BioBacta

Journal of Bioscience and Applied Research
https://jbaar.journals.ekb.eg/

SPBH

The Effects of Age and Sex on Amylin, Preptin Hormones and Some Biochemical Parameters in Cardiovascular Disease with Type 2 Diabetic

Redaa Jaafar Abdul Hussein, Alyaa Majid *

Department of Chemistry, College of Science, University of Thi-Qar, Thi-Qar, 64001, Iraq

*Corresponding author: e-mail: aliaa.s_mschem@sci.utq.edu.iq

DOI: 10.21608/jbaar.2024.297722.1051

Abstract

Risk factors for cardiovascular disease (CVD) include hyperglycemia, high blood pressure, a high body mass index (BMI), and hypercholesterolemia. The two sexes have an increased risk of CHD with age, but the rise has been found greater in women. The research aimed to assess the effects of sex and age on parameters of amylin, preptin, SOD, MDA, fasting blood glucose (FBG), and CAT in CVD patients without and with type 2 diabetes (T2D) in comparison to healthy individuals.

There were 150 participants in the study: 50 normal volunteers, or control subjects who were thought to be healthy, and 100 patients with cardiovascular disease, of which 50 had type 2 diabetes and the remaining 50 did not. Participants in the study varied in age from 40 to 70 years old and had type 2 diabetes and CVD but were not obese. The study's findings demonstrated a substantial relationship between sex and the concentrations of CAT, preptin, amylin, MDA, and SOD. Age affects the parameters that are evaluated in patients with cardiovascular disease, including those with and those without type 2 diabetes. The primary cardiovascular risk factors have accounted for a considerable fraction of sex difference in CHD risk. Higher levels of risk factors were associated with an age-related increase in the incidence of CHD and death in the two genders, yet in women more so.

Keywords: Amylin, preptin, oxidant-antioxidants status, cardiovascular disease, Type 2 diabetic

---

Introduction

People with Type 2 Diabetes Mellitus (T2DM) have a higher risk of developing coronary artery disease (CAD), which has also been known as DM-CAD, which raises mortality and morbidity rates. Its complex etiology is caused by many factors, including genetic susceptibility, endogenous factors, and diverse environmental influences such as a high-fat diet, a sedentary lifestyle, and ongoing stress [1]. Inadequate glycemic control in type 2 diabetes will impact heart pathophysiology even in the absence of CAD and hypertension. An increase in body fat is believed to affect how tissues react to insulin, leading to insulin resistance and a decline in the balance between fat and glucose. Prolonged elevation in blood sugar levels can result in severe consequences such as impaired vision, renal failure, and nerve damage. These can cause abnormalities in the functioning of the urinary, cardiovascular, and gastrointestinal systems [2]. Since myocardial infarction (MI) represents a common CVD indicator, the World Health Organization (WHO) recommended utilizing MI rates as a proxy for CVD rates in epidemiological research [3,4].

MI represents a clinical condition defined as acute myocardial necrosis resulting from an imbalance

Received: June 15, 2024. Accepted: August 26, 2024. Published: September 1, 2024

between myocardial demand and coronary blood supply, according to Azmi and Kesarwani (2014) [5]. MI, which leads to tissue death, is brought on by the sudden blockage of at least one coronary artery which supplies the heart muscle with oxygen-rich blood [6, 7]. An increase in heart mass in reaction to an external stimulus is known as cardiac hypertrophy, which is a broad term for a higher workload. [8]. Congestive heart failure (HF), the last stage of most cardiac disorders, is defined as a progressive illness [9], a result of the prolongation of such a process. MI is characterized by ventricular dilatation, decreased systolic and diastolic function, and in the end congestive heart failure (HF) [10]. Patients who have acute MI might present with a broad spectrum of nonspecific symptoms. Even though they are not frequently used in diagnostics, being aware of their presence concerning infarction is crucial to avoiding incorrect interpretation or diagnosis of other disorders [11, 12]. Smoking, advanced age, high blood pressure, using amphetamines and cocaine, elevated levels of some lipids (TG and LDL cholesterol) and low HDL cholesterol levels, high blood pressure, diabetes, chronic renal illness, obesity, and excessive alcohol consumption are all associated with an early onset of CVD [13, 14]. Hyperamylinemia (also known as hyperinsulinemia) represents one of the common conditions in patients with insulin resistance (IR) and obesity that results in amyloid accumulation. Amyloidosis is frequently observed as a pancreatic disorder in patients with T2D. However, excessive blood amylin levels could result in the accumulation of amylin and proteotoxicity in the heart as well as other peripheral organs [15]. Numerous intricate and little-understood mechanisms contribute to the mortality of smokers and the development of CVDs. It was shown that endothelial dysfunction is a crucial early event in development of the majority of CVDs. One pathological indicator of cigarette smokers is impaired endothelial function [16]. In patients getting catheter-assisted cardiovascular treatment, increased preptin levels might be a good predictor of better etiology. Elevated preptin levels could contribute significantly to the progression of cardiovascular disorders. They have been related to atherosclerosis, which has been considered to be one of the main CVD causes [17]. According to recent research, oxidative stress plays a significant part in the onset, course, and consequences of diabetes, including macrovascular and microvascular problems [18, 19, 20]. There is a concomitant rise in free radical generation with the pathogenic alteration of the body under oxidative stress. Oxidative stress causes several factors to interact with biological processes, which is why low emotional states are associated with environmental adversity [21]. Antioxidants, the body's defense mechanism, combat free radicals. Each antioxidant, including ROS (Reactive Oxygen Species) degradation enzymes [22, 24], lessens the effects of free radicals in a distinct way [22, 23, 19]. One element of the antioxidant defense system against mitochondrial superoxide radicals is superoxide dismutase 2 (SOD2). Hydrogen peroxide can be neutralized through various enzymes. Those enzymes include NADH oxidase, glutathione peroxidase, catalase, and other peroxidases such as cytochrome c [25]. One of the vital enzymes, which is referred to as the catalase uses hydrogen peroxide, which is a non-radical ROS, as substrate. This enzyme is responsible for degrading hydrogen peroxide to neutralize it and keeping the molecule at the right concentration within the cell, which is necessary for processes related to cellular signaling. Enzyme's participation in several infections and diseases, both indirectly and directly, serves as evidence of its relevance [26]. This study compared patients with acute myocardial infarction who had T2D to those who did not, looking at the effects of age and gender on levels of oxidants and antioxidants, amylin hormone, preptin hormone, and FBG.

Materials and Methods

Design of Study

The presented work was carried out from October 2022 to April 2023 at the AL-Nasiriyah Heart Center, ALAzher Privet Hospital, the College of Science's Biochemistry Laboratory, and specialized clinical settings. It included (150) subjects, which have been classified into controls (50) and patients (100). The investigation was carried out on the entire population of presumably healthy people and patients, who were split into:

Control group*:* Fifty (50) ostensibly healthy participants, 25 of whom were male and 25 of whom were female, with ages that range from 40 to 70, made up the control group.

DM/AMI group*:* included fifty (50) patients with T2DM and Acute myocardial infarction [22 females and 28 males] with age range (40—70) years.

AMI group*:* included fifty (50) patients with Acute myocardial (40-70) years [27 males and 23 females] without any history of systematic illness at (40−70) years of age range.

Inclusion

Participants in the study varied in age from 40 to 70 years old and had type 2 diabetes and cardiovascular disease but were not obese. Similar pharmacological guidelines were in place, but insulin injections were not.

Excluding Criteria

The study excluded patients with neuropathy, retinopathy, thyroid problems, and liver disorders

Table 1: Data of the studied groups

Groups		**Sex (M/F)**	**Age (40-70years)**			**BMI (Kg/m^2)**		
			G1 40-50 years	**G2 51-60 years**	**G3 61-70 years**	**Normal (18.5-24.99)**	**Overweight (25-29.99)**	**Obesity (BMI ≥ 30)**
Controls (50)		(25/25)	18	17	15	30	20	……..
Patients (100)	**AMI with T2DM**	(28/22)	33	37	30	54	46	……..
	AMI without T2DM	(27/23)						

Collection of Blood Samples

Unless they were used right away, serum samples were separated and kept at a temperature of -20^{o}C for the ensuing measurement of biochemical markers. Five milliliters (mL) of blood were extracted from patients suffering from AMI, T2D MI patients, and controls. The samples were left to clot at room temperature in disposable, empty tubes before being centrifuged at 3000xg for ten minutes to separate the components. Serum amylin, SOD, preptin, and CAT were measured with the use of ELISA technology through a spectrophotometer,

serum malonaldehyde (MDA) was assessed utilizing the thiobarbituric acid method, and serum blood glucose was measured with the use of a Biolabo (France) kit, according to Fong et al. [27].

Statistical Analysis

The results of the statistical analyses have been represented in the form of (mean ±SD) with LSD with the use of SPSS version 15.0. The one-way ANOVA test has been utilized for examining the variables between the various research groups. A P-value has been deemed statistically significant if it was (P≤0.050).

Results and Discussion

Comparison for all studied Parameters based on Age

Fasting Blood Glucose Concentration

In study group C and group B, there has been a significant difference (p≤0.050) in blood FBG concentration between age groups G2, G1, and G3. Nonetheless, it was shown that there has been a significant (p≤0.05) difference in serum FBG concentration across age groups (G2 & G1). In study group A, there has not been any significant variation in serum FBG concentrations across any of the age groups (G2, G1, and G3) (p≤0.05). In age groups G2, G1, and G3, there has been a significant difference (p≤0.05) in blood FBG concentrations between study groups B, A, and C (Sivakami and George, [28] indicates that glucose is vital to the aging process and age-related disorders since the signs of hyperglycemia and natural aging, including cataracts, are identical. It seems that more complex glycosylation end products will emerge as a result of the subsequent hyperglycemia. Permanent physiological changes brought on by aging have been related to increased risks of disease [29]. Age-related declines in insulin sensitivity and changes in or insufficient beta cell activity compensation in response to increased insulin resistance are the main contributing factors [30, 31]. A decline in beta cell proliferative potential and an apoptotic sensitivity increase are factors associated with aging [31].

Table 2: Serum FBG levels for all age groups.

FBG leves (mg/ml) Mean ±SD				
Age groups	**A**	**B**	**C**	**LSD**
G1	89.17±13.10 a, C	189.33±19.56 b, A	102.00±11.16 b, B	8.41
G2	96.06±13.08 a, C	188.39±24.66 b, A	100.00±11.29 b, B	9.72
G3	93.39±12.84 a, C	216.06±27.29 a, A	112.22±16.66 a, B	11.11
LSD	7.26	13.44	7.42	

Note: Every value displays the mean ± standard deviation. Non-identical superscripts (a, b, or c, for example) have been considered statistically different (P < 0.05) when being compared horizontally, and significantly different (P ≤ 0.05) compared vertically.

G1: First age group range from (41-50 years).

G2: The second age group ranges from (51-60 years).

G3: The third age group ranges from (61-70 years).

A: represents the Control Group.

B: represents the acute myocardial infarction with T2D patients' group.

C: represents the acute myocardial infarction without T2D patients' group.

Serum Amylin and Preptin Concentrations

Table 3 shows that there has been a significant difference in serum amylin concentrations across all age groups (G1, G2, and G3) in study groups A, B, and C ($p \leq 0.050$).

Between research groups B, A and C and age groups G2, G1, and G3, there was a significant variation in blood amylin levels ($p \leq 0.05$). There has been a significant difference ($p \leq 0.05$) in the blood amylin levels between research groups B, A, and C in age groups G2, G1, and G3. In study groups B, A, and C, there has been a significant difference ($p \leq 0.05$) in serum preptin concentration across all age groups (G2, G1, and G3) in Table 3. In the age groups G2, G1, and G3, there has been a significant ($p \leq 0.05$) difference in serum Preptin concentration between study groups B, A, and C. However, there has not been any discernible difference in serum Preptin levels between study groups A and C ($p \leq 0.05$). In the presented study, we found that serum amylin was elevated in the G3 age group. Amyloid aggregation results in the eventual formation of amyloid deposits. It was proposed that such deposits constitute the main β-cell toxicity source, which leads to β-cell mortality and, subsequently in T2D, a decrease in insulin production and amylin levels [32].

Table 3: Serum Amylin and Preptin levels for all age groups.

Amylin levels (pg/ml) Mean ±SD				
Age groups	**A**	**B**	**C**	**LSD**
G1	8.80±2.60 c, B	44.18±8.02 c, A	8.49±2.91 c, B	4.45
G2	10.06±0.98 b, B	48.23±0.98 b, A	9.85±2.54 b, B	2.79
G3	11.33±1.98 a, B	53.18±13.24 a, A	12.92±1.88 a, B	1.64
LSD	1.05	3.99	1.25	
Preptin levels (pg/ml) Mean ±SD				
Age groups	**A**	**B**	**C**	**LSD**
G1	9.64±3.29 c,B	46.13±7.89 c, A	9.88±1.17 c,B	4.28
G3	10.59±2.93 b,B	49.93±12.54 b, A	11.52±2.80 b,B	2.74
G3	12.65±0.99 a, B	54.43±0.99 a, A	13.20±1.16 a,B	1.77
LSD	0.92	3.78	0.98	

- Legend as in table 2.

Serum Malondialdehyde (MDA) Concentration

Within study group A, there has been no significant variation in the serum MDA concentrations between age groups (G2, G1, & G3) ($p \leq 0.050$). In study group B, there has been a statistically significant difference in blood MDA levels between age groups G1 and G2 and age group G3 ($p \leq 0.05$). Even though the serum MDA concentrations of age groups G1 and G2 didn't significantly differ ($p \leq 0.05$). In study group C, there has been a statistically significant variation in serum MDA concentrations between age groups (G2, G1, and G3) ($p \leq 0.050$). For age groups G2, G1, and G3, there has been a significant difference ($p \leq 0.05$) in serum MDA concentrations between study groups B, A, and C. Table 4. It is not thought of aging as a disease in and of itself. Free radicals and nonradical reactive oxygen or nitrogen species (ROS/RNS), which are endogenously generated due to the regular metabolism or exogenously as a result of environmental stressors, are responsible for at least some of the cellular stress that is induced. Those organisms harm biological macromolecules like DNA, lipids, and proteins through their interactions with them. Since our bodies' capacity to respond to stress is reduced as we age, oxidized or altered macro-molecules accumulate and, in the case of lipids and proteins, agglomerate [33]. Diabetes type 1 and type 2 are related to increased production of free radicals and decreased antioxidant capacity, which may lead to macro- and microvascular complications. Research shows that oxidative stress is higher in older T2D patients, however, persons with IGT have higher levels of antioxidant defense, which could partially counteract this [34].

Table 4: Serum MDA levels for all age groups.

MDA levels (µmol/L) Mean ±SD				
Age groups	**A**	**B**	**C**	**LSD**
G1	2.06±0.38 a, C	7.03±1.46 b, A	6.27±1.35 c, B	0.68
G2	2.19±0.26 a, C	7.55±1.87 b, A	7.11±0.30 b, B	0.77
G3	2.30±0.63 a, C	9.20±2.98 a, A	7.98±.49 a, B	1.05
LSD	0.25	1.23	0.77	

- Legend as in Table 2

Serum Superoxide Dismutase (SOD) and Catalase (CAT) Concentrations.

Within study group A, there has been no significant variation in the serum SOD concentrations between age groups (G2, G1, and G3). In study groups B and C, there has been a significant difference ($p \leq 0.050$) in the blood SOD levels between G1 and G2 and G3 age groups. Even though the levels of serum SOD did not significantly change between age groups G2 and G3. In the age groups G2, G1, and G3, there has been a significant ($p \leq 0.050$) difference in blood SOD concentrations between study groups A, B, and C. Table 5. In study group A, there has not been any significant variation in the serum CAT concentrations between age groups (G2, G1, and G3). In study groups B and C, there has been a significant difference ($p \leq 0.050$) in serum CAT levels between the G1, G2, and G3 age groups. Despite this, there has been a significant difference ($p \leq 0.050$) in serum CAT levels between G3 and G2 age groups. In the age groups G1, G2, and G3, there has been a significant ($p \leq 0.050$) difference in serum CAT concentrations between study groups A, B, and C. Several studies have shown that the heart's resistance to oxidative stress decreases with age because antioxidant enzyme levels, including GSH-Px and SOD, decrease. This, in turn, causes alterations in the cardiovascular system. Vascular endothelial dysfunction is also caused by an accumulation of oxidative stress as people age [34]. By serving as oxidant scavengers, antioxidants can protect the biological redox stable states. Since the oxidative stress theory was proposed, antioxidants have consequently been hypothesized to potentially have a preventative effect against aging as well as age-related disorders [35].

Table 5: Serum SOD and CAT levels for all age groups.

SOD levels (ng/ml) Mean ±SD				
Age groups	**A**	**B**	**C**	**LSD**
G1	6.07±1.14 $^{a, A}$	2.49±0.52 $^{a, C}$	3.19±0.72 $^{a, B}$	0.59
G2	5.91±0.96 $^{a, A}$	2.13±0.96 $^{b, C}$	2.87±0.67 $^{b, B}$	0.46
G3	5.75±1.68 $^{a, A}$	2.04±0.38 $^{b, C}$	2.82±0.63 $^{b, B}$	0.75
LSD	0.66	0.21	0.31	
CAT levels (pg/ml) Mean ±SD				
Age groups	**A**	**B**	**C**	**LSD**
G1	55.61±5.62 a, A	32.11±5.67 a, C	42.72±4.41 a, B	3.65
G2	54.19±0.95 a, A	28.98±2.24 b, C	39.03±6.25 b, B	2.68
G3	52.78±7.37 $^{a, A}$	25.05±3.98 b, C	38.33±7.22 b, B	1.87
LSD	2.99	2.04	2.37	

- Legend as in table 2.

Comparison of all studied Parameters According to Sex

Fasting Blood Glucose Concentration

The serum FBG concentrations of the male and female research groups (A, B, & C; p≤0.05) did not significantly differ from one another. Furthermore, the blood FBG concentrations in the male and female sex groups as well as the three study groups (A, B, and C) show significant differences (p≤0.05).

Serum Amylin and Preptin Concentrations

Table 7 demonstrates that the serum amylin levels in the male and female study groups (B and C) differed significantly (p≤0.05). In study group (A), there has not been any significant difference in serum amylin levels between the female and male groups. For female as well as male sex groups, Table 6 shows a statistically significant difference (p≤0.05) in the serum amylin concentrations between Study Group B and Study Groups A and C. The female and male study groups (C and A) did not significantly differ in their serum amylin levels. Table 7 shows that the serum preptin levels in the female and male study groups (C and B) differed significantly (p≤0.05). Nevertheless, in the study group (A), there has not been any appreciable variation in the serum preptin concentrations between female and male groups (p≤0.05). For both the female and male sex groups, there is a significant difference (p≤0.05) in serum concentration of preptin between study groups B, A, and C. The female and male study groups (C and A) did not significantly differ in their serum preptin concentrations, though (p≤0.05). Women reported greater prevalence levels of Amylin and Preptin (10%) compared to men, which is comparable to the 20% higher percentage of women compared to men who have impaired glucose tolerance [36]. Since the molecular explanations that have been proposed have centered on the effects of estrogen, which could decrease after menopause and raise the risk of CHD in women, women have higher quantities of amylin and preptin [37].

Table 6: FBG levels for all sex groups

FBG levels (mg/ml) **Mean ±SD**				
Sex groups	**A**	**B**	**C**	**LSD**
Male	93.72±12.62 c	190.82±27.22 a	100.29±15.60 b	7.68
Female	92.64±14.23 c	198.95±19.85 a	105.60±12.97 b	7.92
P. value	0.297	0.068	0.249	

Note: every value represents mean ± SD values with the non-identical superscript (a, b, or c…etc), which have been considered as significant differences (P≤ 0.05).

-No: Number of subjects.

-LSD: Least Significant Difference.

-SD: Standard deviation.

-A: Control Group.

-B: Acute myocardial infarction with type 2 diabetic patient group.

-C: Acute myocardial infarction without type 2 diabetic patient group.

Table 7: Serum Amylin and preptin levels for all sex groups

Amylin levels (pg/ml) **Mean ±SD**				
Sex groups	**A**	**B**	**C**	**LSD**
Male	10.38±2.07 b	47.11±8.13 a	9.61±2.52 b	2.06
Female	11.72±2.33 b	56.93±10.08 a	10.34±1.77 b	2.91
P. value	0.610	0.039	0.003	
Preptin levels (pg/ml) **Mean ±SD**				
Sex groups	**A**	**B**	**C**	**LSD**
Male	11.00±2.58 b	54.06±8.52 a	12.20±1.65 b	2.11
Female	11.30±2.64 b	59.37±8.76 a	13.61±3.13 b	2.60
P. value	0.268	0.046	0.031	

- Legend as in Table 6

Serum Malondialdehyde (MDA) Concentration

Table 8 showed that there has not been any statistically significant difference in serum MDA levels between study group (A) male and female groups. The male and female groups in (B and C) groups had significantly different serum MDA levels ($p \leq 0.05$). Furthermore, all three study groups (A, B, and C) show a significant difference in blood MDA concentrations ($p \leq 0.05$) between male and female sex groups. Oxidative stress is a significant player in CVD pathogenesis. Postmenopausal women are more susceptible to CVD since they have lower levels of accessible estrogen and higher levels of oxidative stress. Menopause causes a systemic pro-oxidant situation because it reduces the production of estrogen, a naturally occurring antioxidant [38].

Serum Superoxide Dismutase (SOD) and Catalase (CAT) Concentrations

Table 9 showed that there has been no significant difference in blood SOD levels between study group (A) female and male groups. The female and male groups in the (C and B) groups had significantly different serum SOD levels ($p \leq 0.05$). Furthermore, in all three research groups (B, A, and C), there is a significant difference ($p \leq 0.05$) in serum SOD concentration levels between female and male sex groups, as shown in this table. Table 9 shows that there has been no significant difference in the serum CAT levels between the study group (A) male and female groups. The female and male groups in the (B and C) groups had significantly different serum CAT concentrations ($p \leq 0.05$). Furthermore, all three study groups (B, A, and C) show a significant difference ($p \leq 0.05$) in blood CAT concentrations between the female and male sex groups. Oxidative stress arises from an imbalance between the body's antioxidant defense systems and ROS/RNS. When ROS generation

exceeds cellular antioxidant capacity, it might upset the delicate balance. This can therefore result in lipid and protein peroxidation, DNA mutagenesis, and other possibly hazardous effects. In addition to causing direct damage to cells [39]. This study shows that women have lower amounts of antioxidants (CAT and SOD) than men. Following menopause, a crucial stage of female senescence takes place. Premenopausal women have a lower incidence of CVD in comparison to men, whereas postmenopausal women have a much higher incidence of CVD than males, according to epidemiological data. This incident proves that estrogen does protect the cardiovascular system. From the perspective of oxidative stress, estrogen functions through the estrogen receptor to regulate the cardiovascular system, providing menopausal women with heart issues with therapy choices [40].

Table 8: Serum MDA levels for all sex groups

MDA levels (µmol/L) **Mean ±SD**				
Sex groups	**A**	**B**	**C**	**LSD**
Male	2.15±0.51 c	7.28±1.7 a	6.32±1.32 b	0.63
Female	2.18±0.44 b	8.93±2.23 a	7.98±2.06 b	0.60
P. value	0.661	0.031	0.012	

- Legend as in Table 6

Table 9: Serum SOD and Catalase levels for all sex groups.

SOD levels (ng/ml) Mean ±SD				
Sex groups	**A**	**B**	**C**	**LSD**
Male	5.94±0.66 a	2.62±0.57 c	2.98±0.36 b	0.26
Female	5.88±1.58 a	2.03±0.50 c	2.58±0.88 b	0.48
P. value	0.121	0.039	0.048	
CAT levels (pg/ml) Mean ±SD				
Sex groups	**A**	**B**	**C**	**LSD**
Male	54.83±7.07 a	32.77±3.85 c	39.06±4.47 b	1.90
Female	53.76±4.33 a	30.26±3.66 c	37.53±5.52 b	2.59
P. value	0.214	0.040	0.048	

- Legend as in table 6.

Conclusion

Based on the data, the following conclusions were drawn: -

1- Acute myocardial infarction caused by T2D results in abnormalities in FBG, amylin, and preptin.

2- Acute myocardial infarction patients with and without T2D both have abnormalities in their antioxidant systems.

3- Amylin, preptin, MDA, SOD, and CAT concentrations are significantly impacted by sex.

4- Age affects the parameters that are evaluated in patients who have acute myocardial infarction, including those with and those without type 2 diabetes.

Conflict of interest

The authors declared there is no Conflict of interest.

Funding: None

REFERENCES

1. Aravindhan, V. Madhumitha, H. Meta inflammation in diabetic coronary artery disease: Emerging role of innate and adaptive immune responses, J Diabetes Res 2016, 2016(1), 6264149.
2. Ahmad, A. J. Khan, A. Khan, S. Manzoor, K. Causes, complication and management of diabetes mellitus, Chronicle Journal of Food and Nutrition 2017, 1(1), 1-4.
3. Mendis, S. Thygesen, K. Kuulasmaa, K. Giampaoli, S. Mähönen, M. Ngu Blackett, B K. Lisheng, L. Writing group on behalf of the participating experts of the WHO consultation for revision of WHO definition of myocardial infarction. World Health Organization definition of myocardial infarction: 2008–09 revision, International Journal of Epidemiology 2011, 40(1), 139-146.
4. Al-Abbas, W. Evaluation the Role of Interleukin-8 and Interleukin-10 in Myocardial Infarction Patients in Al-Najaf City, University of Thi-Qar Journal of Science 2019, 7(1), 84-88.
5. Kesarwani, N. Azmi, L. Evaluation of Cardioprotective Effect of Tinospora Cordifolia against Isoprenaline Induced Myocardial Infraction in Rats, International Journal of Current Microbiology and Applied Sciences 2014, 5, 543–55.
6. Bishop, M L. Fody, E P. Schoeff, L. Clinical Chemistry: Principles, Procedures, Correlations, 5th Edn. eds.Lippincott Williams and Wilkins.Philadelphia 2005, 200–202,285,290, 370,372,503–508.
7. Majid, A. Auda, M A. Al-Fartosi, K G. Using polyphenolic extract for tubers *Cyperus rotundus* to prevent myocardial Infarction, Journal of Education for Pure Science-University of Thi-Qar 2021, 11(2), 34-41.
8. Akazawa, H. Komuro, I. Roles of cardiac transcription factors in cardiac hypertrophy, Circulation research 2003, 92, 1079.
9. Bénitah, J P. Kerfant, B G. Vassort, G. Richard, S. Gómez, A M. Altered communication between L-type calcium channels and ryanodine receptors in heart failure, Front Biosci. 2002, 7, 263.
10. Shiny, K S. Kumar, S H. Farvin, K H. Anandan, R. Devadasan, K. Protective effect of myocardial infraction, J. Physiol Pharmacol 1989, 1235.
11. Majid, A. Faraj, H R. Affat, S S. Clinical Study Of Some Physiological Parameters in Patients With Acute Coronary Syndrome (ACS) in Thi-Qar Governorate / Iraq, International Journal of Scientific & Engineering Research 2014, 5, 645.
12. Majid, A. Sayer, S A. Protective effect of phenolic extract of *Cyperus rotundus* rhizomes on myocardial infarction induced by isoproterenol in female rats, IOP Conf. Series: Materials Science and Engineering 2018, 454 (2018), 012005.
13. Graham, I. Atar, D. Borch-Johnsen, K. Boysen, G. Burell, G. Cifkova, R. Dallongeville, J. De Backer, G. Ebrahim, S. Gjelsvik, B. European

Guidelines on Cardiovascular Disease Prevention in Clinical Practice, Heart J. 2007, 28, 2375–414.

14. Auda, M A. Majid, A. AlFartosi, K G. Protective role of polyphenolic compounds extracted from *cyperus rotundus* rhizomes and taurine on troponin-I and some oxidant/antioxidants parameters of female rats treated with isoproterenol-induced myocardial infraction, Journal of Thi-Qar University 2018, 13(2), 61-76.
15. Despa, S. Margulies, K B. Chen, L E. Knowlton, A A. Havel, P J. Taegtmeyer, H.... Despa, F. Hyperamylinemia contributes to cardiac dysfunction in obesity and diabetes: a study in humans and rats, Circulation research 2012, 110(4), 598-608.
16. Münzel, T. Hahad, O. Kuntic, M. Keaney, Jr J F. Deanfield, J E. Daiber, A. Effects of tobacco cigarettes, e-cigarettes, and waterpipe smoking on endothelial function and clinical outcomes, European heart journal 2020, 41(41), 4057-4070.
17. Hasan, M S S. Mashkur, M S. Siadat, S O R. Ali, H A. Assessment of serum afamin and preptin levels as a potential diagnosis markers for cardiovascular patients undergoing catheterization, Medico-Legal Update 2020, 20, 479-484.
18. Banerjee, M Vats P. Reactive metabolites and antioxidant gene polymorphisms in type 2 diabetes mellitus, Redox Biol 2013, 2,170-177.
19. Pawar, V., Sontakke, A., Pawar, S. Interconnection between oxidative stress and type 2 diabetes mellitus. *Journal of Bioscience and Applied Research*, 2023; 9(4): 192-198. doi: 10.21608/jbaar.2023.325677
20. Folli, F. Corradi, D. Fanti, P. Davalli, A. Paez, A. Giaccari, A. et al. The role of oxidative stress in the pathogenesis of type 2 diabetes mellitus micro- and macrovascular complications: avenues for a mechanistic-based therapeutic approach, Curr Diabetes Rev 2011,7(5), 313-324.
21. Majid, A. Adem, S. Kadhim, A S. Evaluation of Adiponectin hormone and some biochemical parameters with unstable angina and acute myocardial infarction patients, Journal of Bioscience and Applied Research 2022, 8(3), 138-142.
22. Rahimi, R. Nikfar, S. Larijani, B. Abdollahi, M. A review on the role of antioxidants in the management of diabetes and its complications, Biomed Pharmacother. 2005, 59(7), 365-373.
23. Tiwari, BK. Pandey, KB. Abidi, AB. Rizvi, SI. Markers of oxidative stress during diabetes mellitus, J Biomark 2013, 2013, 378790.
24. Houldsworth, A. Hodgkinson, A. Shaw, S. Millward, A. Demaine, AG. Polymorphic differences in the SOD-2 gene may affect the pathogenesis of nephropathy in patients with diabetes and diabetic complications, Gene 2015, 569(1), 41-45.
25. Halliwell, B. Gutteridge, J M. Oxidative stress: adaptation, damage, repair and death," in Free Radicals in Biology and Medicine, Chapter 2, pp. 36–104, Oxford Science Publications, New York, NY, USA, 3rd edition, 1999.
26. Nandi, A. Yan, L. Jana, C K. Das, N. Role of Catalase in Oxidative Stress- and Age-Associated Degenerative Diseases, Oxidative Medicine and Cellular Longevity 2019, 1-19.
27. Fong, K L. McCay, P B. Poyer, J L. Keele, B B. Misra, H. Evidence that peroxidation of lysosomal membranes is initiated by hydroxyl free radicals produced during flavin enzyme activity, Journal Biology Chemistry 1973, 248(22), 7792-7.
28. George S. Sivakami S. Glucose, glycation and aging. Biogerontology. 2004; 5(6): 365-373.
29. Kasapoglu, M. Ozben, T. Alterations of antioxidant enzymes and oxidative stress markers in aging, Exp Gerontol 2001, 36(2), 209-20.

30. Chang, A M. Halter, J B. Aging and insulin secretion, Am J Physiol Endocrinol Metab 2003, 248(1), E7-12.
31. Maedler, K. Schumann, D M. Schulthess, F. Oberholzer, J. Bosco, D. Berney, T. Donath, M Y. Aging correlates with decreased-cell proliferative capacity and enhanced sensitivity to apoptosis. A potential role for FAS and pancreatic duodenal homeobox-1, Diabetes 2006, 55(9), 2455-2462.
32. Patrick, S. Corrigan, R. Grizzanti, J. Mey, M. Blair, J. Pallas, M.... Casadesus, G. Neuroprotective effects of the amylin analog, pramlintide, on Alzheimer's disease are associated with oxidative stress regulation mechanisms, Journal of Alzheimer's Disease 2019, 69(1), 157-168.
33. Press, M. Jung, T. König, J. Grune, T. Höhn, A. Protein aggregates and proteostasis in aging: Amylin and β-cell function, Mechanisms of ageing and development 2019, 177, 46-54.
34. Liguori, I. Russo, G. Curcio, F. Bulli, G. Aran, L. Della-Morte, D.... Abete, P. Oxidative stress, aging, and diseases, Clinical interventions in aging 2018, 757-772.
35. Luo, J. Mills, K. le Cessie, S. Noordam, R. Van Heemst, D. Ageing, age-related diseases and oxidative stress: what to do next?, Ageing research reviews 2020, 57, 100982.
36. Ashraf, G M. Ebada, M A. Suhail, M. Ali, A. Uddin, M. Bilgrami, A. L…. Barreto, G E. Dissecting Sex-related cognition between Alzheimer's disease and diabetes: from molecular mechanisms to potential therapeutic strategies, Oxidative Medicine and Cellular Longevity 2021, 1-19.
37. Fourny, N. Beauloye, C. Bernard, M. Horman, S. Desrois, M. Bertrand, L**.** Sex differences of the diabetic heart, Frontiers in physiology 2021, 12, 661297.
38. Bourgonje, A R. Abdulle, A E. Al-Rawas, A M. Al-Maqbali, M. Al-Saleh, M. Enriquez, M B.... Saleh, J. Systemic oxidative stress is increased in postmenopausal women and independently associates with homocysteine levels, International Journal of molecular sciences 2020, 21(1), 314.
39. Kong, A S Y. Lai, K S. Hee, C W. Loh, J Y. Lim, S H E. Sathiya, M. Oxidative stress parameters as biomarkers of cardiovascular disease towards the development and progression, Antioxidants 2022, 11(6), 1175.
40. Xiang, D. Liu, Y. Zhou, S. Zhou, E. Wang, Y. Protective effects of estrogen on cardiovascular disease mediated by oxidative stress, Oxidative Medicine and Cellular Longevity 2021, 1-15.