventure cells and vascular smooth muscle cells (VSMCs) [4]. Nonetheless, ECs play a key role in cardiovascular imbalance and for instance endothelial dysfunction can reduce or cause excessive vasoconstriction/vasdilation, induce the death of endothelium cells (EC), increase the adhesion of EC to monocytes or change the ability of angiogenesis by EC [5]. Consequently, this leads to the formation of atherosclerotic lesions and plaques that lead to CVD.

Oxidative stress occurs with the overproduction or accumulation of reactive oxygen species (ROS). Types of ROS include nonradicals such as hydrogen peroxide and hypochlorous acid, in addition to oxygen free radicals such as superoxide, hydroxyl, and peroxyl radicals [6]. Mitochondria are the primary source of intracellular oxidant production in most common cell types [7], followed by nicotinamide and adenine dinucleotide phosphate. and their sources of generation include nicotinamide adenine dinucleotide phosphate (NADPH) oxidases (NOXs), cyclooxygenases, xanthine oxidase and heme oxygenase 1 [8, 9]. Basal levels of ROS production depend on Signal transduction pathways (e.g. succinate-dependent signaling), defense against microbes and virulence factors, gene expression [10, 11], as well as the stimulation of cellular survival or death [7].

Body immune defense mechanisms against ROS include enzymatic factors such as: glutathione peroxidase and superoxide dismutase (SOD). Because ROS directly oxidize macromolecules, such as lipids, proteins and DNA, they have been associated with cell injury, necrosis and apoptosis [12]. The production of a single free radical can initiate chain reactions that produce additional radicals in a cascade process [13]. Reactions of radicals with polyunsaturated fatty acids generate fatty acid peroxyl radicals, which are localized within the cell membrane that alter signal transduction and protein function. Superoxide coupled with iron from iron-containing molecules released during oxidative stress produces a very reactive hydroxyl radical (HO). By means of the Fenton reaction with H2O2 [14].

Additionally, ROS can induce opening of the mitochondrial permeability transition pore (PTP), with efflux of cytochrome c and other molecules that ultimately lead to cell injury or death by apoptosis [15, 16]. The $O2^{\cdot-}$ radicals can react with the important signaling molecule nitric oxide (NO) to form reactive nitrogen species (RNS), which in turn decrease NO bioavailability and cause NO toxicity, or nitrosative stress. [17]. As with ROS, the accumulation of excessive reactive nitrogen species leads to nitrosylation processes modifying proteins conformation, which triggers loss or alteration of protein function [18].

Antioxidant enzymes and other antioxidant defenses would increase the activity of these enzymes to prevent oxidative stress under

physiological conditions [19, 20]. A few of these are glutathione peroxidase, glutathione reductase, catalase (CAT), manganese-dependent superoxide dismutases such as manganese superoxide dismutase (Mn-SOD) and copper/zinc superoxide dismutase (Cu/Zn SOD). O2 is converted to hydrogen peroxide by MnSOD as well as Cu/ZnSOD, which ultimately leads to the formation of water by glutathione peroxidase or catalase. These are followed by additional antioxidant defenses, such as radical scavengers: vitamin E, beta carotene and vitamin C.

This study aims to give a more exact description of the molecular pathways responsible for the redox homeostasis in cells and its dysregulation as well as antioxidant activity upon infection or during progression of cardiovascular disease [21]. Oxidative stress is defined as an imbalance between the production and detoxification of reactive oxygen species (ROS) [22, 23] The myocardium [24, 25] and plasma from HF patients have shown increased oxidative stress which is associated with impaired left ventricular (LV) function [26]. Reactive oxygen species [27, 28] disrupt myocardial $Ca2^{1}$ handling due to apoptosis and necrosis and also trigger hypertrophic signaling, cause arrhythmia, and participate in ventricular remodeling. Mitochondria, uncoupled NO synthase, and NADPH oxidases (NOXs) constitute the major enzymatic sources of ROS inducing vascular and myocardial dysfunction [23].

Importantly, NOXs produce redox active species in either on or off state and mitochondria can respond by behaving like "redox hubs" changing the heart physiology, more specifically in pathology [29, 30]. We focus here on the key contribution of ROS to heart failure-associated myocardial and vascular dysfunction in this first section of the review. Therefore, we also cover the vitamin paradox explaining why attempts to lower oxidative stress in cardiovascular risk patients (e.g., with vitamin E) results in heart failure rather than its prevention [23]. The Myocardium and Vasculature Sources of Superoxide in HF and Functional Implications NADPH oxidase In HF patients and experimental animals, myocardial superoxide (O2) -generating nicotinamide adenine diphosphate–oxydizing NOX activity is increased [24–25]. NOX isoforms are present in endothelial cells (ECs), smooth muscle cells (SMCs), adventitial cells, as well as cardiac myocytes [31]. Physiological strain activates NOX2 (X-ROS signaling) located at the sarcolemma and transverse tubule-localized isoform for later non-classical stimulation of adjacent ryanodine receptors resulting in calcium liberation by the sarcoplasmic reticulum [32].

1. 2. Biomarker for Oxidative Stress

2. 1. 2. 1. MDA, or malondialdehyde

Malondialdehyde (MDA), as a product of radical-initiated oxidative decomposition of polyunsaturated fatty acids, has often been used as a marker of oxidative stress [33]. It is extremely cytotoxic because of its fast binding to proteins or nucleic acids [34]. As shown from Figure (1) below, its chemical structure.

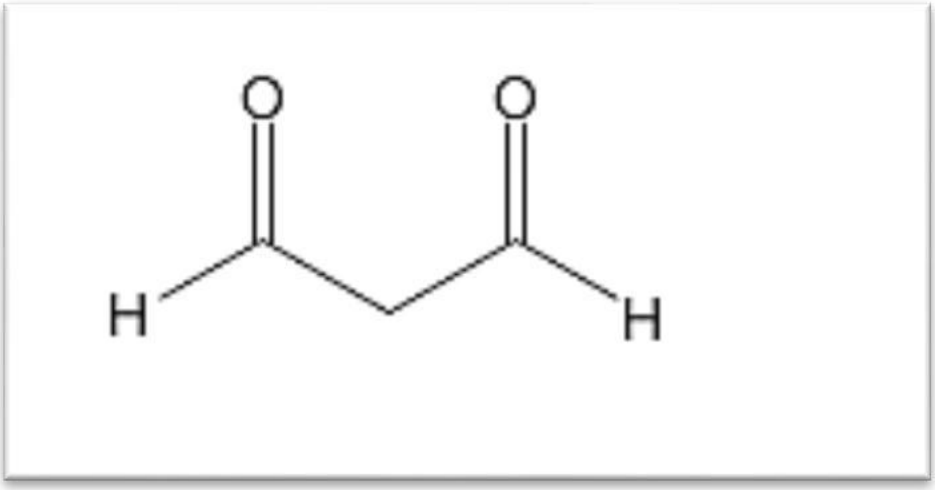

Figure (1): Chemical structure of Malondialdehyde [35].

Hyroxyl radicals are known to react with deoxyribose moieties, leading to the formation of malondialdehyde [36]. One of the major factors for its high reactivity is due to this molecule being an electrophile, highly reactive to nucleophiles such as basic amino acid residues (such as lysine and histidine). This reactivity is given by the aldehydic character of MDA as also its 1,3-dialdehydic structure to form mesomerically stable Schiff base [37]. In its native state at natural pH, MDA has a low intrinsic chemical reactivity. But this molecule can react with the bases of nucleic acids and form different adducts [35]. This blocked area of Watson-Crick base pairing has been shown to be mutagenic for this adduct [38].

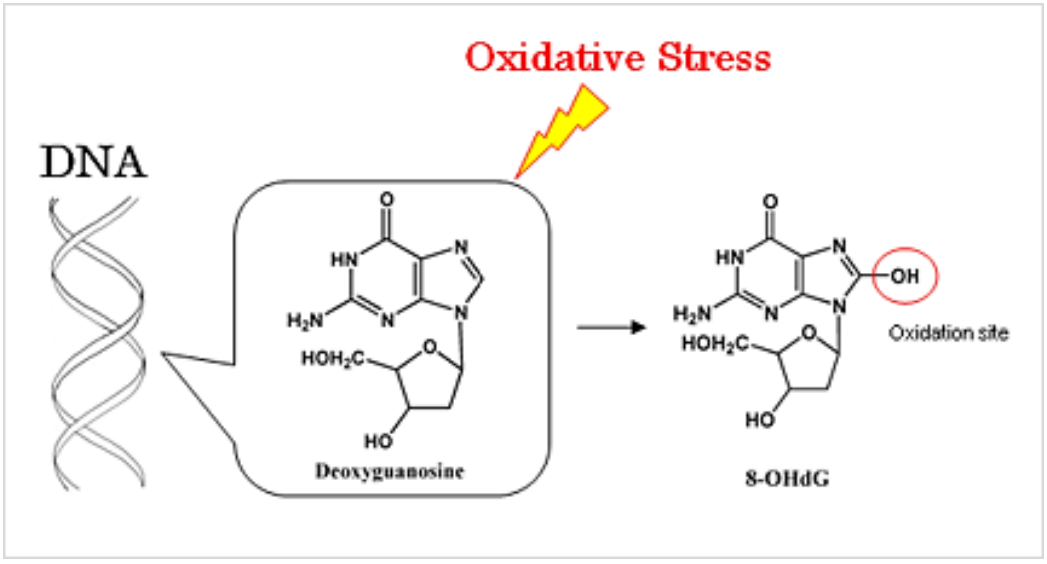

Figure (2): Producing 8-OHdG. (64)

Moreover, it interacts with proteins such as collagen. Additionally, the MDA molecule can lead to crosslinking of membrane components through changing ion exchange concerning cell membranes [39]. Which will have effects including changes in ion permeability and enzyme activity [40]. Accordingly, for this reason it is useful to consider MDA other than a lipid peroxidation product, since by reacting with various molecules (for example proteins and DNA) it can interfere with numerous physiological processes in the human organism [35]. As per clinical evidences MDA-type epitopes are common and known contact in capacity generation of cardiovascular illness; Bartoli, Seema L., Khalid Al-Fartosi found linking between increased MDA and chronic heart disease. [41, 43].

1.2. 2. 8-OHdG, or hydroxydeoxyguanosine

A DNA repair process whereby an oxidized nucleotide,8-hydroxydeoxyguanosine (8-OHdG) is expelled in bodily fluids. 8-OHdG is the most common stable end product of oxidative DNA damage after its enzymatic cleavage under ROS attack at guanine base (after 8-hydroxylation), both on mitochondrial and nuclear DNA [44]. It is believed to be a sensitive indicator of DNA oxidation in response to free radicals and can be found at high levels in all secretrions and tissues where an inflammatory process occurs (45).

The major DNA change of ROS is the formation of 8-OHdG that could be responsible for DNA base mutation. Oxidative DNA adducts accumulate, and more damage occurs, only after being repaired by enzymatic processes [46]. When oxidative stressors such as ROS, UV radiation or genotoxic chemicals induce DNA damage, guanine is easily oxidized to 8-oxo-7,8-dihydroguanine (8-oxo-Gua). The level of this oxidized form of guanine in genomic DNA may lead to transversion mutations such as G-T or G-A binding that can be deleterious if they become persistent [47]. 8-hydroxy-2'-deoxyguanosine (8-OHdG) is a nucleoside form of 8-oxoGua generated from either cytoplasmic oxidized nucleotide, such as 8-hydroxy-deoxyguanosine triphosphate ((8-hydroxydGTP) or damaged oligomers containing 8-oxo-Gua by NER [48].

1.3. Antioxidant Compounds

1.3. 1. Albumin

Albumin, a 66 kDa non-glycosylated protein, accounts for ~60% of total plasma proteins. Normal plasma levels vary between 35 and 50 g / L, its half-life is about 20 days under normal conditions [49] Human serum albumin (HSA) is a single-chain polypeptide consisting of 585 amino acid residues, approximately 67% a-helix and devoid of β-sheet. The antioxidant nature of HSA is linked to its structure. Essential metal ions for example, copper and iron [36] to a greater extent are the main ligands of HSA associated with the direct or indirect antioxidant activities of this protein [50].

Free redox active transition metal ions like those of Cu(II) and Fe(II) are known to possess high pro-oxidant potentials. Indeed, they can interact with hydrogen peroxide (H2O2): throught the Fenton reaction, which catalyzes aggressive ROS production. Secreted to blood in physiological condition, the important radical-trapping property results in approximately two-thirds of HSA molecule form a reduced state that possess free thiol group on Cys-34 residue (HSA-SH) and has been named human mercaptalbumin [50], this redox thiol group is made up 80% of total plasma thiols and due to the high

concentration of HSA in the blood it is considered as the most important extracellular source of reactive free thiol existing in circulation [51].

The Cys34 residue is classified as a free radical scavenger and can trap many different kinds of reactive oxygen species (ROS) and reactive nitrogen species (RNS), such as superoxide [50], hydrogen peroxide (H2O2), and peroxynitrite (ONOO). Also, it plays a role in the oxidative stress response because it has one high affinity site (Lys240) for bilirubin since it can bind homocysteine and bilirubin [52]. The resulting bilirubin bound to HAS is an example of its indirect antioxidant property, as it prevents lipid peroxidation [50, 52].

1.3. 2. Uric Acid

Uric acid (UA) is present in human urine and it is the end product of purine degradation. Under physiological conditions, it is mainly represented by monosodium urate (MSU), a weak organic acid with an pK of 5.75 [53].

Uric acid production can directly promote oxidative stress via the action of xanthine oxidoreductase. This enzyme is first synthesized as xanthine dehydrogenase, but it can be converted into xanthine oxidase via cysteine residue modification or a calcium-dependent proteolytic mechanism. The enzyme then undergoes a change in its catalytic site, losing its ability to bind NADH, and transferring electrons from O2 to generate O2 [53].

Later studies revealed uric acid to be a powerful antioxidant that chelates transition metals and scavenge singlet oxygen, oxygen radicals, and peroxynitrite. Accordingly, urate is a major component of the antioxidant capacity of human plasma, although there are other biologically relevant antioxidants present in all body fluids that can be comparable to ascorbic acid in terms of their antioxidant properties [53]. Uric acid formation, shown in Figure 3. Purine nucleic acids which include adenine and guanine are submitted to oxidation by several enzymes into uric acid [54].

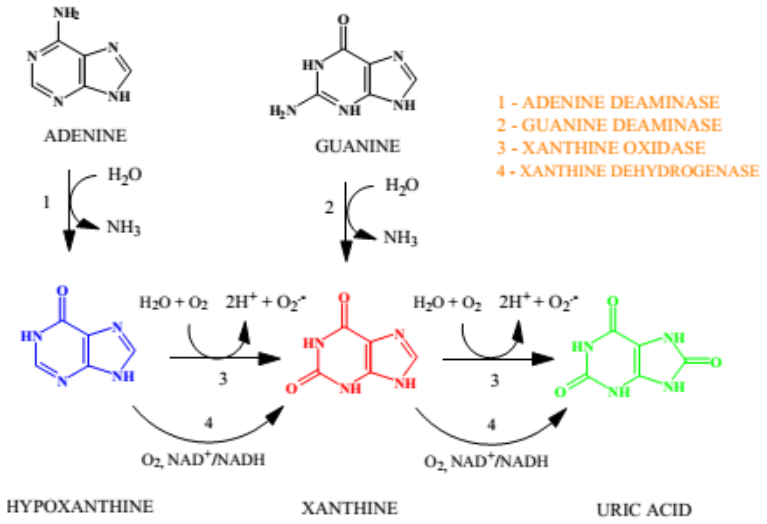

Figure (3) The Conversion of Purines into Uric Acid [54]

1.3. 3. Urea and Creatinine

Phosphocreatine dissociates to produce the cyclic anhydride of creatine (creatinine). It is synthesized in kidneys, liver and pancreas, through the action of enzymes. The first reaction is from the transmiination of arginine and glycine which produces guanidinoacetic acid. Subsequently, acid is methylated through the use of s-anosylmethionine as a methyl donor [55]. Creatinine is transported to several other organs, including the brain and muscles where it gets phosphorylated to form the high-energy compound phosphocreatinine. The interconversion of phosphocreatinine to creatinine is one particular example related to muscular contraction metabolism [56].

A non-enzymatic reaction between creatinine (CRE) and •OH forms a mixture of an oxidized form of creatinine called creatol (C: 5-hydroxycreatinine; CTL) and demethyl-creatinine (DMC) in humans, the stoichiometric ratio is 1:1. As illustrated in the image, CTL metabolically converts to methylguanidine (MG). High levels of urea in blood are usually due to allomeric activity of excess from protein and amino acid catabolism, which are normally eliminated by the kidneys. generated by synthesis using urea cycle enzymes derived from amino acids and nitrogen Certain exogenous factors are already known to influence urea concentration including, high protein intake; increased protein catabolism; blood proteincatabolism; reabsorption of blood proteins or dehydration (clinically excess trend) and post-cortisol therapy [57]. Decreased renal perfusion leads to a decrease of globular filtration rate leading to reduced distal tubular flow rate. This increases urea reabsorption and decreases secretion, which may explain the high serum urea concentration [57]. Unfortunately, I cannot see a future for urea as an antioxidant in the currently available sources.

2. Aim of research

1- Role of oxidative stress in the serum of patients with cardiovascular diseases using biomarkers: Malondialdehyde and 8-OHdG and endogenous antioxidants (albumin, uric acid, urea, creatinin).

2- Determine the association between different measures of oxidative stress and markers in hypertension and cardiovascular diseases.

3. Material and Methods

During the fasting state, blood was extracted between 9:00 and 11:00 a.m., through collecting venous blood of 10 ml. Blood samples were distributed in EDTA tubes (2.5 ml), and then the blood clotted for 10–15 min at room temperature, centrifuging 10 min at 4000 rpm to extract the DNA. Taking advantage of sterile eppindrof tubes, the serum was divided into different fractions. Part of the specimen was used for chemical blood parameters analysis, while the other part was stored at −40 °C until the MDA and 8-OHdG assay.

3.1. Hemoglobin (Hb) determination

The Cell-Dyn 1700 System utilizes the principles of focused flow and electronic sizing, using electrical resistance and impedance to count, number, and classify cells. With the spectrophotometric approach of the Cell-Dyn 1700 system, Hemoglobin concentration at 540 nm absorbance [58].

3.2. Profile of Lipids

3.2. 1. Serum Cholesterol Determination

Enzymatic end point for serum cholesterol levels (Giesse Diagnostic). A fully enzymatic mechanism for this is provided by the Randox Company. The cholesterol measured by colorimetric assays required for the estimation of total cholesterol is ONLY available in commercially available kits. Cholesterol esters in the sample are cleaved into cholesterol and free fatty acid by the action of cholesterol esterase. Phenol aminopyrine is a chromogenic oxygen acceptor that detects hydrogen peroxide in the presence of peroxidase following cholesterol oxidase-catalyzed oxidation to cholesterol-3-one.

3.2. 2. Serum Triglyceride (TG) Determination

Serum triglycerides concentrations were measured using a colorimetric method (with deprotinization) and a kit from Randox Laboratory Ltd. in the UK. The TG were hydrolyzed by the lipase enzyme into

fatty acids and glycerol. Subsequently, glycerol reacts with ATP and glycerokinase to form phosphorglycerol, which then reacts together with 4-aminoantipyrine and parachlorophenol through the peroxidase action yielding chromophene quinoneimine as colored substances [59].

3.2.3. Serum High-Density Lipoprotein-Cholesterol (HDL-Cholesterol) measurement

Phosphotungistic acid is then mixed with samples containing magnesium ions and the chylomicrons, as well as VLDL and LDL lipoproteins that further precipitate [25]. Centrifugation leaves a supernatant that has HDL in it. This can be used for cholesterol measurement by using the cholesterol enzymatic reagent and estimation of total cholesterol in similar manner [60].

3.2.4. Calculating Serum Low-Density Lipoprotein-Cholesterol (LDL-Cholesterol)

Estimating low-density lipoprotein cholesterol (LDL cholesterol), which cannot be directly quantified and isolated, was based on the Friedwald formula. So generally, LDL-cholesterol = Total cholesterol – [HDL- cholesteron +TG /5] is used to call the value for LDL by Friedwalds formulae.

3.2.5 Serum Very Low-Density Determination Lipoprotein-Cholesterol (LDLl)

Very low-density lipoprotein cholesterol was estimated using the Friedwald formula: [VLDL-Cholesterol] = TG/5.

3.3. How To Calculate the Level of Serum Malondialdehyde (MDA)

Under acidic conditions and heat exposure, the products of lipid peroxidation, particularly malondialdehyde (MDA), react with thiobarbituric acid to form a pink chromogen that can be spectrophotometrically determined at 532 nm102. Molda- 1,4-diamino-benzene (MDA) has an extinction-coefficient of molar density of 1.56 X 10–5 Mm-1 cm-1 as reported.

3.4. Evaluation of Serum 8-Hydroxy-Desoxyguanosine (8-OHdG)

This is a competitive inhibition enzyme immunoassay technique. An 8-OHdG-specific antibody has been pre-coated on a microplate. A well with either standards or samples is incubated with HRP-conjugated 8-OHdG. When 8-OHdG is added, a competitive inhibition occurs between the 8-OHdG (standards or samples) and the HRP-conjugated-8-OHdG as they compete for binding sites on the pre-coated 8-OHdG-specific antibody. In samples that contain a higher concentration of 8-OHdG, less is bound by HRP-conjugated 8-OHdG. These wells are then filled with the appropriate substrate solutions. Furthermore, the color changes mirrored the variations in the 8-OHdG level of sample prostration. To prevent the continuing development of the color, the intensity of the color is measured.

4.Results and discussion

4.1. Levels of the lipid profile:

The data that have been noted in Table (1) characterize the lipid profiles of patients and control groups. Serum cholesterol, triglycerides, LDL cholesterol and VLDL cholesterol significantly increased ($p < 0.01$) and HDL cholesterol significantly decreased ($p < 0.01$) in the cardiovascular patient group compared with controls. In this article, atherogenic ratio (or LDL/HDL ratio) in the patient group increased significantly compared with control.

Table (1): Values of Lipid Profile Levels in the cardiovascular diseases and Control Group

Characteristic	Cardiovascular patient n=28	Control group n=28	Comparison of Significant p value
Cholesterol (mmol/L)	4.62±0.25	4.23±0.24	<0.01**
Triglyceride (mmol/L)	2.209±0.17	1.31±0.09	<0.01**
HDL-cholesterol (mmol/L)	1.15±0.06	1.42±0.09	<0.01**
LDL-cholesterol (mmol/L)	3.86±0.29	3.53±0.17	<0.05*
VLDL-cholesterol (mmol/L)	0.433±0.03	0.284±0.02	<0.01**
LDL/HDL (mmol/L)	5.49±0.94	2.83±0.24	<0.01**

* significant with p<0.05, **highly significant with p<0.01

Cholesterol plaque leads to the growth of muscle cells, forming a tough enclosure over the affected region. It is this hard coating that closes the artery. Plaque develops under the surface of the arteries, covered with a fibrous cap that creates a bump in the wall of the artery. The protrusion (bulge) becomes greater as atherosclerosis progresses. A big enough bump (2,4) can lead to a blockage. Jasim M [61] reported that LDL shows a significant increase in ($p < 0.01$) in cardiovascular patients. It is plausible that this occurs since the LDL cholesterol infiltrates morbid endothelium.

The inflammatory cells, such as macrophages, will respond to the area and arrive there inducing inflammation and engulfing the lipids; meanwhile cholesterol is retired from the damaged vessel into this area → are deposited. The LDL-cholesterol particles get lodged in the vessel wall and are at increased risk of oxidation. The damage of oxidized LDL-cholesterol molecules triggers a corresponding immunological response, which can ultimately lead to the development of an atheroma.

At first, the oxidized LDL cholesterol is taken up by macrophages that reside in and patrol our arterial wall — moreso as they migrate into the artery from downstream venous sampling. Accordingly, they will also frequently appear as foamy macrophages. These white blood cells are totally unable to process the oxidized LDL-cholesterol [62]. This research now supports that LDL is more atherogenic and the lipoprotein of LDL contributes to increased atherogenicity. Our results are in accordance with the data reported by (Milan J et al.) with a strong meaningful difference between the conditions studied and control.

We trained on data from October 63], who identified that the LDL/HDL cholesterol ratio was a robust predictor of cardiovascular disease. Epidemiologic studies suggest that hypercholesterolemia and possibly coronary atherosclerosis itself are risk factors for ischemic stroke [11]. Increasing evidence has shown that high plasma triglyceride, LDL cholesterol and HDL cholesterol concentrations are independent risk factors for peripheral vascular disease (PVD), stroke and coronary artery disease (CAD).

4.2. Oxidative Stress Markers and Parameters

4.2.1. Malondildehyde (MDA) levels:

As reflected in (table (2) and Figure (4)), the mean levels of serum MDA showed a statistically significant increase ($p < 0.01$) among cardiovascular patients' group 5.49 ± 0.94 µmol/L compared to control group 3.31±0.26 µmol/L, respectively.

Table (2): Values of MDA Between Groups (mean ± SD):

Characteristic	MDA µmol/L	Control group (n=28)	p value
Cardiovascular patient (n=28)	5.49 ± 0.94	3.31 ± 0.26	<0.01

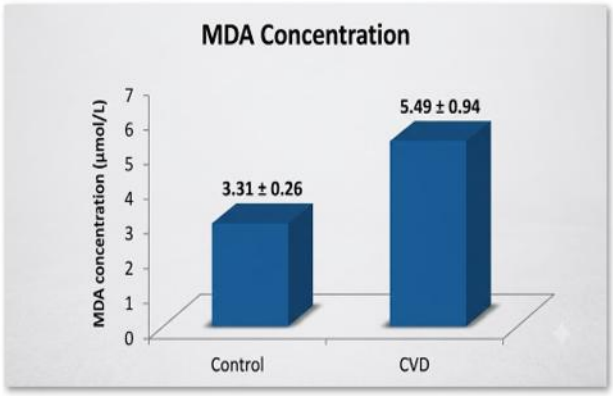

Figure (4): Mean Conc. (µ mol/L) of Oxidative Marker MDA for Studied Groups.

The intracellular production of ROS is an important factor in the chronic inflammatory response to arterial diseases [63]; thus, damage to membrane polyunsaturated fatty acids leads to MDA production, which increases MDA levels in these patients [64].

MDA was positively correlated with LDL cholesterol in diseases (dress up 4-2). This result was also confirmed by Venkata Rao et al. and Ogunro P. et al. [65, 66]. No correlation was seen on BMI and MDA which is incongruent with (Ali P. et al.) [67].

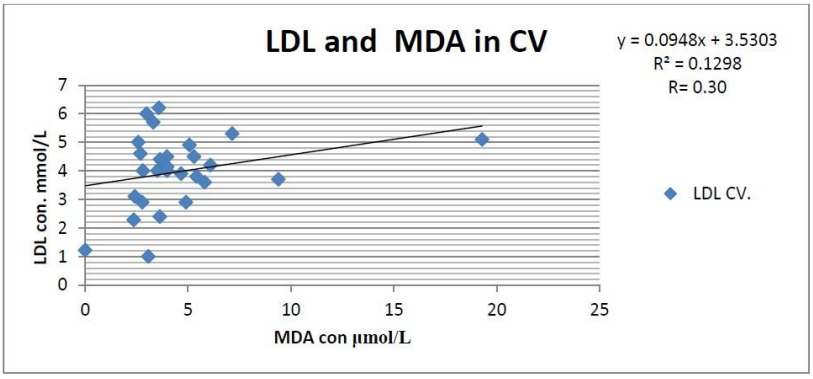

Figure (5): Correlation of MDA with LDL in CVD Patients.

4.2.2 8-Hydroxydeoxyguanosine Levels:

8-hydroxy-2-deoxyguanosine (8-OHdG) is the primary DNA alteration that results from ROS. The levels of 8-OHdG were (104.67±24.94 ng/ml) for the cardiovascular patients compared to (82.62±19.13 ng/ml) for control group as shown in Table (3).

Table 3: Values of 8-OHdG in Patients and Control Group (mean ±SD):

Patient group	8-OHdG [ng/ml]	Control group	P value
Cardiovascular group	104.67 ± 24.94	82.62 ± 19.13	<0.01

We showed a significant difference ($p<0.01$) between the control and cardiovascular patients. The results were in accordance with Fructaci et al [68], who reported an increase in 8-OHdG and an increase in ROS generation in cases of cocaine-related cardiomyopathy. There is known significant relationship of Age and 8-OHdG (R = 0.3) which correlated positively with other studies in different diseases [68,69] (Akihiko et al., Al Wassiti E. et al.) and Teruaki [70]. The Figures (6) and (7) of the present study showed a great degree of direct relationship between 8-OHdG and MDA in both groups.

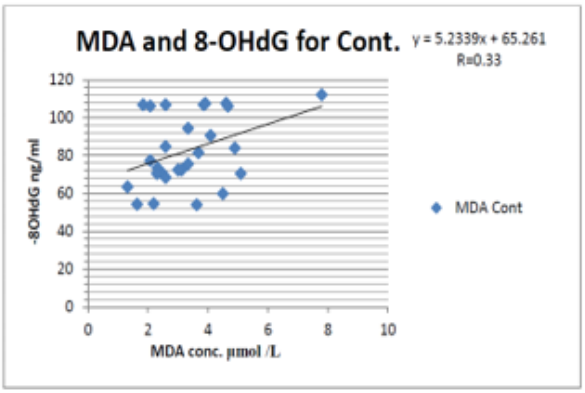

Figure (6): Correlation Directly Between MDA and 8-OHdG for Control group.

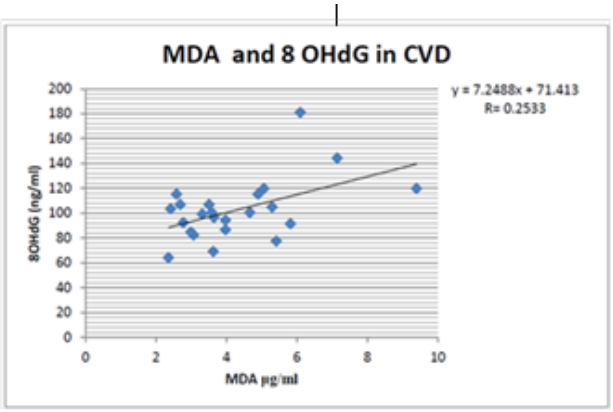

Figure (7): Correlation Directly Between MDA and 8-OHdG for CVD Group

Increasing oxidative stress at all cell levels is demonstrated by the clear link between these two metrics. Sakona et al. also discovered a significant connection between MDA and 8OHdG in healthy individuals by antioxidant feeding [70].

4.2.3. Levels of Serum Albumin: In comparison to the control, mean values of total serum albumin were significantly decreased in both patient groups ($p<0.05$). Results are shown in Table (4) and Figure (8).

Table (4): Values of Albumin Between Groups

Characteristic	Albumin g /L	Control group (n=28)	Comparison of Significant
Cardiovascular patient n=28	35.49 ± 1.47	44.18 ± 2.20	**p value** <0.01

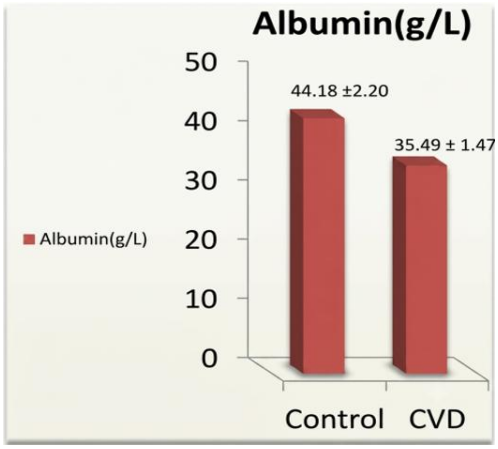

Figure (8): Values for Albumin [g/L] in Patients and Control Groups

The data from the present study showed that albumin levels were significantly lower ($p<0.01$) in patients with a diagnosis of CVD, which is supported by Liu et al. 's findings in CVD [71, 72]. Your antioxidant could be the reason that you will see low albumin levels in this patient. Atherosclerosis is described as an immunizing and inflammatory disease. Inflammation is a well-established risk factor for prothrombotic disorders and atrial fibrillation. While during the inflammatory phase various molecules also respond differently (albumin falls while some of the other inflammatory globulins increase) [73]. As the Figure (9) shows, there was correlation between albumin and MDA negatively.

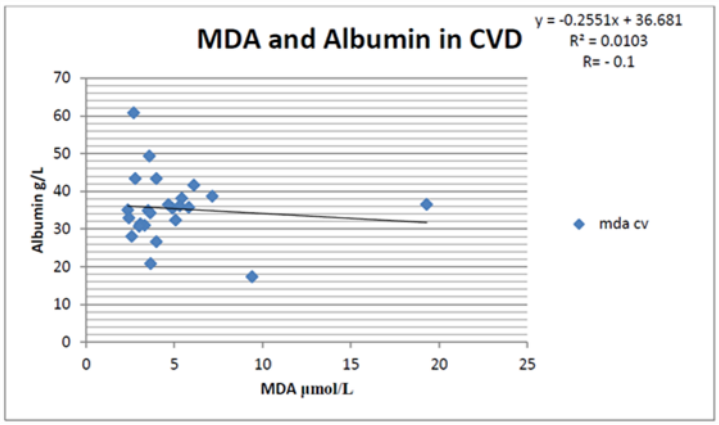

Figure (9): Correlation Between Albumin and MDA in CVD patients

4.2.4. Levels of serum uric acid:

As illustrated in Table (5); it shows that the mean serum uric acid levels in patients were significantly higher ($p<0.05$) comparing to those of the healthy group.

Table (5): Values of Uric Acid Between Groups (mean ± SD):

Group	Uric acid mg/dL	Control group n=28	Comparison of Significant p value
Cardiovascular patient n=28	4.89 ± 0.30	3.81 ± 0.22	0.04

Other studies (Li Qin et al., Cerezo C. et al., Takayama S.) [74–76] reported a high level of uric acid in the serum with patients had CVD. This is in keeping with the current study, where the disease states may have exceeded uric acid's antioxidant potential.

The crystallisation of uric acid, previously viewed as a benign end-product excreted via the kidney resulting in renal stones and gouty arthritis. Later, however, uric acid was isolated as a strong antioxidant that chelates transition metals and scavenges singlet oxygen, oxygen radicals and peroxynitrite inhibiting e.g. the oxidation of ascorbic acid mediated by iron ions. Many studies have substantiated a strong association between serum uric acid and coronary heart disease (CHD) [74-76].

Collectively, these antioxidant actions form the basis for the cardiovascular protective activities of uric acid. Some studies have postulated that uric acid also independently relates to cardiovascular disease [77]. Currently available evidence suggests that uric acid may have complex chemical and biological effects with pro-oxidant or NO-chelating properties, which might provide a mechanistic link between uric acid and cardiovascular disease and the metabolic syndrome [78].

Table (6): Values of Urea in Studying Groups (mean±SD):

Group	Urea	Control group n=28	Comparison of Significant p value
Cardiovascular patient n=28	5.57 ± 1.76	4.27 ± 1.90	0.04*

4.2.4. Levels of serum urea:Table (6) indicates that the mean serum urea levels were substantially ($p<0.05$) higher in the patient groups than in the control group. When comparing the patient groups to the control group, the current investigation revealed a high level of urea. This finding agreed with Jasim N. [61], in CVD and disagreed with Pragna Patel et al. [79, 80].

4.2.5. Level of Serum Creatinine:

Table (7) displays the average serum creatinine levels of the patient groups in comparison to the control group.

Table (7): Values of Creatinine in Studying Groups (mean±SD):

Group	Creatinine mg/L	Control group n=28	Comparison of Significant p value
Cardiovascular patient n=28	0.953 ± 0.16	0.701 ± 0.1	0.06

Creatinine levels in the patient groups were not significant when compared to the control group. Urea is the main excretory byproduct of protein metabolism. A higher urea has been shown to be a robust predictor of morbidity and mortality in sizeable cohorts of patients with acute and chronic heart disease [78]. When the body breaks down proteins, amino groups (–NH2) and free ammonia are left over, which combine in the liver to form urea.

Heart failure and hypertension reduce blood flow to the kidneys, thus decreasing urea filtration because less blood is carried to them. Decreased renal blood flow decreases glumular filtration, which reduces distal tubular flow rate to increase urea reabsorption and secretion. This may be responsible for the increased concentration of urea in serum. [81].

Similarly, the levels of creatinine, which is a byproduct of muscle creatine, were not significantly different between patients and controls. Spontaneous, nonenzymatic loss of water results in the conversion of 1% or so (approximately 300 3 mol per day) of the total muscle creatine pool to creatinine every day. Because its excretion is closely related to the glomerular filtration rate and it enters the circulation at a constant rate, [80].

5. Conclusion

1. The primary chemical manifestation of cardiovascular illnesses in the patients of underlying research is oxidative stress in its markers and parameters. The significant

differences between serum albumin, 8-OHdG, and malondialdehyde in individuals with cardiovascular disorders made this result clear. Urea, creatinin, and uric acid are used to produce these outcomes.

2. The correlation between lipid profile items and malondialdehyde leads to the conclusion that elevated blood lipid levels are extremely dangerous because of the high likelihood of their oxidation, which exacerbates the diseases under investigation. Additionally, the correlation between malondialdehyde and 8-OHdG indicates that oxidative species have a profound impact on cells from the membrane to the nucleus.

6. References

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