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Evaluation of some Biomarkers Adiponectin, Troponin, and C-reactive protein (CRP) for Atherosclerosis Obese and non-obese patients and related with oxidation, antioxidation parameters in Kerbala Governorate

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Abstract

Background: *The most widespread pathological condition of peripherals, coronary artery disorders, and of cerebellar problems, is atherosclerosis (AS). Obesity is the most common nutritional disorder worldwide and is one of the major risk factors for atherosclerotic cardiovascular diseases. Adiponectin is a "adipokine" that is mostly formed by adipose tissue. Adiponectin levels are low and have limited capacity to control inflammatory reactions in obese individuals. Troponin releases into the circulation when myocytes are injured. Oxidative stress (OS) refers to a series of actions that frequently initiates and follows molecular/cellular pathogenic events that cause a number of human illnesses, such as atherosclerosis. Malondialdehyde (MDA) plasma levels indicate the degree of lipid peroxidation, additionally the severity of OS. Antioxidant is a molecule that is capable of "neutralizing" the oxidation of reactive oxidant species (ROS) before they react with cellular biomolecules and change their structure function.* ***Methods****: A case-control study was used in the design of the study. 100 male participants, comprising 60 atherosclerosis individuals, 30 obese patients, 30 normal weight patients, and 40 healthy people, 20 of whom were obese and 20 of whom were of normal weight. Age between (40-65).* ***Results****: The result demonstrated a very high significant decrease in the concentration of adiponectin ($p \leq 0.001$) in both atherosclerosis obese and normal patients groups as compared to control normal groups. Also showed a highly significant increase ($p \leq 0.001$) in the concentration of Troponin I in atherosclerosis obese, normal patients' groups as compared to control obese and normal groups. Additionally found a highly significant increase ($p \leq 0.001$) in the concentration of C-reactive protein in all study groups (atherosclerosis obese, atherosclerosis normal, and control obese) as compared to control normal. Also found a highly significant increase ($p \leq 0.001$) in the concentration of (MDA) in all study groups as compared to the normal control, the highest increase was in the atherosclerosis obese patient group. TAOC showed a highly significant decrease ($p \leq 0.001$) in all study groups, the highest decrease found in athero obese and control obese as compared to control normal.* ***Conclusion****: Adiponectin plays a role in the development of atherosclerosis in obese individuals. A person with an increased body mass index is more susceptible to development of atherosclerosis. The end result of lipid peroxidation, increased MDA concentration, indicates that the rate of oxidative stress is high. Decrease in concentration of TAOC in all obese groupings, which means increased body mass index leads to decreased antioxidant.*

Keywords: *Atherosclerosis, Obesity, Adiponectin. Malondialdehyde. Oxidative stress.*

1. Introduction

Atherosclerosis

German physician Félix Marchand first used the term "atherosclerosis" (AS) in 1904; it is derived from the Greek words "athere" and "sclerosis," which indicate gruel and hard, respectively, is the primary contributor to diseases of the coronary arteries, the brain, and the peripheral blood vessels (1). Cholesterol deposition and chronic inflammation are two crucial factors in the pathogenesis of AS, AS includes three main stages, including the generation of fatty streaks, the induction of atheroma, and atherosclerotic plaques (2). This condition begins when oxidized low-density lipoproteins (Ox-LDLs) build up in the artery intima (3). This resulted in the production of proinflammatory oxidized lipids by the overlapping endothelial cells (ECs) (4). Within the intima of the artery, monocytes develop into proinflammatory the macrophages locally enhance the inflammatory reaction, eventually, macrophages ingest lipoproteins to produce foam cells rich in lipids, which cause early atherosclerosis lesions to appear (5).

Obesity

Obesity is a significant worldwide health problem linked to higher morbidity and mortality rates (6). According to the WHO, obesity is defined as “abnormal excessive fat accumulation that presents risk to health” (7). The buildup of too much body fat results in a variety of metabolic disorders and diseases, such as resistance to insulin and atherogenic dyslipidemia (8). Obesity poses a serious threat to public health since it adversely affects almost all bodily physiological processes and raises the chance of acquiring a number of disease conditions, including DM and CVD (9). By causing arterial inflammation and oxidative stress, proinflammatory adipocytokines and free fatty acids generated by malfunctioning fatty tissue can systematically accelerate atherosclerosis (10).

Adiponectin

Adiponectin is a type of adipokines released by adipose tissue, which is a tissue that is found throughout the body and is considered an important endocrine system (organ), adipokines are essential for the control of immunological and energy responses (11). Adiponectin is a factor exclusive to adipocytes that was originally identified in 1995 (12). Adiponectin has a molecular weight of 28 kDa and 244 amino acids, and is involved in a number of physiological processes, such as lipid metabolism, energy control, immunological response, and inflammation (13). Multiple names for adiponectin include (Acrp30, AdipoQ), it exerts its physiologic effects through three widely dispersed receptors called AdipoR1, AdipoR2, and T-cadherin (14). Adiponectin's physiological actions are triggered by related receptors in conditions like obesity, diabetes, inflammation, asthma, and CVD (15). Adiponectin is a multimeric protein that can occur as trimmers (lower molecular weight, LMW), hexamers (middle molecular weight, MMW), and high molecular weight (HMW) multimers (16). HMW adiponectin may be particularly significant since it possesses insulin-sensitizing and vasoprotective effects via its interactions with AdipoR1 and AdipoR2 receptors (17). Adiponectin is inversely connected with fat mass, makes up to 0.05% of the total proteins in the plasma, and is low in obese individuals (18). Decreased adiponectin levels have been linked to metabolic syndrome, cardiovascular disease (CVD), and hypertension; it has a wide range of biological effects, including anti-diabetic, anti-atherogenic, anti-inflammatory properties (19). In skeletal muscle, adiponectin deficiency promotes fatty acid oxidation (20). In contrast to several other "adipokines" that rise with obesity, such as tumor necrosis factor (TNF), leptin, and resistin (21). It has been demonstrated that adiponectin levels are inversely correlated with carotid artery intima-media thickness (IMT), a marker of early atherosclerosis (22). Additionally, adiponectin changes the pro- inflammatory M1 macrophage phenotype to the anti-inflammatory M2 (23).

Troponin

Troponin is a protein, which is a member of the contractile apparatus in skeletal and cardiac muscle, controls and promotes the connection between actin and myosin filaments, as part of the sliding filament process of muscle contraction (24). Troponin releases into the circulation when myocytes are injured

(25. Troponin T (TnT), Troponin I (TnI), and Troponin C (TnC) are the three troponin isoforms (subunits) that make up the troponin complex, which is the most significant regulation of the contraction/relaxation of striated muscle tissues (26). The processes of cTnI and cTnT leakage in the early stages of many pathological illnesses may be linked to a rise in the permeability of cell membranes and/or intracellular fragmentation of cTnI and cTnT molecules into smaller pieces that may easily flow through intact cell membrane (27). After strenuous activity, cardiac troponin is connected to measures of plaque susceptibility or coronary atherosclerosis (28). Although cTnT and cTnI are expressed in heart tissue in approximately equal amounts in patients with myocardial necrosis, such as in acute myocardial infarction (MI), cTnI frequently reaches peak levels ten times higher than cTnT (29).

C-Reactive protein

is a type of protein, mainly produced by liver organs, it can be elevated in plasma patients with acute inflammation (30). Structurally, CRP is a 206 amino acid cyclic pentameric protein with five identical subunits that are not covalently bonded, excessive body weight that has been associated with elevated CRP levels (31). Since fat cells secrete a variety of inflammatory molecules called adipocytes, including leptin, adiponectin, and others, obese people constantly have high levels of inflammation (10). Because of CRP's capacity to bind to change LDL and its effect on the functionality of ECs, the stability of plaque, and thrombosis, CRP is believed to have a part in atherogenesis (32). Subclinical atherosclerosis, intima media thickness (IMT), the presence of plaque, and total plaque area are all associated with CRP (33).

Malondialdehyde

Malondialdehyde (MDA), a small, reactive chemical complex containing 2 groups of aldehyde at the carbon 3 and carbong1 positions, is present in all eukaryotes (34). MDA, a particular aldehyde that has been used as a biomarker of OS, is believed to be a common result of lipid peroxidation (35). MDA is a toxic aldehyde that can covalently bond to other biomolecules including DNA, lipids, or proteins and is frequently employed as an indicator of stress caused by oxidation in biological materials (36). MDA is a constant end product of a chain event known as peroxidation of lipids, which produces a constant supply of radicals called free radicals that start more peroxidation (37).

Total Antioxidant Capacity

An antioxidant is a substance that may prevent oxidation of a substrate while operating at lower levels than the substrate being protected (38). Enzymes neutralize free radicals, proteins like transferrin may bind to metals that promote their formation, vitamins E and serve as free radical scavengers, and vitamin C, which is a water-soluble molecule, usually scavenges hydroxyl radicals, vitamin E, lipid soluble vitamin, breaks down the chain reactions of lipid peroxidation (39). Important physiological processes involving glutathione have consequences that are relevant to a variety of diseases and pathologies, including the preservation of redox balance, decreased oxidative stress, improvement metabolism detoxification, and control of the immune system's activity (40). It is recognized as the most important antioxidant for protecting the cell membrane from oxidative damage brought on by free radicals (41).

An antioxidant is a molecule that is capable of “neutralizing” the oxidation of ROS before they react with cellular biomolecules and change their structure or function (42).

2. Materials And Methods

Study designs

A case-control study was used in the design of the current investigation. 100 participants, comprising 60 atherosclerosis individuals, 30 obese patients, 30 normal weight patients, and 40 healthy people, 20 of whom were obese and 20 of whom were of normal weight. In Karbala, Iraq, the work was finished during November 2022 and May 2023. Aging between (40-65)

Collection Data

The study's participants were all affected by the condition atherosclerosis. Their BMI was calculated based on their height and weight. To determine Adiponectin or MDA or T-AOC using a specific ELISA

kit and add a sample to the well of the ELISA plate, Measurement of CRP and Troponin by Abbott C40000.

3. Results and Discussion

Table (1): the concentration of Adiponectin in atherosclerosis obese-non obese patients compared with obese-non obese control

Groups	N	Adiponectin (mg/dl)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Athero Obese	30	*0.8204 c*	0.13375	0.02442	.7704	0.8703
Athero Normal	30	1.4266 b	0.19148	0.03496	1.3551	1.4981
Control Obese	20	0.8740 c	0.30127	0.07779	.7072	1.0408
Control Normal	20	4.0717 a	0.68467	0.17678	3.6925	4.4508

P value = 0.001* LSD= 0.384 *different letters means significant differences

The result of table (1) demonstrated very high significant decrease in the concentration of adiponectin ($p \leq 0.001$) in both atherosclerosis obese and normal patients groups (0.8204± 0.02442), (1.4266±0.03496) respectively as compared to control normal groups (4.0717± 0.17678), also found significant decrease ($p \leq 0.001$) between control obese (0.8740 ± 0.07779) and control normal groups. This disease may be related to many reasons such as elevated levels of detrimental adipokines secreted in states of increased adiposity, such as TNF, which inhibit adiponectin secretion, leading to reduced plasma levels.(43). The manner by which adipose tissue expands (increases in size, hypertrophy, and/or in number of cells, hyperplasia) could regulate synthesis and secretion of adiponectin. Drolet et al. demonstrated an inverse relationship between mean adipocyte diameter and adiponectin secretion. AdipoR1 and AdipoR2 expression is significantly decreased in T2DM and obesity state.(44). The results in the table (4-3) have been addressed and supported by other studies, it is well established that levels of the hormone adiponectin decrease as BMI rises, and that obese people have a lower level of this hormone than lean people (45). In obese people, the ability of adiponectin levels to regulate inflammatory responses is limited (46). Decreasing serum levels of adiponectin are linked to metabolic conditions with chronic inflammation, such as Type 2 diabetes, obesity, and atherosclerosis (47). In obese people, hypoadiponectinemia can possibly lead to endothelial dysfunction and a proatherogenic effect (48). Adiponectin levels have been shown to be related to intima-media thickness (IMT), a measure of early AS (49). Additionally, research showed that adiponectin overexpression reduces the development of atherosclerotic plaque (50). This corresponds to the result in the table (4-3), a control who is non obese has a high concentration of adiponectin. By preventing macrophages from transforming into foam cells and monocytes from adhering to endothelial cells, adiponectin has antiatherogenic actions (51). It additionally inhibits smooth muscle cell proliferation, increases nitrogen oxide synthesis, and promotes blood vessel development (52).

Table (2): the concentration of Troponin I in atherosclerosis obese-non obese patients compared with obese-non obese control

Groups	N	Troponin I (ng/dl)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Athero Obese	30	*6901.8100 b*	14978.23	2734.6397	1308.8437	12494.7763
Athero Normal	30	16916.490 a	22778.66	4158.7957	8410.7977	25422.1823
Control Obese	20	6.0400 c	1.61679	0.41745	5.1447	6.9353

Control Normal	20	0.7400 c	0.48226	0.12452	0.4729	1.0071

P value = 0.001* LSD= 7031.647 *different letters means significant differences

The present data showed highly significant increase ($p \leq 0.001$) in the concentration of Troponin I in atherosclerosis obese , normal patients groups (6901.8100 ±2734.6397), (16916.490±4158.7957) respectively as compared to control obese and normal groups table (2). This increase may be caused by Troponin release into the circulation when myocytes are injured (25). The results agree with other studies. Another investigation demonstrated a direct correlation between elevated troponin levels and the severity of coronary stenosis (53). There is a correlation between low levels of high-sensitivity cardiac troponin (hs-cTn) and a low risk of atherosclerotic cardiovascular disease (54). It is well established that body mass index (BMI) and troponins are independently associated (55).Heart troponin release with exercise is connected to coronary atherosclerosis or indications of plaque susceptibility (28). Because one of the primary risk factors for developing cardiac angina is coronary atherosclerosis, this condition may induce discomfort or retrosternal pain (56).

Table (3): the concentration of C-reactive protein (CRP) in atherosclerosis obese-non obese patients compared with obese-non obese control

Groups	N	CRP (mg/dl)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Athero Obese	30	*23.1833 a*	52.86916	9.65254	3.4417	42.9250
Athero Normal	30	13.8333 ab	25.99900	4.74675	4.1251	23.5415
Control Obese	20	8.2600 ab	3.02154	.78016	6.5867	9.9333
Control Normal	20	1.3600 b	.86504	.22335	.8810	1.8390

P value = 0.004* LSD= 19.784 *different letters means significant differences

In table (3) result found highly significant increase ($p \leq 0.001$) in the concentration of C-reactive protein in all study group (atherosclerosis obese, atherosclerosis normal, and control obese) (23.1833 ± 9.65254), (13.8333 ± 4.74675),(8.2600±0.78016) respectively as compared to control normal (1.3600±0 .22335). This increase related to fat cells secrete a variety of inflammatory molecules called adipocytes, including adiponectin, and others, obese people constantly have high levels of inflammation. Because of the capacity of CRP to bind to change LDL and its effect on the functionality of ECs, the stability of plaque, and thrombosis, CRP is believed to have a part in atherogenesis (57). The result agrees with other studies, obesity is the main factor that contributes to high CRP in people with the metabolic syndrome (58). Obesity is related to elevated CRP levels (59). Excessive body weight has been associated with elevated CRP levels (60).

Table (4): the concentration of Malondialdehyde (MDA) in atherosclerosis obese-non obese patients compared with obese-non obese control

Groups	N	MDA (Mmol/l)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Athero Obese	30	*21.5940 a*	7.61587	21.5940	18.7502	24.4378
Athero Normal	30	16.7450 b	5.48130	1.00074	14.6982	18.7918
Control Obese	20	12.9060 c	2.32618	.60062	11.6178	14.1942
Control Normal	20	4.6367 d	2.64245	.68228	3.1733	6.1000

P value = 0.001* LSD= 3.251 *different letters means significant differences

Based on the results in the table (4) found highly significant increase ($p \leq 0.001$) in the concentration of (MDA) in all study groups as compared to the normal control, the highest increase was in the atherosclerosis obese patient group (21.594 ±1.390). This increase may be related to endothelial cells deposit cholesterol-rich low density lipoprotein (LDL) in the membrane's inner layer of the vascular wall, where it is oxidized and transformed into oxidized LDL under conditions of elevated oxidative stress (61). the initial phase of atherosclerosis is demonstrated by the oxidation of lipids in the form of Ox-LDL, while MDA, a marker of elevated oxidative stress that indicates the level of lipid peroxidation (62). The result was supported by other studies. MDA levels in obese individuals were significantly higher than those in normal (63). The level of lipid peroxidation and the severity of OS are both reflected in MDA plasma levels (64). MDA is one of the significant end products of lipid peroxidation, which is one of the most often used biomarkers to measure oxidant status since it is connected to the severity of lipid peroxidation (65). The lipid hypothesis regarding atherosclerosis suggests that peroxidation of lipids and the oxidation of LDL cause the onset and persistent progression of atherosclerosis (66).

Table (5): the concentration of TAOC in atherosclerosis obese-non obese patients compared with obese-non obese control

Groups	N	TAOC (mmol/l)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Athero Obese	30	*2.8874 c*	.52922	.09662	2.6898	3.0850
Athero Normal	30	3.9696 b	.87166	.15914	3.6442	4.2951
Control Obese	20	2.7647 c	.55250	.14266	2.4587	3.0706
Control Normal	20	6.7857 a	.71502	.18462	6.3897	7.1816

P value = 0.001* LSD= 0.908 *different letters means significant differences

In table (5) Total antioxidant capacity (TAOC) showed highly significant decrease ($p \leq 0.001$) in all study groups, the highest decrease found in athero obese and control obese (2.8874

±0.9662), (2.7642 ± .14266) respectively as compared to control normal (6.7857 ± .18462). This decrease may be related to many reason such as the level of expression and action of antioxidant enzymes decreased in the adipose tissue of obese people, although the fact that adipose tissue has compared high levels of antioxidant defense enzymes for controlling high ROS generation (67). The main center of ROS production, particularly in obese individuals, is in the mitochondria of white adipose tissue, where NDPH (nicotinamide adenine dinucleotide phosphate) oxidase is overexpressed and antioxidative enzyme expression is diminished (68). The result supported by another study, one of the causes of obesity-related diseases such atherosclerosis, hypertension, and obesity is oxidative damage to essential cellular components (69).

Study limition

The participants chosen may not have been autoimmune disease (systemic lupus erythematosus,rheumatoid arthritic, et al), DM , liver diseases, Kidney Diseases.

4. Conclusion

Adiponectin plays a role in the development of atherosclerosis in obese individuals. Increased concentration of adiponectin protects individuals from atherosclerosis, because it has an antiatherogenic effect. A person with an increased body mass index is more susceptible to development of atherosclerosis. The end result of lipid peroxidation, increased MDA concentration, indicates that the rate of oxidative stress is high. Decrease in concentration of T-AOC in all obese groupings, which means increased body mass index leads to decreased antioxidant.

Recommendations

Study the relationship of the study biomarkers in their occurrence of atherosclerosis in obese and non obese females. Comparison of Study biomarkers between male and female atherosclerosis patients. Comparison of study biomarkers with diabetic atherosclerosis and non diabetic atherosclerosis.

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