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Ministry of Higher Education and
Scientific Research
University of Thi-Qar
College Of Science**



Clinical Study for Some Biochemical Parameters in Type 2 Diabetic Patients with and without Metabolic Syndrome

**A Thesis
Submitted to the College of Science
University of Thi-Qar
In partial Fulfillment of the Requirements
For the Master Degree of Science in Biochemistry**

By

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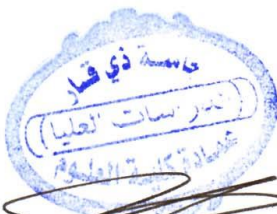
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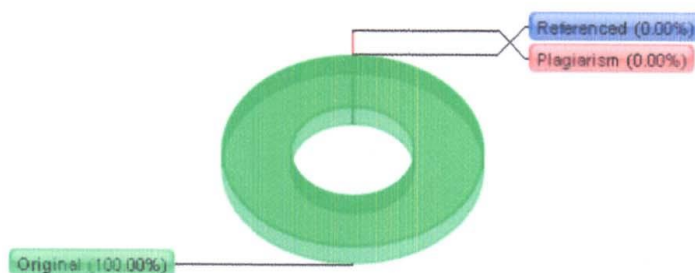
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نتعهد بالتقيد التام بما جاء في مضمون كتاب وزارة التعليم العالي والبحث العلمي/جهاز الاشراف والتقويم المرقم ج ت/425 الصادر بتاريخ 2014/3/24، والمبلغ اليها بكتاب رئاسة جامعة ذي قار/قسم البحث والتطوير المرقم 4704/54/7 والصادر بتاريخ 2014/3/31، عند أعداد الرسالة أو الاطروحة الموسومة:

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- 2- تطبق استمارة التعهد هذه على السادة المشرفين على الرسالة أو الأطروحة وعلى طلبة الماجستير والدكتوراه.
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- 3- أ.د. مزاحم هادي

عنوان الرسالة أو الاطروحة: clinical study For some Biochemical parameters in type 2 Diabetic patients with and without Metabolic Syndrome

اني الطالب: عبد الله فاخر يوسف. أتعهد بتولي وتنظيم الدراسة الاحصائية بنفسني من دون المساعدة بكتابة الجانب الاحصائي من قبل أساتذة.

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CERTIFICATE

We certify that this thesis, entitled **Clinical Study for Some Biochemical Parameters in Type 2 Diabetic Patients with and without Metabolic Syndrome**, was prepared by **Abdullah Fakhir Yousif** under your supervision at the Department of Chemistry, College of Sciences, University of Thi-Qar (Iraq) in partial fulfillment of the requirements for the Master degree of science in chemistry.



Supervisor

Prof.

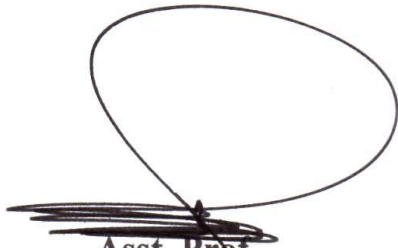
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In view of the available recommendation, I forward this thesis for debate by the examining committee.



Asst. Prof.

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Head of the Department of Chemistry

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Certificate

We the examining committee, after reading this thesis "**Clinical Study for Some Biochemical Parameters in Type 2 Diabetic Patients with and without Metabolic Syndrome**" and examining the student **Abdullah Fakhir Yousif** in its content, find that it is qualified for pursuing the degree of master of science in Biochemistry with grade of **(Excellent)**.

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The Dean of college

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University of Thi-Qar

الإهداء

إلى صاحب الإسراء والمعراج .. إلى سيد المرسلين .. إلى نبي الرحمة ونور العالمين ..
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وحنانها بلسم جراحي ..

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ABBREVIATIONS

Abs	Absorbance
ADA	American Diabetes Association
Alb	Albumin
ANOVA	Analysis of Variance
ATP	Adenosine triphosphate
BCG	Bromocresol Green
BMI	Body Mass Index
CE	Cholesterol esterase
CETP	Cholesterol Ester Transfer Protein
CH	Cholesterol
CHD	Coronary Heart Diseases
CM	Chylomicron
CO	Cholesterol oxidase
CVD	Cardio Vascular Diseases
D	Dilution Factor
D.W	Distilled Water
Da	Dalton
DBP	Diastolic Blood Pressure
DKA	Diabetic ketoacidosis
DM	Diabetes Mellitus

DM 2	Diabetes Mellitus Type 2
DMMS	Type 2 Diabetes Mellitus with Metabolic Syndrome
DMSO	Dimethyl Sulfoxide
DNA	Deoxyribonucleic Acid
DTNB	5,5-dithio-bis(2-nitrobenzoic Acid)
EDTA	Ethylene diamine tetra acetic acid
FA	Fatty Acid
FBG	Fasting Blood Glucose
FRs	Free Radicals
GDM	Gestational Diabetes Mellitus
GH	Growth Hormone
GK	Glycerol kinase
GPO	Glycerol-3-phosphate oxidase
GPX	Glutathione Peroxidase
GR	Glutathione Reductase
GSH	Glutathione
GSSG	Glutathione disulfide
GTF	Glucose Tolerance Factor
Hb	Hemoglobin
HbA _{1c}	Hemoglobin A _{1c}

HC	Hollow Cathode
HDL-c	High Density Lipoprotein-Cholesterol
HIV	Human Immunodeficiency Virus
HNE	4-hydroxy-2-nonenal
HNKS	Hyperosmolar Non-Ketotic State
IDDM	Insulin Dependent Diabetes Mellitus
IDF	International Diabetes Federation
IDL	Intermediate Density Lipoprotein
IGT	Impaired Glucose Tolerance
IR	Insulin Resistance
IU/L	International Unit per Liter
L	Light Path
L•	Lipid radical
LDL-c	Low Density Lipoprotein- Cholesterol
LMW	Low Molecular Weight
LOO•	Lipid peroxy radical
LOOH	Lipid hydro peroxide
LPL	Lipoprotein lipase
LPO	Lipid Peroxidation
LSD	Least Significant Difference
MDA	Malondialdehyde
MENA	Middle East and North Africa

MODY	Maturity-Onset Diabetes of the Young
MS	Metabolic Syndrome
MW	Molecular Weight
NIDDM	Non insulin Dependent Diabetes Mellitus
OGTT	Oral Glucose Tolerance Test
PEG	Poly Ethylene Glycol
POD	Peroxidase
PUFA	Poly Unsaturated Fatty Acid
PVD	Peripheral Vascular Disease
R	Reagent
RNS	Reactive Nitrogen Species
ROS	Reactive Oxygen Species
RPM	Rotor Per Minute
SBP	Systolic Blood Pressure
SD	Standard Deviation
SOD	Superoxide dismutase
T3	Triiodothyronine Hormone
T4	Thyroxin Hormone
TBA	Thio Barbituric Acid
TC	Total Cholesterol
TCA	Trichloro Acetic Acid
TG	Triglyceride

US	United States
UV	Ultra Violate
VIS	Visible
VLDL-c	Very Low Density Lipoprotein- Cholesterol
WHO	World Health Organization
ϵ	Molar Extinction Coefficient

Summary

Type 2 diabetes constitutes a major threat to public health; non ideal control leads to chronic hyperglycemia. This kind occurs due to the resistance to the body's cells to the action of insulin hormone, or may be due to the lack of production of a sufficient quantity of insulin by the pancreas and it is caused by multiple factors, most notably the overweight and lack of physical activity.

The metabolic syndrome is a complex set of disorders that significantly increases the risk of heart disease. The American Diabetes Association (ADA) criteria were used for the diagnosis of metabolic syndrome.

The present study is designed to determine the levels of FBG, HbA_{1c}, lipid profile (TG, TC, and HDL-c), Oxidative Stress status (Malondialdehyde, Albumin, and Glutathione) and some trace elements (chromium, and selenium) in type 2 diabetic patients with and without metabolic syndrome.

The measured parameters were studied on the basis of four variables: general comparison, Age, body mass index (BMI) and sex.

Patients and controls were divided, in the general comparison, into three groups:

- 1- Control group: included 50 supposed healthy subjects aged (41-70 years)
- 2- DM group: included 64 type 2 patients diabetes aged (41-70 years)
- 3- DMMS group: included 36 patients with type 2 diabetes and metabolic syndrome aged (41-70 years).

Patients and controls were divided according to their ages, into three age groups: A1 (41-50 years), A2 (51-60 years), and A3 (61-70 years).

Patients and controls were divided according to BMI, into three groups: Normal range (18.5-24.99), Overweight (25-29.99) and Obese (≥ 30.00).

As for the sex, the patients and controls were divided into (Male, Female).

The results obtained in this study show a significant increase in the concentration of FBG, HbA_{1c}, TG, TC and MDA in all patients groups in comparison with the control group ($P \leq 0.05$).

Also the results show a significant increase in the concentration of FBG, HbA_{1c}, TG, TC and MDA in type 2 diabetes with metabolic syndrome group in comparison with the type 2 diabetes without metabolic syndrome group ($p \leq 0.05$).

The present study show a significant decrease in the concentration of HDL-c, Alb, GSH, chromium and selenium in all patients groups in comparison with the control group ($P \leq 0.05$).

Aging has a negative effect on the studied parameters in diabetic patients with and without metabolic syndrome.

Also BMI has a negative effect on the studied parameters in diabetic patients with and without metabolic syndrome.

There is a significant impact for gender on concentrations of FBG, HbA_{1c}, TG, TC, HDL-c, and chromium.

Chapter One

Introduction and Literature Review

1- INTRODUCTION AND LITERATURE REVIEW

The term diabetes was discovered by Aretaeus of Cappadocia. It was derived from Greek verb (diabainein). Diabetes is first registered in English, in the form diabetes, in a medical text written around (1425). In (1675), Thomas Willis added the word (Mellitus), the Latin meaning "honey" a reference to the sweet taste of the urine. In (1776), Matthew Dobson confirmed that the sweet taste was because of an excess of a kind of sugar in the urine and blood of people with diabetes (Marshall, 2000). In 1889 (Joseph and Oskar) discovered the role of the pancreas in diabetes disease when removed the pancreas completely from the dogs, where they showed signs and symptoms of diabetes led to their deaths (Patlak, 2002).

In (1921), Banting and Best induced diabetes in dogs by extract the pancreatic islets of Langerhans of healthy dogs (Murray, 1971). Banting, Best and their colleagues went on to purify the insulin hormone from bovine pancreases. This led to the availability of an effective treatment by insulin injections and the first patient was treated in 1922 (Murray, 1971). Despite the availability of treatment, diabetes has remained a major cause of death. Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases. In 2012, an estimated 1.5 million deaths were directly caused by diabetes (WHO, 2012).

According to International Diabetes Federation in 2013, an estimated 425 million people had diabetes. More than 39 million people have diabetes in the Middle East and North Africa (MENA) Region; by 2045 this will rise possibly to 67 million (International Diabetes Federation (IDF), 2013).

In Iraq in 2015 there were 1.2 million cases of diabetes (IDF, 2015). Globally, an estimated 422 million adults are living with diabetes mellitus, according to the 2016 data from the World Health Organization (WHO, 2016).

Diabetes mellitus is the most common of metabolic disorders and it is a major threat care worldwide (Mandrup-Poulsen, 2008).

1.1. Diabetes Mellitus:

1.1.1. Definition:

Diabetes mellitus (DM) is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both. In both cases the glucose is unable to enter the cells, leading to its accumulation in the blood and the excess levels of this sugar are excreted in the urine (Priyanka *et al.*, 2011).

1.1.2. Classification of Diabetes Mellitus:

Diabetes can be classified into the following general categories:

1.1.2.1. Type 1 Diabetes:

Type 1 diabetes occurs as a result of auto-immune beta-cell destruction in the pancreas, characterized by a total absence of insulin production (Deshpande *et al.*, 2008). This type of diabetes is a relatively homogeneous disease in which the insulin secretion of beta cells in the pancreas declines and eventually ceases totally (Matveyenko and Butler, 2008). Type 1 diabetes is usually diagnosed during childhood or early adolescence and it affects about 1 in every 600 children (ADA, 2006). This form, previously called “insulin dependent diabetes” or “juvenile-

onset diabetes” accounts for about 5% to 10% of all diagnosed cases of diabetes (ADA, 2017).

1.1.2.2. Type 2 Diabetes :

Occurs due to a progressive insulin secretory defect on the background of insulin resistance (ADA, 2017). It accounts for about 90% to 95% of all diagnosed cases of diabetes (Deshpande, 2008). It usually develops above the age of 40 years (Harris *et al.*, 1995). This form was previously referred to as non insulin dependent diabetes mellitus (NIDDM) (Gardner, 2011).

1.1.2.3. Gestational Diabetes Mellitus (GDM):

Gestational diabetes occurs when pregnant women without a previous history of diabetes develop a high blood glucose level (Malik and Taplin, 2014 ; Retnakaran *et al.*, 2015). Gestational diabetes diagnosed in the second or third trimester of pregnancy is not clearly overt diabetes. It occurs in about 2–5% of all pregnancies and may improve or disappear after delivery (ADA, 2017).

1.1.2.4. Specific Types of Diabetes:

Occurs due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY], diseases of the exocrine pancreas (such as cystic fibrosis), and drug-or chemical-induced diabetes [such as in the treatment of HIV (Human Immunodeficiency Virus) /AIDS or after organ transplantation] (ADA, 2017).

1.1.3. Symptoms of Type 2 Diabetes Mellitus:

There are common symptoms of diabetes mellitus include:

Polydipsia, Polyuria, Weight loss, Increased appetite, Blurred vision, Sores that do not heal, General lethargy and Tiredness (Gittoes and Kendall, 2007).

1.1.4. Diagnosis of Type 2 Diabetes Mellitus:

Diabetes mellitus is diagnosed by demonstrating any one of the following:

- 1- Fasting blood glucose concentration ≥ 126 mg/dL (7 mmol/L) plus classic symptoms of diabetes, which include polyuria, polydipsia, and unexplained weight loss. (Fasting is defined as no caloric intake for at least 8 hours).
- 2- Casual plasma glucose concentration ≥ 200 mg/dL (11.1 mmol/L) plus classic symptoms of diabetes. Casual is defined as any time of day irrespective of meal time.
- 3- Two hours post load glucose concentration ≥ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT). The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 gm anhydrous glucose dissolved in water.
- 4- HbA_{1c} ratio $\geq 6.5\%$ (WHO, 2006 ; ADA, 2017).

1.1.4.1. Role of Hemoglobin in Diagnosis and Monitoring of Glucose Levels :

Hemoglobin is the predominant protein in red blood cells and is also the oxygen carrying pigment that gives blood its red color. About 97% of hemoglobin is hemoglobin A. Although one chemical component accounts for 92% of hemoglobin A, approximately 8% of hemoglobin A is made up of minor components that are chemically slightly different.

These minor components include hemoglobin A_{1c}, A_{1b}, A_{1a₁} and A_{1a₂}. Hemoglobin A_{1c} (HbA_{1c}) is a minor component of hemoglobin to which glucose is bound. HbA_{1c} is also sometimes referred to as glycosylated hemoglobin or glycohemoglobin. In addition to random, fasting blood glucose levels, HbA_{1c} levels are routinely measured in monitoring people with diabetes (Jeppsson *et al.*, 2002).

HbA_{1c} levels depend on the blood glucose concentration. That is, increase in the glucose concentration in blood leads to increase in the level of HbA_{1c}. Levels of HbA_{1c} are not influenced by daily fluctuations in the blood glucose concentration. HbA_{1c} is a useful indicator of how well the blood glucose level has been controlled in the recent past (over two to three months) and may be used to monitor the effects of diet, exercise, and drug therapy on blood glucose in people with diabetes (Jeppsson *et al.*, 2002).

1.1.5. Causes of Type 2 Diabetes Mellitus:

The pathophysiology of type 2 diabetes is simply characterized by insulin resistance, impairment of hepatic glucose production regulation and reduced β cells function subsequently leading failure of β cells (Weyer *et al.*, 1999). The decreased insulin biological response (insulin resistance) occurs because insulin is unable to bind to its receptor due to defects in the insulin receptor binding sites or disturbances in the insulin signal transduction pathway. Overcoming insulin resistance requires the pancreatic β cells to increase the amount of insulin secreted, a state called hyperinsulinaemia. Because accelerated endogenous glucose output occurs simultaneously with hyperinsulinaemia, at least in early and middisease stages, insulin resistance in hepatic cells becomes the major driver of hyperglycemia in type 2 diabetes (Weyer *et al.*, 1999).

1.1.6. Risk Factor of Type 2 Diabetes Mellitus:

Several risk factors have been associated with the development of type 2 diabetes. Genetic factors in some ethnic groups, family history of diabetes, and increasing population age are examples of unmodifiable risk factors. However, lifestyle factors associated with unhealthy diet, physical inactivity and smoking usually leading to overweight, dyslipidemia, high blood pressure and impaired glucose tolerance (IGT) are the most common risk factors for escalating diabetes mellitus (Joshi and Shrestha, 2010).

1.1.7. Complication of Type 2 Diabetes Mellitus:

Risk of complications increase in people who are not keen to balance the level of sugar in the blood. Controlling blood sugar levels can help to prevent these complications (Tintinalli *et al.*, 2011) and there are two types of complications, acute and chronic.

1.1.7.1. Acute Diabetic Complications

Hypoglycemia , Hyperosmolar non-ketotic state (HNKS) (Asareer *et al.*, 2010).

1.1.7.2. Chronic Diabetic Complications

1. Microvascular complications include:

Retinopathy, Diabetic Neuropathy, Diabetic Nephropathy, Diabetic foot.

2. Macrovascular complications include:

Atherosclerosis, Hypertension, Coronary heart disease (CHD), Peripheral vascular disease (PVD), Cerebrovasculare disease (Asareer *et al.*, 2010).

1.2. Metabolic Syndrome (MS):

The metabolic syndrome is a complex set of disorders that can increase the risk of cardiovascular disease, type 2 diabetes and all-cause mortality. It containing of a cluster of risk factors including elevated fasting blood glucose, dyslipidemia, elevated blood pressure and abdominal obesity (Okosun *et al.*, 2014).

According to (ADA, 2017) the criteria to diagnosis this syndrome are by the presence of three or more of these risk factors as shown in table (1-1).

Table (1-1): Criteria for diagnosis of metabolic syndrome:

Fasting blood glucose	Fasting blood glucose of 100 mg/dL or more or taking drugs for high blood glucose.
Serum triglyceride	Serum triglyceride of 150 mg/dL or more or taking drugs for high triglyceride
Low serum HDL-c	Less than 40 mg/dL for men
	Less than 50 mg/dL for women
Blood pressure	Blood pressure of 130/85 mm Hg or more or taking drugs for high blood pressure
Central obesity (waist circumference)	More than 40 inch for men
	More than 35 inch for women.

1.2.1. Pathogenesis of Metabolic Syndrome:

The exact cause of MS is not yet known, however, most researchers believe it is caused by a combination of genetic and lifestyle choices, including the types of diet and level of physical activity. There are some major factors thought to impact on the development of MS. Insulin resistance with hyperinsulinemia seems to be a central factor in the pathogenesis of the MS. An insulin-resistant state interferes with the hormonal actions taking place in the liver (Bremer *et al.*, 2012).

Insulin produced in the β -cells of the pancreas travels quickly to the liver via the portal vein, and in the presence of the MS, insulin has a selective dysfunction so that it does not diminish the hepatic glucose output, but rather increases it, and still as the normal state and increases the lipolysis, thereby releasing triglycerides to the circulation, causing dyslipidemia (Bremer *et al.*, 2012). Moreover insulin resistance causes increased sodium renal reabsorption and stimulate the nervous system which can result in hypertension (Sarafidis and Ruilope, 2006). In addition to that excessive nutrient intake can result in obesity which lead to excessive of adipose tissue, which also contribute to the development of MS (Kern *et al.*, 1995).

1.3. The Hormonal Role in Carbohydrate Metabolism:

Hormone is a chemical messenger that carries a signal from one cell or group of cells to another, by the blood. Generally hormones regulate, the function of their target cells (the cells receiving the hormone) (Neave, 2008).

Insulin hormone:

This hormone is synthesized in the pancreas within the beta cells (β -cells) of the islets of Langerhans. Insulin is polypeptide has a molecular weight of 5808 Da (Dunning *et al.*, 2006). The active form of insulin consists of 51 amino acids arranged into two polypeptide chains designated A (21 amino acids) and B chain with (30 amino acids). Both chains are held together by two disulphide bonds between the cysteine in Cys A7 and Cys B7 respectively, Cys A20 and Cys B19 positions. Another disulphide bond is internal, within the A chain itself (Cys A6 and Cys A11) (Michael *et al.*, 2014). Active structure of insulin hormone of human is shown in figure (1-1):

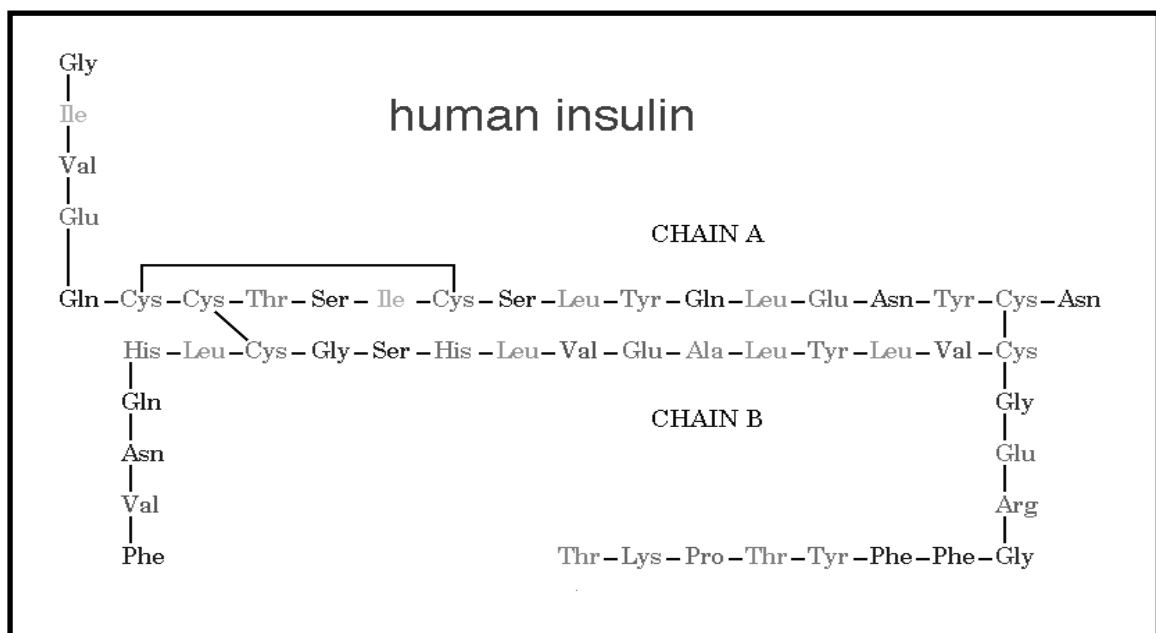


Figure (1-1): Active structure of insulin hormone of human (Michael *et al.*, 2014).

The effect of insulin on glucose metabolism include:

1-Insulin binds to its receptor 2-produces many activation cascades
3-glycogen synthesis 4-fatty acid synthesis 5-protein synthesis
6-glycolysis (Holz and Oleg, 2005) as shown in the figure (1-2):

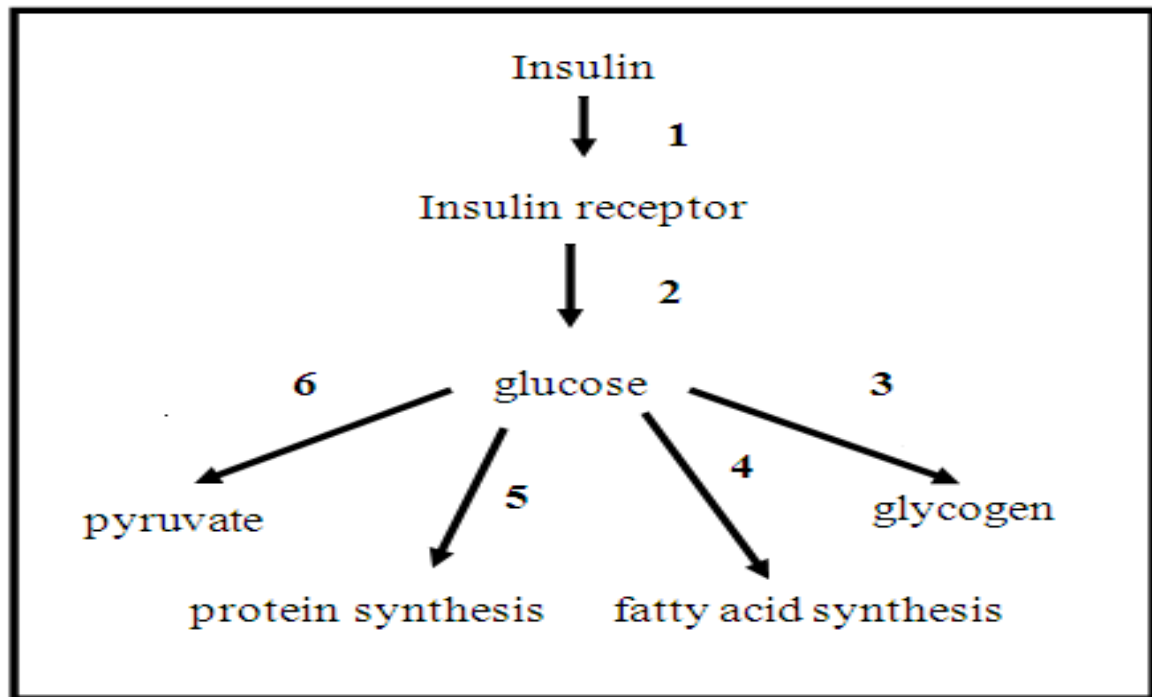


Figure (1-2): The effect of insulin on glucose metabolism.

Glucagon hormone:

Glucagon is produced by the α -cell of the islets of Langerhans of pancreas, it is an important hormone involved in glucose metabolism (De Lean *et al.*, 2006). Glucagon polypeptide, consists 29 amino acids. This hormone has a molecular weight of 3485 Da (David, 1992). Its primary structure in human is shown in figure (1-3):

NH₂-His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr-COOH

Figure (1-3): Structure of glucagon hormone (David, 1992).

The two major effects of glucagon on glucose metabolism are :

- 1- breakdown of glycogen (glycogenolysis)
- 2- increased gluconeogenesis (Pilkis and Granner, 1992).

Other Hormones:

Thyroid hormones: The two major active hormones secreted by the thyroid gland are thyroxine, and triiodothyronine, commonly called T4 and T3, respectively. Hyperthyroid patients apparently utilize glucose at normal or increased rate, hypothyroid patients have decreased ability to utilize glucose. In addition, hypothyroid patients are much less sensitive to insulin than are normal or hyperthyroid individuals (Murray *et al.*, 1988).

Growth hormone (GH) synthesized, stored, and secreted by the somatotroph cells within the anterior pituitary gland (Salam and Reetu 2011). GH prevents glucose utilization by peripheral tissues, thus preserving (sparing) it for such tissues as the brain. The main reason for this is that GH blocks insulin mediated glucose uptake and utilization by peripheral tissues, particularly muscles (De Weerth *et al.*, 2002).

Epinephrine hormone is produced by the adrenal medulla and consist from the amino acids phenylalanine and tyrosine (Ober, 2000). During periods of emotional stress, such as anger or fright, adrenalin is secreted by the adrenal glands. It is transported by the blood to the muscles and liver where it promotes glycogen breakdown, thus increasing the amount of glucose in the blood. Making that glucose readily available as the body needs it to meet the emergency situation (Burant *et al.*, 1991).

Cortisol hormone is produced by the adrenal cortex within the adrenal gland. Cortisol counteracts insulin by increasing gluconeogenesis and promoting breakdown of lipids (lipolysis). This leads to increased circulating glucose concentrations in the blood by increasing gluconeogenesis. It also causes increase in glycogen breakdown in the

liver. Therefore the prolonged cortisol secretion causes hyperglycemia (Yamashima, 2003).

1.4. Lipids and Lipoproteins:

1.4.1. Lipids:

Lipids are a diverse and ubiquitous group of compounds which have many key biological functions, such as acting as structural components of cell membranes and serving as energy storage sources (Fahy *et al.*, 2011). Plasma lipids consist of triacylglycerol (triglycerides) 16%, cholesterol 14%, phospholipids 30%, cholesterol esters 36% and a much smaller fraction of unesterified long-chain fatty acids or free fatty acids 4% (Murray *et al.*, 2003 ; Princy *et al.*, 2013).

1.4.1.1. Cholesterol (CH):

Cholesterol is an essential cellular nutrient. Very nearly all of the cholesterol in a cell is found in cell membranes where it fulfils two important functions. First, together with the fatty acids of phospholipids it modulates cell membrane fluidity. Second, in conjunction with the phospholipid sphingomyelin, it forms lipid rafts or caveolae where signalling molecules such as hormones congregate (Stanley, 2008).

1.4.1.2. Triglyceride (TG):

Triglycerides are fatty acid esters of glycerol, each containing three fatty acids (Mayne , 2002). They are derived from three primary sources: the diet, storage depots in adipocytes and biosynthesis particularly in the liver (Mathews *et al.*, 2001).

1.4.2. Lipoproteins:

Lipids synthesized in the liver and intestine has to be transported to the various tissues to accomplish their metabolic functions. Because of their insolubility, they are transported in plasma bound with protein as macromolecular complexes called lipoproteins (Rifai,1986).

1.4.2.1. Chylomicrons (CM):

Chylomicrons are the lipoprotein particles contain the highest percentage of lipid and the smallest percentage of protein in compare to other lipoproteins. Chylomicrons are assembled in the intestinal mucosa as a means to transport dietary TG to the rest of the body. The main sites for removal of chylomicrons are the muscle and liver by lipoprotein lipase, an enzyme bound to the capillary endothelium of extra hepatic tissues, hydrolyzes triacylglycerol in chylomicrons, into free fatty acids and glycerol (Philippa and Easterbrook 1999).

1.4.2.2. Very Low Density Lipoprotein (VLDL):

It is produced in liver and chief carrier of endogenous hepatic triacylglycerol in blood, then migrate into pre- β -globulin region in electrophoretic field (Attman *et al.*, 1993).

1.4.2.3. Intermediate Density Lipoprotein (IDL):

Small amounts of IDL are produced by the liver. The effect of lipoprotein lipase (LPL) is to hydrolyse triacylglycerol, thus reducing the size of VLDL and increasing the percentage of denser molecules (i.e., it degrades VLDL to IDL). After hydrolysis, the fatty acids are taken up by nearby cells or by serum albumin for transport to more peripheral cells. A similar process leads from IDL to LDL (August *et al.*, 2007).

1.4.2.4. Low Density Lipoprotein (LDL):

Low density lipoprotein is a sort of lipoprotein that transfers cholesterol from the liver to peripheral tissues (Segrest *et al.*, 2001).

1.4.2.5. High Density Lipoprotein (HDL):

Particles promote vascular health by extracting cholesterol from tissues and delivering it back to the liver. Particles of HDL prevent coronary artery disease by serving as transport particles for excess cholesterol to the liver, where it is converted into bile acids and excreted (Daniels *et al.*, 2009).

1.5. Type 2 Diabetes Mellitus with Free Radicals (FRs) and Reactive Oxygen Species (ROS):

Free radicals can be defined as chemical species associated with an odd or unpaired electron, these short lived, neutral, unstable and highly reactive to pair up the odd electron and finally achieve stable configuration (Alam *et al.*, 2013). It is a highly reactive due to the presence of unpaired electron and they are electrically charged molecules, i.e., they have an unpaired electron, which causes them to seek out and capture electrons from other substances in order to neutralize themselves (Oparil *et al.*, 2003).

Although the initial attack causes the free radical to become neutralized, another free radical is formed in the process, causing a chain reactions to occur and until subsequent free radicals are deactivated. Thousands of free radical reactions can occur within seconds of the initial reaction (Marr, 1995). However, free radicals are capable of attacking the healthy cells of the body, causing them to lose their structure and

function. The damage of cell caused by free radicals appears to be a main contributor to aging and degenerative diseases of aging such as diabetes mellitus, cardiovascular disease, cataracts and renal failure (Alam *et al.*, 2013). Furthermore, the excessive production of free radical leads to oxidation of cellular lipids, proteins and nucleic acid, which may ultimately lead to cell death (Leutner *et al.*, 2005).

Any free radical involving oxygen can be referred to as reactive oxygen species (Leutner *et al.*, 2005). Reactive oxygen species is a term which contains all highly reactive, oxygen-containing molecules, including free radicals (Oparil *et al.*, 2003). Reactive oxygen species are a by-product in type 2 diabetes, these generated during protein glycation and as a consequence of advanced glycation end products-receptor binding, they impair insulin signalling pathways and induce cytotoxicity in beta cells of pancreas (Sarah *et al.*, 2011).

However, free radicals are formed especially in patients with unregulated or poorly regulated diabetes mellitus because of increasing oxidative activity (Meyers *et al.*, 1996 ; Rattan, 2006). The increasing of free radical in diabetes mellitus over time plays a role in the development of diabetic complication. ROS regulate vascular function by modulating cell growth, migration and secretion. An imbalance in redox states where pro-oxidants over antioxidant capacity results in oxidative stress. This oxidative stress causes the vascular injury and cardiovascular diseases, hypertension and diabetes (Cefalu and Hu, 2004). In general increased oxidative stress at the cellular level can come about as a consequence of many factors, including medications, infections, poor diet, trauma, radiation, toxins and cigarette smoke (Oparil *et al.*, 2003).

The mechanism of oxidative stress is due to persistent hyperglycemia, which leads to overt generation of ROS in mitochondria is shown in figure (1-4).

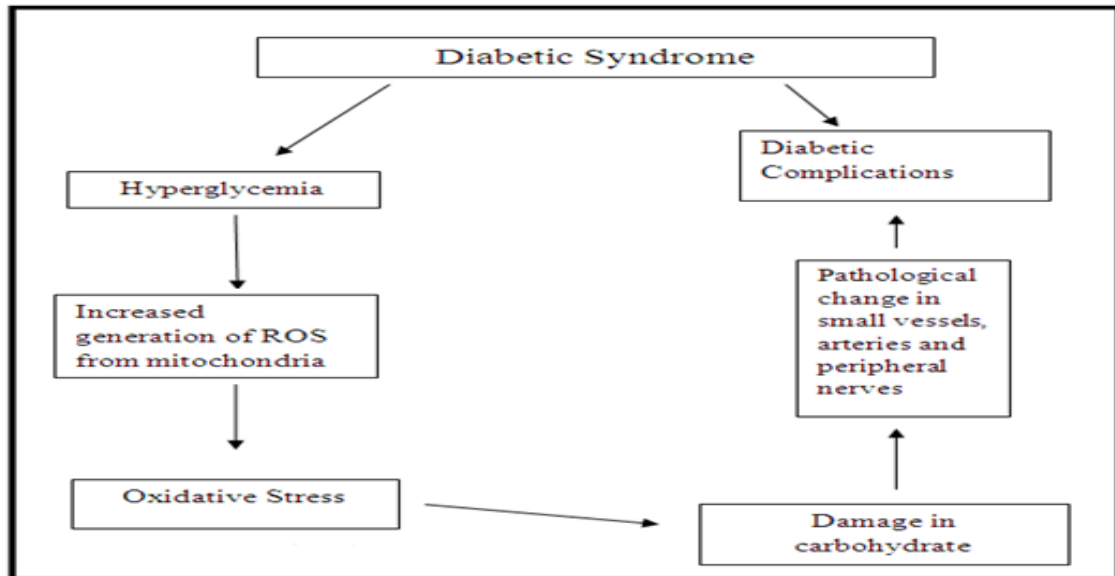


Figure (1-4): Mechanism of hyperglycemia which leads to generation of ROS in mitochondria (Racek *et al.*, 2006).

1.6. Lipid Peroxidation (LPO):

Lipid peroxidation is a chain reactions initiated by the attack of reactive oxygen species (ROS) and reactive nitrogen species (RNS) on polyunsaturated fatty acid (PUFA), leading to cell membrane damage and consequently to cell death (Domijan *et al.*, 2015). The overall process of lipid peroxidation consists of three steps: initiation, propagation, and termination as shown in figure (1-5).

Step1. In Initiation, pro oxidants like hydroxyl radical abstract the allylic hydrogen forming the carbon-centered lipid radical ($L\cdot$).

Step2. In the propagation phase, ($L\cdot$) rapidly reacts with oxygen to form a lipid peroxy radical ($LOO\cdot$) which abstracts a hydrogen from another

lipid molecule generating a new $L\cdot$ (that continues the chain reaction) and lipid hydro peroxide (LOOH).

Step3. In the termination reaction, antioxidants like vitamin E donate a hydrogen atom to the $LOO\cdot$ species and form a corresponding vitamin E radical that reacts with another $LOO\cdot$ forming non radical products.

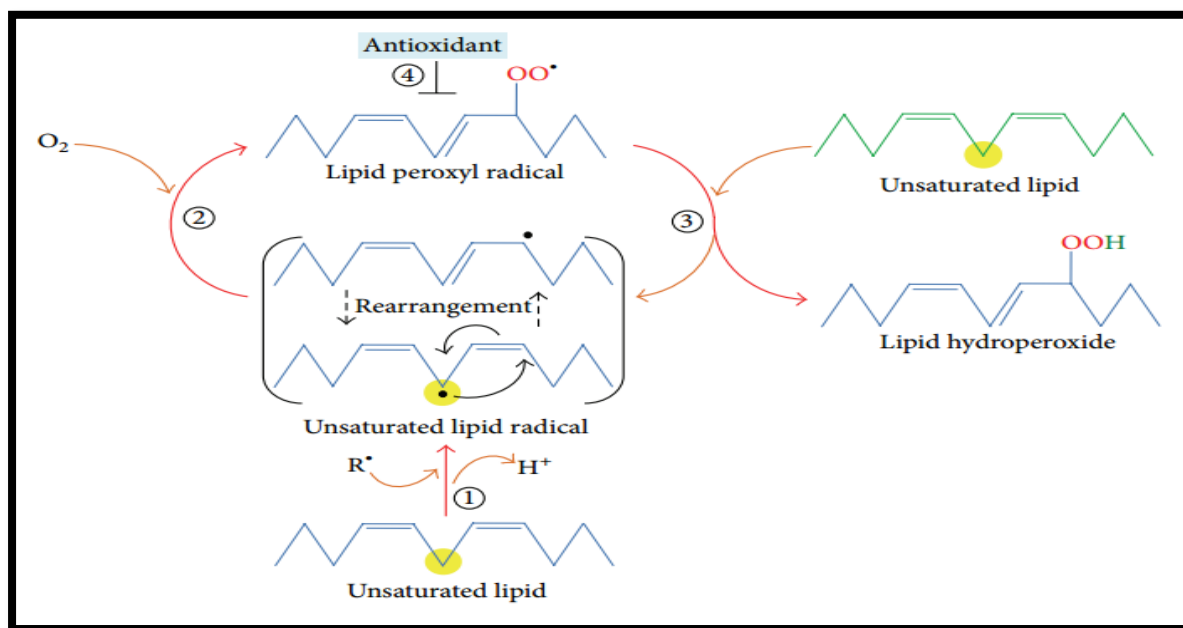


Figure (1-5): Lipid peroxidation process (Antonio *et al.*, 2014).

Primary products of LPO are unstable hydro peroxides that decompose to various secondary products, among which are stable aldehydes, malondialdehyde, 4-hydroxy-2-nonenal (HNE) and acrolein (Domijan *et al.*, 2015).

Malondialdehyde is a good marker of free radical-mediated damage and oxidative stress and the main source of MDA in biological samples is the peroxidation of polyunsaturated fatty acids. MDA is able to impair several physiological mechanisms of the human body through its ability to react with molecules such as deoxyribonucleic acid (DNA) and

proteins. It is therefore useful to consider this molecule as something more than a lipid peroxidation product (Del *et al.*, 2005).

1.7. Antioxidant Defense System:

Antioxidant is a molecule that inhibits or prevent the oxidation of other molecules (Abner *et al.*, 2011 ; Goran *et al.*, 2013), protecting our body from the detrimental effects of free radicals (Rahman, 2007). Antioxidant is necessary to scavenge free radicals by give up their own electrons to free radicals which start a chain reactions that damages cells (Liu, 2000).

The general classification of antioxidants depends on their functions.

Consequently they are divided into three types :

Primary antioxidants which arrest new free radicals generation such as catalase, superoxide dismutase, glutathione peroxidase, ceruloplasmin, ferritin and transferrin. The secondary antioxidants perform removal newly formed free radicals before they can initiate chain reactions which leads to cell damage and further free radical generation e.g. vitamins such as E, C and A, uric acid, bilirubin as well albumin. Finally, the tertiary antioxidants repair cell structure damaged by free radicals attack e.g. DNA repair enzymes and methionine sulphoxide reductase (Ingold *et al.*, 1987 ; Burton *et al.*, 1990).

Another classification is adopted for antioxidants. It depends on the type of antioxidant substance. According to this classification, antioxidants are classified into two types, Enzymatic and non enzymatic. The first type includes all antioxidants which have enzymatic activity such as glutathione peroxidase, glutathione-s-transferrase, superoxide dismutase and catalase. As for non enzymatic antioxidants they include

wide range of *in vivo* substances which have not enzymatic activity such as vitamins e.g. E, C and A also uric acid, transferrin, ferritin, albumin and glutathione (Halliwell, 1992).

1.7.1. Albumin (Alb):

Albumin is the most abundant protein of blood plasma. It is a single chain, polypeptide with a molecular weight of 66,500 Da containing 585 amino acids (Yang *et al.*, 2014). Serum albumin represents 60 % of total plasma proteins (Taverna *et al.*, 2013). Albumin synthesis takes place only in the liver. Albumin is not stored by the liver but is secreted into the portal circulation as soon as it is manufactured (Tullis, 1997).

Albumin has many important physiological functions among them, regulates colloidal osmotic pressure, and transports numerous endogenous compounds such as fatty acids (FA), hormones, bile acids, amino acids, metals and toxic metabolites (Yang *et al.*, 2014).

Albumin may have a significant antioxidant potential. It is participation in the scavenging of oxygen free radicals, which has been implicated in the pathogenesis of inflammatory diseases. This may be related to the abundance of sulfhydryl (-SH) groups on the albumin molecule (Tullis, 1977).

1.7.2. Glutathione (GSH):

Glutathione, a water soluble low molecular weight tripeptide, is the most abundant non protein thiol in the body (Dickinson and Forman, 2002). Providing multiple defense mechanisms against the cellular damage caused by oxidative stress, glutathione is particularly effective against the highly toxic hydroxyl radicals ($\cdot\text{OH}$) for which no other enzymatic defense is known (Wu *et al.*, 2004 ; Maher, 2005).

Although glutathione can be directly obtained exogenously from food sources, the majority is synthesized from the amino acids glutamate, cysteine and glycine within the cytosol; a process which requires the consecutive actions of the enzymes glutamate cysteine synthase and glutathione synthase (Maher, 2005). In its reduced state, GSH acts as an electron donor during periods of oxidative stress, forming glutathione disulfide (GSSG) in the reduction of H_2O_2 by the reaction catalysed by the antioxidant enzyme glutathione peroxidase (GPx) (Maher, 2005; Valko *et al.*, 2007). An accumulation of GSSG however can have a detrimental effect on cellular function therefore GSH can be regenerated from GSSG via the activity of the enzyme glutathione reductase (GR) (Maher, 2005). In addition to its role in the reduction of H_2O_2 , glutathione has other protective roles against oxidative stress. These include:

- 1- Assisting amino acid transport through the plasma membrane
- 2- Scavenging $\cdot\text{OH}$ and singlet oxygen directly
- 3- Regenerating important antioxidant vitamins C and E back to their active forms (Valko *et al.*, 2007).

1.8. Type 2 Diabetes Mellitus and Trace Elements:

Trace elements are chemicals that are required by organisms in very small amounts for apropos physiological and biochemical functioning (Vincent, 2000). Every one of trace element contributes differently in many important physiological and biochemical processes in the body, the interaction between trace elements in biological processes play a role in mediating biological and chemical reactions which could be applied to the management of human health (Rasdi *et al.*, 2013).

Although trace elements are essential micronutrients, which benefit organisms that are exposed within certain remedial ranges, at larger doses they may cause a biological damage (Vincent, 2000).

1.8.1. Chromium (Cr):

Chromium is an essential trace element which necessary for glucose and lipid metabolism (Larsen, 1993). It is distributed widely in the body, with the highest levels being found in the kidney, liver, spleen, and bone. Biologic role of chromium was initially thought that chromium potentiated the actions of insulin as part of an organic complex, glucose tolerance factor (GTF) (Imlay and Linn, 1988).

Chromium may function as part of the oligopeptide low-molecular weight chromium (LMWCr)-binding substance (MW=1.500 Da), which is composed of glycine, cysteine, glutamic acid, and aspartic acid. The principal carrier protein for chromium is transferrin, which also plays a major role in the movement of chromium from blood to LMWCr. It has been suggested that migration of transferrin receptors to the plasma membranes of insulin-insensitive cells after the stimulation of insulin receptors is the initial step in this process. Transferrin containing the plasma bound chromium is bound to the transferrin receptors, chromium is released from transferrin, and the resulting free chromium is postulated to be sequestered by LMWCr (Halliwell and Gutteridge, 1992). In this step, chromium is transferred from transferrin to LMWCr, which exists in insulin-dependent cells in the apo, or inactive, form. Binding with chromium ions converts inactive LMWCr to its holo, or active form. It is proposed that LMWCr participates as part of an insulin signal amplification system (figure1-6) (Halliwell and Gutteridge, 1992) as it is bound to insulin-activated insulin receptors. The result of this process is

the activation of insulin receptor kinase and potentiation of the actions of insulin (Fernandez-Real *et al.*, 2005).

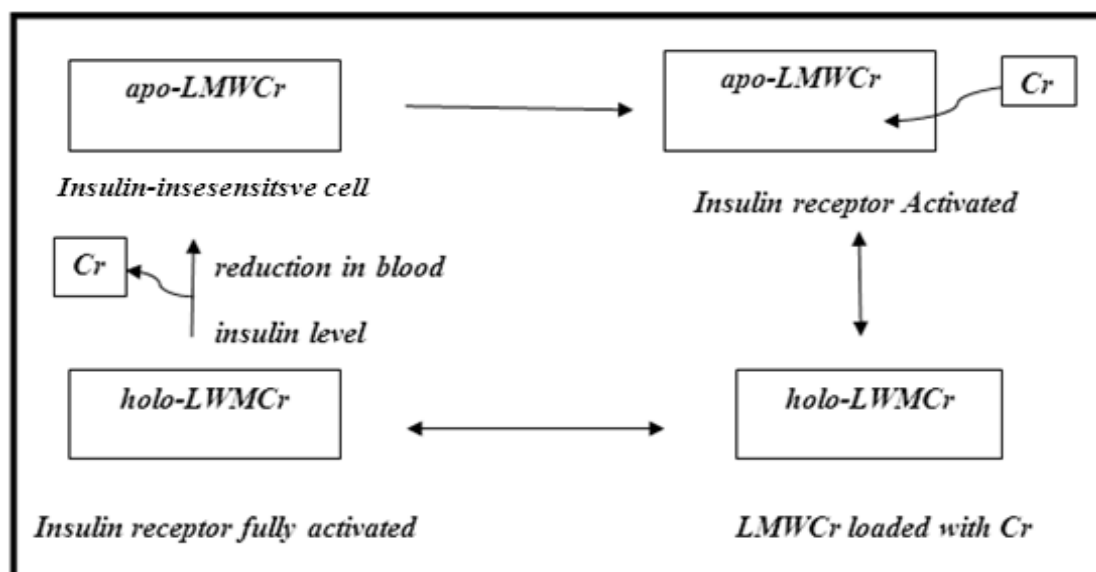


Figure (1-6): Proposed mechanism of action for chromium and LMWCr potentiating the action of Insulin (Fernandez-Real *et al.*, 2005).

1.8.2. Selenium (Se):

Selenium is an essential trace element in human body. It is readily absorbed from the gastrointestinal tract. Selenium has been found to perform a variety of functions. The main one is its role as an antioxidant against oxidative stress produced by free radical activities. Furthermore, selenium gives glutathione peroxidase enzyme the activity to scavenge hydrogen peroxide, the highly active oxygen material (Awasthi *et al.*, 1975). Also, selenium plays an essential role in the control of thyroid hormone (Berry and Larson, 1992).

selenium can protect the body from the toxic effect of heavy metals (Harr and Muth, 1972).

Aims of study

Aims of Study

The present study was designed to shed light on the following aims:

First: To evaluate the synergistic effect of type 2 diabetes mellitus and metabolic syndrome on the following status :

- 1- Fasting blood glucose levels and HbA_{1c} ratio.
- 2- Serum lipid profile.
- 3- Serum oxidant–antioxidant status.
- 4- Serum chromium and selenium.

Second: Studying the above parameters according to some variables Age, BMI, and Sex.

Chapter Two

Materials and Methods

2- Materials and Methods

2.1. Design of Study:

This study is conducted at the Center of Diabetes and Endocrine Glands in Thi-Qar, Biochemistry Laboratory in the College of Science (University of Thi-Qar) at the period between (November, 2016) to (May, 2017). The study included (150) subjects, (50) controls and (100) patients. The ranging of duration of disease from (1-3 years), period of drug consumption ranging from (1-3 years) and all of them take metformin (500 mg) twice daily as treatment. It is notable that the smokers were excluded.

The controls and patients were divided into the groups:

- 1- Control group:** included fifty (50) supposed healthy subjects aged (41-70 years).
- 2- DM group:** included sixty four (64) patients with type 2 diabetes mellitus aged (41-70 years).
- 3- DMMS group:** included thirty six (36) patients with type 2 diabetes mellitus and metabolic syndrome aged (41-70 years).

The major groups were divided into subgroups according to Age, BMI, Sex as shown in tables (2-1) (2-2) (2-3):

Table (2-1): Data of all Age groups

Age groups	Age (years)	No. Control	No. DM	No. DMMS
A1	41-50	21	23	07
A2	51-60	19	18	18
A3	61-70	10	23	11

Table (2-2): Data of all BMI groups

BMI groups	BMI range	No. Control	No. DM	No. DMMS
Normal range	18.5-24.99	22	13	0.0
Overweight	25-29.99	18	27	17
Obese	≥ 30	10	24	19

Table (2-3): Data of all Sex groups

Sex groups	No. Control	No. DM	No. DMMS
Male	20	34	12
Female	30	30	24

2.2. Collection of Blood Samples:

After an overnight fasting for about 8 hr, (10 mL) of venous blood was collected from type 2 diabetic patients with, without metabolic syndrome and controls, then divided into the following:

A- 2 ml of blood sample was transferred to tubes containing EDTA (Ethylene diamine tetra acetic acid) and used for HbA_{1c} estimation.

B- 8 ml were transferred to plain tube and allowed to clot at room temperature to get serum by putting it in empty disposable tubes and centrifuged to separate it at 3000 rotor per minute (rpm) for 10 min, the serum samples were separated and stored at (-20°C) for later measurement biochemical parameters, unless used immediately. The clinical chart of this study describe experimental parameters in the table (2-4).

Table (2-4): The clinical chart of the study

Patient Profile	
Name:	
Age:	
Sex:	
BMI (Kg/m ²)	Weight
	Length
Waist circumference:	
Blood pressure:	
Duration of disease:	
Drug used:	
Duration of treatment:	
Smoking:	
Other disease:	
Biochemical Parameters	
Fasting Blood Glucose (FBG)	
Hemoglobin A _{1c} Ratio (HbA _{1c} %)	
Lipid Profile	Triglyceride (TG) Total Cholesterol (TC) High Density Lipoprotein-Cholesterol (HDL-c)
Lipid Peroxidation	Malondialdehyde (MDA)
Antioxidants	Albumin (Alb) Glutathione (GSH)
Trace Elements	Chromium (Cr) Selenium (Se)

2.3. Chemicals:

The chemicals used in this study with their companies which are showed in table (2-5).

Table (2-5):The chemicals and their suppliers

No.	Chemicals	Supplied Company
1.	Albumin Kit	Biolabo, France
2.	Cholesterol Kit	Biolabo, France
3.	Glucose Kit	Randox, England
4.	HbA _{1c} Kit	Germany
5.	HDL-c Kit	Biolabo, France
6.	Hydrochloric acid	BDH, England
7.	Nitric acid	BDH, England
8.	Perchloric acid	BDH, England
9.	Sodium phosphate acidic	Fluka, Switzerland
10.	Sodium phosphate basic	Fluka, Switzerland
11.	Thiobarabitoric acid (TBA)	BDH, England
12.	Trichloro acetic acid (TCA)	BDH, England
13.	Triglyceride Kit	Biolabo, France
14.	5,5-dithio-bis (2-nitrobenzoic acid) (DTNB)	Fluka, Switzerland

2.4. Instruments:

The instruments are available in the Laboratories of Chemistry Department in the College of Science (University of Thi-Qar) and in the Center of Diabetes and Endocrine Glands which are shown in table (2-6).

Table (2- 6): The instruments and their manufacturers

No.	Instruments	Manufacturers
1.	Atomic absorption spectrophotometer	Shimadzu, Japan
2.	Centrifuge	Universal 16A , Germany
3.	HbA _{1C} analyzer	Nycocard TM , Germany
4.	Incubator	Jard, Japan
5.	Mixer	China
6.	Oil bath	L513-0814, French
7.	pH Meter	PW-9421 Philips, England
8.	Sensitive balance	MO.12307078, Japan
9.	UV/VIS spectrophotometer	T 60, PG Instruments Ltd, Germany
10.	Water bath	L513-0814, French

2.5. Biochemical Parameters:

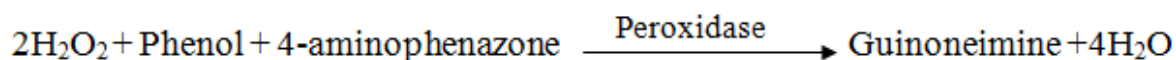
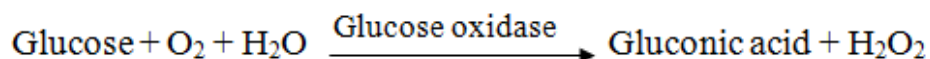
Several considerable methods were used to measure the studied parameters. It is notable that all measurements were duplicated for each sample.

2.5.1. Determination of Blood Glucose Concentration:

Principle: (Trinder, 1969)

Glucose was determined after enzymatic oxidation in the presence of glucose oxidase . The hydrogen peroxide formed reacts under catalysis of peroxidase, with phenol and 4-aminophenazone to form a red-violet quinoneimine dye as indicator.

Reaction scheme was as follows

**Reagents:**

Reagent	Contents	Concentrations
R1: Buffer	Phosphate Buffer Phenol	0.1 mol/L 11 mmol/L
R2: Enzymes	Glucose Oxidase Peroxidase 4-aminophenozone	≥ 1.5 KU/L ≥ 1.5 KU/L 0.77 mmol/L
R3: standard	Glucose	98 mg/dL

Procedure:

	Blank	Standard	Assay
Reagent	1mL	1mL	1mL
Standard	-----	10 μ L	-----
Specimen	-----	-----	10 μ L

Tubes were mixed. Let stand for 5 min at 37 °C or 10 min at room temperature. The absorbance was recorded at 500 nm against reagent blank

Calculation:

The concentration of glucose was calculated as follows:

$$\text{Glucose Conc. (mg/dL)} = \frac{\text{Abs (Assay)}}{\text{Abs (Standard)}} \times 98 \text{ (standard concentration)}$$

2.5.2. Determination of Hemoglobin A_{1c} Ratio:

Nycocard™ HbA_{1c} analyzer is an *in vitro* diagnostic medical device for quantitative determination of HbA_{1c} in human whole blood. For monitoring of long term metabolic control in persons with diabetes mellitus (Lenzi *et al.*, 1987 ; Sacks *et al.*, 2011).

Reagents:

Reagent	Contents
R1: Glycinamide buffer	Dye-bound boronic acid and detergents 0.2 mL
R2: Washing Solution	Morpholine buffered NaCl solution and Detergent 2.0 mL

Procedure:

5µL of whole blood was added to the test tube with R1 Mixed well. Leaved the tube for 3 minutes. Remixed to obtain a homogenous suspension. 25 µL of the mixture were applied to a test device. Allowed the mixture to soak completely into the membrane. Waited for minimum 10 seconds. 25 µL of R2 were applied to the test device. Allowed the reagent to soak completely into the membrane. Waited for minimum 10 seconds. Read the test result within 5 minutes using the Nycocard™ HbA_{1c} analyzer (Lenzi *et al.*, 1987).

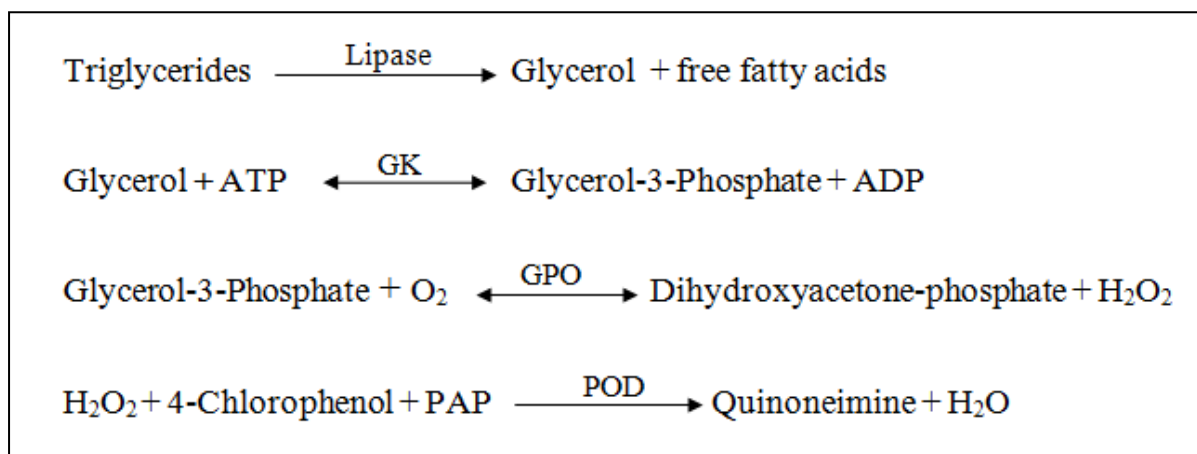
2.5.3. Determination of Serum Lipid Profile:

2.5.3.1. Determination of Serum Triglyceride Concentration:

Principle: (Trinder, 1969 ; Fossati and Prencipe, 1982)

Fossati and Prencipe method associated with Trinder reaction.

Reaction scheme was as follows:



Reagents:

Reagent	Contents	Concentrations
R1: Buffer	Pipes	100 mmol/L
	Magnesium chloride	9.8 mmol/L
	Chloro-4-phenol	3.5 mmol/L
R2: Enzymes	Lipase	≥ 1000 IU/L
	Peroxidase (POD)	≥ 1700 IU/L
	Glycerol-3-phosphate oxidase (GPO)	≥ 3000 IU/L
	Glycerol kinase (GK)	≥ 660 IU/L
	4-amino-antipyrine	0.5 mmol/L
	Adenosine triphosphate (ATP)	1.3 mmol/L
R3: Standard	Triglycerides	200 mg/dL

Procedure:

	Blank	Standard	Assay
Reagent	1 mL	1 mL	1 mL
Distilled water (D.W)	10 μ L	-----	-----
Standard	-----	10 μ L	-----
Specimen	-----	-----	10 μ L
Tubes were mixed. Let stand for 5 min at 37°C or 10 min at room temperature. The absorbance was recorded at 500 nm against reagent blank.			

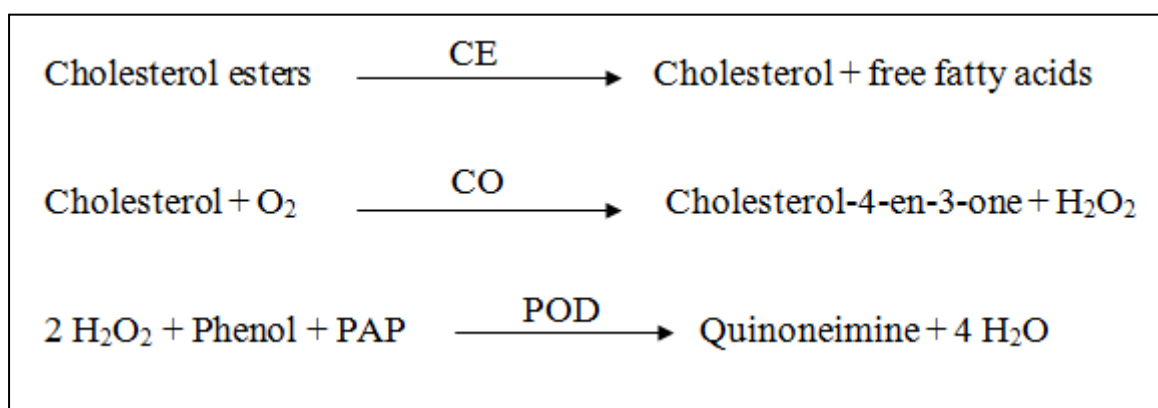
Calculation:

The concentration of serum TG was calculated as follows:

$$\text{TG Conc. (mg /dL)} = \frac{\text{Abs (Assay)}}{\text{Abs (Standard)}} \times 200 \text{ (standard concentration)}$$

2.5.3.2. Determination of Serum Total Cholesterol Concentration:**Principle:**

Enzymatic method described by (Allian *et al.*, 1974). Reaction scheme was as follows:



Reagents:

Reagent	Contents	Concentrations
R1: Buffer	Phosphate buffer	100 mmol/L
	Chloro-4-phenol	5 mmol/L
	Sodium cholate	2.3 mmol/L
	Triton x 100	1.5 mmol/L
R2: Enzymes	Cholesterol oxidase (CO)	≥ 100 IU/L
	Cholesterol esterase (CE)	≥ 170 IU/L
	Peroxidase (POD)	≥ 1200 IU/L
	4-Amino-antipyrine	0.25 mmol/L
	Poly Ethylene Glycol (PEG) 6000	167 μmol/L
R3: Standard	Cholesterol	200 mg/dL

Procedure:

	Blank	Standard	Assay
Reagent	1 mL	1 mL	1 mL
D.W	10 μL	-----	-----
Standard	-----	10 μL	-----
Specimen	-----	-----	10 μL
Tubes were mixed. Let stand for 5 min at 37°C or 10 min at room temperature. The absorbance was recorded at 500 nm against reagent blank.			

Calculation:

The concentration of serum TC was calculated as follows:

$$\text{TC Conc. (mg /dL)} = \frac{\text{Abs (Assay)}}{\text{Abs (Standard)}} \times 200 \text{ (standard concentration)}$$

2.5.3.3. Determination of Serum HDL-c Concentration:**Principle:** (Tietz, 1999)

Low density lipoproteins, very low density lipoproteins and chylomicrons from the sample are precipitated by phosphotungstic acid and magnesium chloride. HDL obtained in supernatant after centrifugation is then measured with total cholesterol reagent.

Reagents:

Reagent	Contents	Concentrations
R1: Precipitant	Phosphotungstic acid	13.9 mmol/L
	Magnesium chloride	570 mmol/L
R2: Standard	Cholesterol	100 mg/dL

Procedure:

Pipetted in centrifuge	Micro method
Specimen	500 µL
Precipitant	50 µL
Tubes were mixed. Let stand for 5 min at 37°C or 10 min at room temperature, then centrifuged for 15 min at 4000 rpm.	

	Blank	Standard	Assay
Reagent (Cholesterol)	1 mL	1 mL	1 mL
D.W	25 µL	-----	-----
Standard	-----	25 µL	-----
Supernatant (HDL)	-----	-----	25 µL

Tubes were mixed. Let stand for 5 min at 37°C or 10 min at room temperature. The absorbance was recorded at 500 nm against reagent blank.

Calculation:

The concentration of serum HDL-c was calculated as follows:

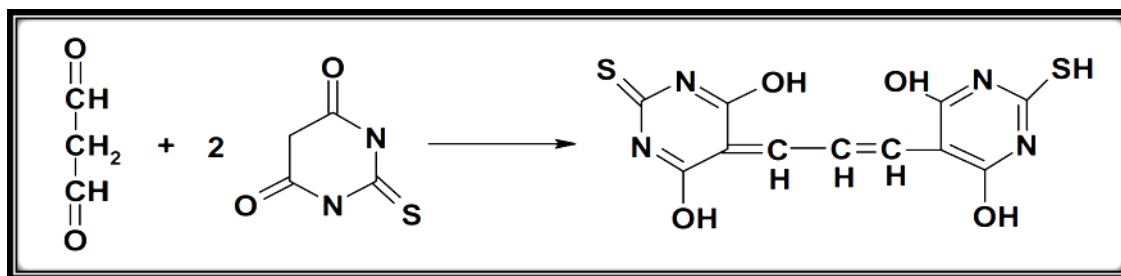
$$\text{HDL-c Conc. (mg /dL)} = \frac{\text{Abs (Assay)}}{\text{Abs (Standard)}} \times 100 (\text{standard concentration}) \times 1.1$$

2.5.4. Determination of Oxidative Stress Parameters:

2.5.4.1. Determination of Serum Malondialdehyde Concentration:

Principle:

Lipid peroxidation was determined by using the thiobarbituric acid method. In this method, Malondialdehyde formed from the breakdown of polyunsaturated fatty acids were identified as the product of LPO that react with thiobarbituric acid, in coexisting trichloro acetic acid, to give a red chromophore absorbing at 532 nm (Fong *et al.*, 1973). MDA concentration were calculated, using the molar extinction coefficient of MDA (ϵ MDA) equal to $1.56 \times 10^5 \text{ mol}^{-1} \text{L cm}^{-1}$ (Wills, 1969). MDA formed from breakdown of polyunsaturated fatty acid, serves as a convenient index of peroxidation reaction.



Procedure:

The level of serum MDA was determined spectrophotometrically with a TBA solution. In brief, to 150 μ L serum sample the following were added: 1mL (17.5%) TCA and 1mL of 0.66% TBA, mixed well by vortex, incubated in boiling water for 15 minutes, and then allowed to cool. One mL of 70% TCA was added and the mixture was allowed to stand at room temperature for 20 minutes, and centrifuged at 2000 rpm for 15 minutes; the supernatant was taken out for scanning spectrophotometrically at 532nm (Muslihet *et al.*, 2002).

Calculation:

The concentration of serum MDA was calculated as follows:

$$\text{MDA Conc. } \left(\frac{\mu\text{mol}}{\text{L}} \right) = \frac{\text{Abs at 532 nm}}{L \times \epsilon} \times D \times 10^6$$

Where:

L: Light path (1cm)

ϵ : Molar Extinction coefficient $1.56 \times 10^5 \text{ mol}^{-1} \text{ L cm}^{-1}$

D: Dilution factor = 21

2.5.4.2. Determination of Antioxidant Parameters:**2.5.4.2.1. Determination of Serum Albumin Concentration:****Principle:** (Webster, 1974)

One of the most important serum proteins produced in the liver is albumin. There are techniques which have been developed to determine Alb concentration. The simplest technique is the bromocresol green (BCG) method, colorimetric method. The principle of measurement is based on the relatively high affinity of BCG towards Alb. Albumin in the presence of BCG at a slightly acid pH = 4.2, produces a color change of the indicator from yellow green to green-blue. The intensity of the color formed is proportional to the Alb concentration in the sample, serum or plasma free of hemolytic.

Reagents:

Reagent	Contents	Concentrations
R1: Bromocresol Green	Succinic acid Bromocresol green Sodium hydroxide Polyoxyethylene monolauryl ether	83 mmol/L 167 μ mol/L 50 mmol/L 1 gm/L
R2: Standard	Albumin	50 g/L

Procedure:

	Blank	Standard	Assay
Reagent	2mL	2mL	2mL
D.W	10 µL	-----	-----
Standard	-----	10 µL	-----
Specimen	-----	-----	10 µL
Mixed well. Record absorbance at (630) nm within 3 min against reagent blank.			

Calculation:

The concentration of serum Alb was calculated as follows:

$$\text{Alb Conc. (g / L)} = \frac{\text{Abs (Assay)}}{\text{Abs (Standard)}} \times 50 \text{ (standard concentration)}$$

2.5.4.2.2. Determination of Serum Glutathione Concentration:

Principle: (Ellman, 1959).

This method depend on the reaction of 5,5-Dithio-bis (2-nitrobenzoic acid) (DTNB) with aliphatic thiol compounds at pH=8 to produce one mole of p-nitrothiol phenol anion per mole thiol. Since this anion highly colored ($\epsilon=13600$ at 420 nm), it can be used to measure the thiol concentration

Reagents:

R1: Phosphate buffer solution with pH =7 and the concentration of 0.2 M consists of:

-The solution A: Solution of Sodium phosphate acidic (NaH_2PO_4) with 0.2 M is prepared by melting 2.4 g of (NaH_2PO_4) into an amount of water and completed to 100 mL.

-The solution B: Solution of Sodium phosphate basic (Na_2HPO_4) with 0.2 M is Prepared by melting 2.83 g of (Na_2HPO_4) into an amount of water and completed to 100 mL.

R1 is prepared by mixing 19.5 mL of the solution A with 30.5 mL of the solution B and completed to 100 mL by distilled water.

R2: Phosphate buffer solution with pH=8 and the concentration of 0.2 M this buffer solution is prepared by mixing 2.62 mL of 0.2 M (NaH_2PO_4) with 47.38 mL of 0.2 M (Na_2HPO_4) and completed to 100 mL by distilled water.

R3: DTNB solution which is prepared by melting 39.6 mg of DTNB into 10 mL of the R1.

Procedure:

- 1- Adding 20 μL of the serum to 9 mL of water.
- 2- Adding 1 mL of R2 to the solution.
- 3- Mixing 3 mL of the previous solution with 20 μL of R3.
- 4- Keeping the result solution for 60 seconds at the room temperature.
- 5- Preparing the equivalent solution (Blank) as the steps 1 and 2.
- 6- Measuring the absorbance of the result solution by using optical spectrum at the wavelength of 420 nm.

Calculation:

The concentration of serum GSH was calculated as follows:

$$GSH(\mu\text{mol/L}) = (T - B) \times \frac{D}{\varepsilon} \times 1000$$

Where:

T: Absorbance of the solution

B: Absorbance of the equivalent solution (Blank)

D: Dilution factor = 501

ε: Molar Extinction Coefficient equal to $13600 \text{ mol}^{-1} \text{ L cm}^{-1}$

$$\frac{D}{\varepsilon} = 36.8 \times 10^{-3}$$

2.5.5. Determination of Serum Chromium and Selenium Concentrations:**Principle:**

Concentrations of two elements in serum samples were measured by flame atomic absorption method. In this method, light of hollow cathode (HC) lamp is absorbed by ground state atoms in a lean air-acetylene flame. The amount of light absorbed is directly proportional to the concentration of atoms in the gaseous state in the light path and hence to the concentration of chromium and selenium in the solution.

Digestion of samples:

The serum samples were digested by adding 2 mL of conc. nitric acid and 1 mL of conc. Perchloric acid to 0.5 mL serum in Pyrex tube. Heated for 1 hour at 160 °C using oil bath, then samples were cooled, and the volume was completed to 10 mL by 0.3 N hydrochloric acid.

2.6. Statistical Analysis:

The statistical analysis was done by using Microsoft Excel 2010. The results were expressed as mean $\pm$ standard deviation (mean $\pm$ SD) with LSD test. One way analysis of variance (ANOVA) was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

Chapter Three

Results and Discussion

3. Results and Discussion

3.1. Clinical and Characteristic Features of the Studied Groups:

There are 150 subjects included in the present study, with difference in clinical characteristic type 2 diabetes with and without metabolic syndrome patients groups and control group. Characteristic data for all studied groups shown in table (3-1).

Table (3-1): Characteristic data for studied groups

Characteristic							
Groups	No.	Sex (M/F)	Age (years) Mean $\pm$ SD	BMI (Kg/m ²) Mean $\pm$ SD	DBP (mm Hg) Mean $\pm$ SD	SBP (mm Hg) Mean $\pm$ SD	Waist circumference (inch) Mean $\pm$ SD
Control	50	20/30	50.34 $\pm$ 7.50	24.12 $\pm$ 3.26	78.30 $\pm$ 5.71	118.22 $\pm$ 10.43	33 $\pm$ 4.25
DM	64	34/30	55.12 $\pm$ 8.89	27.81 $\pm$ 2.32	82.85 $\pm$ 6.36	126.63 $\pm$ 13.68	39 $\pm$ 4.16
DMMS	36	12/24	56.26 $\pm$ 7.59	33.88 $\pm$ 3.65	87.36 $\pm$ 6.35	160.88 $\pm$ 16.76	44 $\pm$ 5.32

-**No**: Number of subjects

-**DM**: Type 2 diabetic patients group

-**DMMS**: Type 2 diabetic with metabolic syndrome patients group

-**DBP**: Diastolic blood pressure

-**SBP**: Systolic blood pressure

3.2. General Comparison for all Studied Parameters:

3.2.1. Fasting Blood Glucose Concentration:

Table (3-2) shows a significant increase in the concentration of FBG in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant increase in the concentration of FBG in DMMS group in comparison with the DM group ($P \leq 0.05$). This result matched with the results of study of (Pizent *et al.*, 2010).

A significant increase in the concentration of FBG in DMMS group is clear because all patients with metabolic syndrome are diabetics type 2. A group of experts tried to develop the common definition of the metabolic syndrome to become more acceptable on a large scale, from the definitions given by the WHO, which is the first organization to propose the criteria for determining metabolic syndrome in 1999, where this organization requires in the diagnosis of metabolic syndrome to substantiate insulin resistance (diagnosed DM 2) through elevation of fasting blood glucose (WHO, 1999).

Table (3 – 2): FBG concentrations

Groups	No.	FBG concentrations (mg/dL) Mean $\pm$ SD
Control	50	89.38 $\pm$ 12.53 ^C
DM	64	192.32 $\pm$ 60.31 ^B
DMMS	36	207.75 $\pm$ 67.87 ^A
LSD		14.37

Note: Each value represents mean $\pm$ S.D values with non-identical superscript (A , B or C...etc.) , were considered significantly differences ($P \leq 0.05$).

-SD: Standard deviation

-LSD: Least Significant Difference

3.2.2. Hemoglobin A_{1c} Ratio:

Table (3-3) shows a significant increase in the ratio of HbA_{1c} in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant increase in the ratio of HbA_{1c} in DMMS group in comparison with the DM group ($P \leq 0.05$). This result matched with the results of study of (Sang *et al.*, 2012).

High concentrations of glucose can increase the glycation of common proteins such as hemoglobin, forming HbA_{1c}. However, it is important to note that HbA_{1c} is neither considered dysfunctional nor harmful. The concentration of the HbA_{1c} predicts diabetes complications because it reflects more harmful glycation sequelae of diabetes, such as retinopathy and nephropathy, which are understood to be due to harmful advanced glycation end products (Castilho *et al.*, 2003).

Table (3 – 3): Hemoglobin A_{1c} ratio

Groups	No.	HbA _{1c} (%) Mean $\pm$ SD
Control	50	5.62 $\pm$ 0.39 ^C
DM	64	8.85 $\pm$ 1.72 ^B
DMMS	36	12.10 $\pm$ 1.79 ^A
LSD		3.11

- Legend as in table (3-2)

3.2.3. Serum Lipid Profile Concentrations:

3.2.3.1. Serum Triglyceride Concentration:

Table (3-4) shows a significant increase in the concentration of serum TG in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant increase in the concentration of TG in DMMS group in comparison with the DM group ($P \leq 0.05$). This increase is not surprising because elevated serum TG levels, and lipid abnormality is an important component of the metabolic syndrome. This result matched with the results of study of (Grundy, 1998) who reported that hypertriglyceridemia commonly occurs along with other components of the metabolic syndrome.

Many investigations reveal that hypertriglyceridemia is closely linked to insulin resistance (Steiner, 1994 ; Despres, 1998) where (Mostaza *et al.*, 1998) found that patients with primary hypertriglyceridemia have an elevated turnover rate of nonesterified fatty acids. This elevation suggests that patients with primary hypertriglyceridemia have insulin resistance at the level of adipose tissue. Considerable study has also indicated an important predictive role of increased serum TG levels contributing to the risk for CHD, especially patients with type 2 diabetes (Ahmad *et al.*, 2005).

3.2.3.2. Serum Total Cholesterol Concentration:

Table (3-4) shows a significant increase in the concentration of serum TC in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant increase in the concentration of serum TC in DMMS group in comparison with the DM group ($P \leq 0.05$). This result matched with the results of study of (Abdoljalal *et al.*, 2015).

The low level of HDL-c in diabetic patients may increase the risk of atherosclerosis due to the important role played by HDL-c in the transfer of cholesterol from the cells of the body to the liver and thus reduce blood cholesterol. The low level of HDL-c in diabetic patients leads to increased cholesterol levels in the blood (Genest *et al.*, 1995).

3.2.3.3. Serum HDL-c Concentration:

Table (3-4) shows a significant decrease in the concentration of serum HDL-c in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant decrease in the concentration of serum HDL-c in DMMS group in comparison with the DM group ($P \leq 0.05$). This result matched with the results of study of (Pizent *et al.*, 2010).

This decrease in serum HDL-c levels may be due to increase in cholesterol ester transfer protein (CETP) activity, which transports cholesterol from the HDL-c to VLDL-c, leaving HDL-c rich in triglycerides and less familiar to apolipoprotein-A, leaving it free to be easily filtered by the kidney. Moreover the decrease in serum HDL-c levels may be due to either increase activity of hepatic lipase (Wafa *et al.*, 2012) or changes in liver function, which inhibit the production of apolipoprotein-A1, which is the main protein for HDL-c (Sayran, 2012).

The low level of HDL-c in diabetic patients may increase the risk of atherosclerosis due to the important role played by HDL-c in the transfer of cholesterol from the cells of the body to the liver and thus reduce blood cholesterol (Genest *et al.*, 1995).

Table (3-4): Lipid profile concentrations for studied groups.

Groups	No.	TG concentrations (mg/dL) Mean $\pm$ SD	TC concentrations (mg/dL) Mean $\pm$ SD	HDL-c concentrations (mg/dL) Mean $\pm$ SD
Control	50	122.53 $\pm$ 38.77 ^C	168.13 $\pm$ 45.17 ^C	51.12 $\pm$ 6.38 ^A
DM	64	137.67 $\pm$ 42.56 ^B	187.65 $\pm$ 42.00 ^B	43.61 $\pm$ 5.41 ^B
DMMS	36	190.14 $\pm$ 58.96 ^A	213.46 $\pm$ 37.87 ^A	34.26 $\pm$ 5.47 ^C
LSD		8.93	13.25	4.62

- Legend as in table (3-2)

3.2.4. Oxidative Stress:

3.2.4.1. Lipid Peroxidation Status (Malondialdehyde):

Table (3-5) shows a significant increase in the concentration of serum MDA in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant increase in the concentration of serum MDA in DMMS group in comparison with the DM group ($P \leq 0.05$). This result matched with the results of study of (Demircan *et al.*, 2008) who observed that MDA levels are higher in MS patients, asserting the hypothesis that oxidative stress is involved in the pathogenesis of this syndrome.

Moreover, oxidative stress plays an important role in the development of cardiovascular diseases (CVD) and diabetes by imbalance of ROS production, and has close relationship with inflammation. It was observed that the lipid peroxidation are increased in patients with MS and it is directly related with the development of atherosclerosis together with establishment of pro-inflammatory state (Jialal *et al.*, 2012 ; Yubero *et al.*, 2013). Also, diabetes can be considered as a pro-oxidant state caused by increased lipid oxidation (Devaraj *et al.*, 2008). Hyperglycemia generates ROS, which in turn cause damage to the cells in many ways. Damage to the cells ultimately results in secondary complications in diabetes mellitus (Ramachandran *et al.*, 2010).

3.2.4.2. Antioxidant System:

3.2.4.2.1. Serum Albumin Concentration:

Table (3-5) shows a significant decrease in the concentration of serum Alb in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant decrease in the concentration of serum Alb in DMMS group in comparison with the DM group ($P \leq 0.05$). This result matched with the results of study of (Wolff *et al.*, 1991). These decreasing are due to the increase of the

synthesis of lipid peroxide and increase formation of free radicals which result in increasing of membranes permeability and leaking the proteins outside the vascular system (Vlassara *et al.*, 1981). In this study, the focus was on the antioxidant activity of Alb because oxidative stress is thought to play a significant role in the pathogenesis of many diseases, including type 2 diabetes and metabolic syndrome.

3.2.4.2.2. Serum Glutathione Concentration:

Table (3-5) shows a significant decrease in the concentration of serum GSH in all patients groups in comparison with the control group ($P \leq 0.05$). There is a significant decrease in the concentration of serum GSH in DMMS group in comparison with the DM group ($P \leq 0.05$).

Hyperglycemia causes an increase in reactive oxygen metabolites and their derivatives (Ceriello and Giugliano, 2001). Since GSH is an important antioxidant, GSH deficiency causes increase in the oxidative stress (Seghrouchni *et al.*, 2002). Hyperglycemia induced oxidative stress and reduction in the levels of GSH in the vascular straight muscles (Powell *et al.*, 2001).

Table (3-5): Oxidative stress for studied groups.

Groups	No.	MDA concentrations ($\mu\text{mol/L}$) Mean $\pm$ SD	Alb concentrations (g/L) Mean $\pm$ SD	GSH concentrations ($\mu\text{mol/L}$) Mean $\pm$ SD
Control	50	1.75 ± 0.35^C	4.42 ± 0.44^A	342.16 ± 34.16^A
DM	64	3.11 ± 0.76^B	4.10 ± 0.28^B	227.92 ± 17.62^B
DMMS	36	4.22 ± 0.85^A	3.64 ± 0.37^C	201.23 ± 19.81^C
LSD		0.32	0.24	18.43

- Legend as in table (3-2)

3.2.5. Serum Trace Elements Concentrations:

3.2.5.1. Serum Chromium Concentration:

Table (3-6) shows a significant decrease in the concentration of serum chromium in all patients groups in comparison with the control group ($P \leq 0.05$). There is no significant difference in the concentration of serum chromium between DMMS group and DM group ($P \leq 0.05$). This result matched with many considerable reports (Ekmekcioglu *et al.*, 2001; Davies *et al.*, 2004; Stupar *et al.*, 2007) that tightly suggest the low concentrations of chromium in serum are significantly correlated with diabetes mellitus.

Some studies (Liu *et al.*, 2000 ; Rajpathak *et al.*, 2004) have reported a relation between type 2 diabetes and chromium concentrations in serum, where (Rukgauer and Zeyfang, 2002) reported that type 2 diabetes patients have lower concentrations of serum chromium. (Davies *et al.*, 2004) compared the serum chromium concentration in patients with type 2 diabetes and the control and reported that the decreased serum chromium concentration play a major role in the development of diabetes. However, the decrease in the concentration of chromium plays an important role in increasing concentration of glucose because it has an effective role on the insulin action.

3.2.5.2. Serum Selenium Concentration:

Table (3-6) shows a significant decrease in the concentration of serum selenium in all patients groups in comparison with the control group ($P \leq 0.05$). There is no significant difference in the concentration of serum selenium between DMMS group and DM group ($P \leq 0.05$).

Patients with DM have significantly lower serum selenium concentrations compared with healthy subjects (Zhao *et al.*, 2008 ; Joshi *et al.*, 2011). Antioxidants in non-diabetic individuals can mitigate free radical-mediated

oxidative stress, but in the chronic hyperglycemia state, increased free radical production may lead to the overconsumption of chain-breaking antioxidants, elevated lipid peroxidation, and enhanced oxidative stress (Whiting *et al.*, 2008).

Selenium is believed to be one of the most important antioxidant nutrients in the human body, and selenoproteins have a protective effect against oxidative stress and inflammation (Rayman, 2012; Rayman and Stranges, 2013). However, the low selenium status measured in DM populations of some case studies might be caused by the disease and its association with inflammation. Other previous studies have suggested that the inflammatory response decreases the expression of selenoprotein P and reduces serum selenium concentrations (Nichol *et al.*, 1998 ; Hesse-Bahr *et al.*, 2000).

Table (3-6): Trace elements concentrations for studied groups.

Groups	No.	Chromium concentrations (µg/L) Mean ± SD	Selenium concentrations (µg/L) Mean ± SD
Control	50	0.52 ±0.11 ^A	135 ±12.11 ^A
DM	64	0.33 ±0.08 ^B	112±14.25 ^B
DMMS	36	0.30±0.07 ^B	108±12.87 ^B
LSD		0.06	10.21

- Legend as in table (3-2)

3.3. Effect of Age on Studied Parameters:

3.3.1. Fasting Blood Glucose Concentration:

Table (3–7) shows a significant increase in the concentration of FBG in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant increase in the concentration of FBG in the Cont-A3 and Cont-A2 groups in comparison with the Cont-A1 group ($p \leq 0.05$). This results show no significant difference in the concentration of FBG between Cont-A3 group and Cont-A2 group ($p \leq 0.05$).

In the DM age groups there is a significant increase in the concentration of FBG in the DM-A3 and DM-A2 groups in comparison with the DM-A1 group ($p \leq 0.05$). The results obtained in this study show a significant increase in the concentration of FBG in the DM-A3 group in comparison with the DM-A2 group.

In the DMMS age groups there is a significant increase in the concentration of FBG in the DMMS-A3 and DMMS-A2 groups in comparison with the DMMS-A1 group ($p \leq 0.05$). Results of the present study show no significant difference in the concentration of FBG between DMMS-A3 group and DMMS-A2 group.

(George and Sivakami, 2004) reports the glucose to be central to the phenomenon of aging and age-related diseases for the reason that the symptoms manifested in natural aging like cataract are similar to those resulting from hyperglycemia. Apparently the resultant hyperglycemia will lead to the formation of more advanced glycosylation end products. Aging is a process of irreversible physiological changes associated with an increasing susceptibility to disease (Kasapoglu and Ozben, 2001). The main factors are that aging induces decrease insulin sensitivity and alteration or insufficient compensation of beta cell functional in the face of increasing insulin resistance (Chang and Halter, 2003). The decrease in beta cell proliferation capacity and enhanced sensitivity to apoptosis are the states related with aging (Maedler *et al.*, 2006).

Table (3-7): FBG concentrations for all age groups.

FBG concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	87.97 $\pm$ 8.35 ^{bB}	21	180.16 $\pm$ 53.14 ^{aC}	23	183.67 $\pm$ 54.32 ^{aB}	07	11.37
A2	90.17 $\pm$ 6.47 ^{cA}	19	189.73 $\pm$ 58.52 ^{bB}	18	210.72 $\pm$ 59.78 ^{aA}	18	13.72
A3	90.83 $\pm$ 10.51 ^{cA}	10	206.50 $\pm$ 57.63 ^{bA}	23	218.21 $\pm$ 63.16 ^{aA}	11	11.48
LSD	1.22		8.17		10.13		

Note: Each value represents mean $\pm$ S.D values with non-identical superscript (a , b or c ...etc.), were considered significantly differences ($P \leq 0.05$) to compare horizontally, and with non-identical superscript (A, B or C ...etc.), were considered significantly differences ($P \leq 0.05$) to compare vertically.

A1: First age group range from (41-50 years)

A2: Second age group range from (51-60 years)

A3: Third age group range from (61-70 years)

3.3.2. Hemoglobin A_{1c} Ratio:

Table (3–8) shows a significant increase in the ratio of HbA_{1c} in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant increase in the ratio of HbA_{1c} in the Cont-A3 and Cont-A2 groups in comparison with the Cont-A1 group ($p \leq 0.05$). This results show no significant difference in the ratio of HbA_{1c} between Cont-A3 group and Cont-A2 group ($p \leq 0.05$).

In the DM age groups there is a significant increase in the ratio of HbA_{1c} in the DM-A3 group in comparison with the DM-A2 and DM-A1 groups ($p \leq 0.05$). The

results obtained in this study show no significant difference in the ratio of HbA_{1c} between DM-A2 group and DM-A1 group ($p \leq 0.05$).

In the DMMS age groups there is a significant increase in the ratio of HbA_{1c} in the DMMS-A3 and DMMS-A2 groups in comparison with the DMMS-A1 group ($p \leq 0.05$). Results of the present study show no significant difference in the ratio of HbA_{1c} between DMMS-A3 group and DMMS-A2 group ($p \leq 0.05$).

Aging process can be faster because of accumulation of toxic metabolic products. These substances can be the products of non enzymatic glycosylation. Glycosylation may therefore play an important role in aging and has been implicated in the pathophysiology of number of diseases, like diabetes, Alzheimer disease, and lung diseases (Trypuc and Czerpak, 2007). Aging is also associated with many risk factors common to the sedentary lifestyle that are expected to be associated with elevated HbA_{1c} levels (Pani *et al.*, 2008).

Table (3–8): HbA_{1c} ratio for all age groups.

HbA _{1c} (%) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	5.28 $\pm$ 0.48 ^{CB}	21	7.92 $\pm$ 1.62 ^{BB}	23	11.17 $\pm$ 1.72 ^{AB}	07	2.53
A2	5.81 $\pm$ 0.32 ^{CA}	19	8.13 $\pm$ 1.93 ^{BB}	18	12.27 $\pm$ 1.42 ^{AA}	18	2.21
A3	5.97 $\pm$ 0.39 ^{BA}	10	10.34 $\pm$ 1.13 ^{AA}	23	12.41 $\pm$ 1.49 ^{AA}	11	4.08
LSD	0.37		0.72		0.94		

- Legend as in table (3-7)

3.3.3. Serum Lipid Profile Concentrations:

3.3.3.1. Serum Triglyceride Concentration:

Table (3–9) shows a significant increase in the concentration of serum TG in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant increase in the concentration of serum TG in the Cont-A3 group in comparison with the Cont-A2 and Cont-A1 groups ($p \leq 0.05$). This results show no significant difference in the concentration of serum TG between Cont-A2 group and Cont-A1 group ($p \leq 0.05$).

In the DM age groups there is a significant increase in the concentration of serum TG in the DM-A3 and DM-A2 groups in comparison with the DM-A1 group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum TG between DM-A3 group and DM-A2 group ($p \leq 0.05$).

In the DMMS age groups there is a significant increase in the concentration of serum TG in the DMMS-A3 group in comparison with the DMMS-A2 and DMMS-A1 groups ($p \leq 0.05$). Results of the present study show no significant difference in the concentration of serum TG between DMMS-A2 group and DMMS-A1 group ($p \leq 0.05$).

Aging is often associated with lipid metabolism disorders. Lipid metabolism disorders that are associated with aging process constitute the early stage in the emergence of a constellation of risk factors for metabolic disorders (Sawabe *et al.*, 2009 ; Gobal and Metha, 2010). With the increase of age the composition of body fat also increases, which especially accumulates in the abdomen triggering the incidence of central obesity. TG composition in the muscle and liver are higher in older age compared with younger age groups (Cree *et al.*, 2004). Increased body fat composition is associated with reduced fat oxidation both at rest and in activity (Nagy *et al.*, 1996). Thus, controlling triglycerides in middle-aged individuals should be targeted to prevent later onset of DM2. Hypertriglyceridemia is associated with an increased risk of cardiovascular events and acute pancreatitis (Robert *et al.*, 2007).

Table (3 –9): Serum TG concentrations for all age groups.

TG concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	120.52 $\pm$ 26.72 ^{cB}	21	130.00 $\pm$ 40.62 ^{bB}	23	179.11 $\pm$ 38.27 ^{aB}	07	8.87
A2	121.43 $\pm$ 29.18 ^{cB}	19	139.13 $\pm$ 42.16 ^{bA}	18	183.37 $\pm$ 51.38 ^{aB}	18	13.62
A3	128.84 $\pm$ 19.41 ^{cA}	10	145.60 $\pm$ 45.19 ^{bA}	23	208.23 $\pm$ 45.73 ^{aA}	11	10.11
LSD	7.10		6.69		6.13		

- Legend as in table (3-7)

3.3.3.2. Serum Total Cholesterol Concentration:

Table (3–10) shows a significant increase in the concentration of serum TC in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant increase in the concentration of serum TC in the Cont-A3 and Cont-A2 groups in comparison with the Cont-A1 group ($p \leq 0.05$). This results show no significant difference in the concentration of serum TC between Cont-A3 group and Cont-A2 group ($p \leq 0.05$).

In the DM age groups there is a significant increase in the concentration of serum TC in the DM-A3 and DM-A2 groups in comparison with the DM-A1 group ($p \leq 0.05$). The results obtained in this study show a significant increase in the concentration of serum TC in the DM-A3 group in comparison with the DM-A2 group ($p \leq 0.05$).

In the DMMS age groups there is a significant increase in the concentration of serum TC in the DMMS-A3 group in comparison with the DMMS-A2 and DMMS-A1 groups ($p \leq 0.05$). Results of the present study show no significant difference in the concentration of serum TC between DMMS-A2 group and DMMS-A1 group ($p \leq 0.05$).

Table (3–10): Serum TC concentrations for all age groups.

TC concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	158.61 $\pm$ 33.14 ^{cB}	21	174.62 $\pm$ 51.16 ^{bC}	23	199.16 $\pm$ 33.72 ^{aB}	07	14.73
A2	174.12 $\pm$ 38.72 ^{cA}	19	187.15 $\pm$ 48.34 ^{bB}	18	202.83 $\pm$ 50.13 ^{aB}	18	11.25
A3	176.74 $\pm$ 40.56 ^{cA}	10	201.10 $\pm$ 42.82 ^{bA}	23	239.95 $\pm$ 52.14 ^{aA}	11	17.62
LSD	10.21		11.56		14.35		

- Legend as in table (3-7)

3.3.3.3. Serum HDL-c Concentration:

Table (3–11) shows a significant decrease in the concentration of serum HDL-c in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant decrease in the concentration of serum HDL-c in the Cont-A3 and Cont-A2 groups in comparison with the Cont-A1 group ($p \leq 0.05$). This results show no significant difference in the concentration of serum HDL-c between Cont-A3 group and Cont-A2 group ($p \leq 0.05$).

In the DM age groups there is a significant decrease in the concentration of serum HDL-c in the DM-A3 and DM-A2 groups in comparison with the DM-A1 group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum HDL-c between DM-A3 group and DM-A2 group ($p \leq 0.05$).

In the DMMS age groups there is a significant decrease in the concentration of serum HDL-c in the DMMS-A3 group in comparison with the DMMS-A2 and DMMS-A1 groups ($p \leq 0.05$). Results of the present study show no significant difference in the concentration of serum HDL-c between DMMS-A2 group and DMMS-A1 group ($p \leq 0.05$).

Table (3–11): Serum HDL-c concentrations for all age groups.

HDL-c concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	55.40 $\pm$ 4.16 ^{aA}	21	46.16 $\pm$ 4.33 ^{bA}	23	36.78 $\pm$ 4.82 ^{cA}	07	5.46
A2	48.27 $\pm$ 4.52 ^{aB}	19	42.50 $\pm$ 4.78 ^{bB}	18	35.82 $\pm$ 3.37 ^{cA}	18	4.32
A3	47.54 $\pm$ 5.37 ^{aB}	10	41.93 $\pm$ 3.24 ^{bB}	23	30.10 $\pm$ 4.15 ^{cB}	11	5.13
LSD	3.67		3.12		2.78		

- Legend as in table (3-7)

3.3.4. Oxidative Stress:

3.3.4.1. Lipid Peroxidation Status (Malondialdehyde):

Table (3–12) shows a significant increase in the concentration of serum MDA in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant increase in the concentration of serum MDA in the Cont-A3 group in comparison with the Cont-A2 and Cont-A1 groups ($p \leq 0.05$). This results show no significant difference in the concentration of serum MDA between Cont-A2 group and Cont-A1 group ($p \leq 0.05$).

In the DM age groups there is a significant increase in the concentration of serum MDA in the DM-A3 group in comparison with the DM-A2 and DM-A1 groups ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum MDA between DM-A2 group and DM-A1 group ($p \leq 0.05$).

In the DMMS age groups there is a significant increase in the concentration of serum MDA in the DMMS-A3 and DMMS-A2 groups in comparison with the DMMS-A1 group ($p \leq 0.05$). Results of the present study show a significant

increase in the concentration of serum MDA in the DMMS-A3 group in comparison with the DMMS-A2 group ($p \leq 0.05$).

Aging is associated with changes in physical characteristics and decline of many physiological functions. The excessive production of free radicals in the organism, and the imbalance between the concentrations of these and the antioxidant defenses may be related to aging (Afanas'ev, 2005 ; Reddy *et al.*, 2008). Oxygen free radical mediated cell damages are implicated in the aging process (Kasapoglu and Ozben, 2001). Oxidative damage to DNA, proteins and lipids induced by the overproduction of ROS accumulate with age and contributes to degenerative diseases and the aging phenomenon by disrupting cellular homeostasis (Armbrecht, 2001 ; Biesalski, 2002 ; Sohal *et al.*, 2002 ; Balaban *et al.*, 2005).

Table (3–12): Serum MDA concentrations for all age groups.

MDA concentrations ($\mu\text{mol/L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	1.56 $\pm$ 0.41 ^{CB}	21	2.92 $\pm$ 0.72 ^{BB}	23	3.36 $\pm$ 0.54 ^{AC}	07	0.34
A2	1.69 $\pm$ 0.49 ^{CB}	19	3.08 $\pm$ 0.78 ^{BB}	18	4.31 $\pm$ 0.81 ^{AB}	18	1.33
A3	2.26 $\pm$ 0.68 ^{CA}	10	3.47 $\pm$ 0.53 ^{BA}	23	4.62 $\pm$ 0.58 ^{AA}	11	0.93
LSD	0.46		0.20		0.26		

- Legend as in table (3-7)

3.3.4.2. Antioxidant System:

3.3.4.2.1. Serum Albumin Concentration:

Table (3–13) shows a significant decrease in the concentration of serum Alb in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant decrease in the concentration of serum Alb in the Cont-A3 group in comparison with the Cont-A2 and Cont-A1 groups ($p \leq 0.05$). This results show no significant difference in the concentration of serum Alb between Cont-A2 group and Cont-A1 group ($p \leq 0.05$).

In the DM age groups there is a significant decrease in the concentration of serum Alb in the DM-A3 group in comparison with the DM-A2 and DM-A1 groups ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum Alb between DM-A2 group and DM-A1 group ($p \leq 0.05$). In this regard, previous studies have described the effect of ageing on serum albumin level (Salive *et al.*, 1992 ; Gomi *et al.*, 2007).

In the DMMS age groups there is a significant decrease in the concentration of serum Alb in the DMMS-A3 and DMMS-A2 groups in comparison with the DMMS-A1 group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum Alb between DMMS-A3 group and DMMS-A2 group ($p \leq 0.05$).

Albumin incurs some damage that affects its antioxidant properties. These modifications can occur in diabetes mellitus, which is one of the pathological condition associated with early occurrence of vascular complications, together with functional alterations of albumin (Saliv *et al.*, 2002).

Table (3–13): Serum Alb concentrations for all age groups.

Alb concentrations (g/L) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	4.68 $\pm$ 0.43 ^{aA}	21	4.50 $\pm$ 0.31 ^{bA}	23	3.92 $\pm$ 0.39 ^{cA}	07	0.15
A2	4.39 $\pm$ 0.61 ^{aA}	19	4.11 $\pm$ 0.38 ^{bA}	18	3.63 $\pm$ 0.41 ^{cB}	18	0.21
A3	3.93 $\pm$ 0.35 ^{aB}	10	3.69 $\pm$ 0.22 ^{bB}	23	3.48 $\pm$ 0.35 ^{cB}	11	0.18
LSD	0.37		0.40		0.25		

3.3.4.2.2. Serum Glutathione Concentration:

Table (3–14) shows a significant decrease in the concentration of serum GSH in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant decrease in the concentration of serum GSH in the Cont-A3 and Cont-A2 groups in comparison with the Cont-A1 group ($p \leq 0.05$). This results show a significant decrease in the concentration of serum GSH in the Cont-A3 group in comparison with the Cont-A2 group ($p \leq 0.05$).

In the DM age groups there is a significant decrease in the concentration of serum GSH in the DM-A3 group in comparison with the DM-A2 and DM-A1 groups ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum GSH between DM-A2 group and DM-A2 group ($p \leq 0.05$).

In the DMMS age groups there is a significant decrease in the concentration of serum GSH in the DMMS-A3 and DMMS-A2 groups in comparison with the DMMS-A1 group ($p \leq 0.05$). Results of the present study show a significant decrease in the concentration of serum GSH in the DMMS-A3 group in comparison with the DMMS-A2 group ($p \leq 0.05$). The progressive decrease in serum GSH values due to the difference in the antioxidant defense during aging (Lang *et al.*, 1992). Type 2 diabetes is associated with increased lipid peroxidation and decreased antioxidant status (Kharb, 2007 ; Hisalkar *et al.*, 2012).

Table (3–14): Serum GSH concentrations for all age groups.

GSH concentrations ($\mu\text{mol /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	368.42 $\pm$ 41.19 ^{aA}	21	238.87 $\pm$ 25.61 ^{bA}	23	223.75 $\pm$ 20.17 ^{cA}	07	13.22
A2	332.26 $\pm$ 38.72 ^{aB}	19	236.96 $\pm$ 18.73 ^{bA}	18	201.36 $\pm$ 15.23 ^{cB}	18	18.96
A3	305.82 $\pm$ 31.59 ^{aC}	10	209.89 $\pm$ 21.15 ^{bB}	23	186.68 $\pm$ 18.58 ^{cC}	11	16.41
LSD	16.52		13.46		11.62		

- Legend as in table (3-7)

3.3.5. Serum Trace Elements Concentrations:

3.3.5.1. Serum Chromium Concentration:

Table (3–15) shows a significant decrease in the concentration of serum chromium in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant decrease in the concentration of serum chromium in the Cont-A3 group in comparison with the Cont-A2 and Cont-A1 groups ($p \leq 0.05$). This results show no significant difference in the concentration of serum chromium between Cont-A2 group and Cont-A1 group ($p \leq 0.05$).

In the DM age groups there is a significant decrease in the concentration of serum chromium in the DM-A3 group in comparison with the DM-A2 and DM-A1 groups ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum chromium between DM-A2 group and DM-A1 group ($p \leq 0.05$).

In the DMMS age groups there is a significant decrease in the concentration of serum chromium in the DMMS-A3 and DMMS-A2 groups in comparison with

the DMMS-A1 group ($p \leq 0.05$). Results of the present study show no significant difference in the concentration of serum chromium between DMMS-A3 group and DMMS-A2 group ($p \leq 0.05$).

Table (3–15): Serum chromium concentrations for all age groups.

Chromium concentrations ($\mu\text{g /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	0.55 ± 0.10^{aA}	21	0.38 ± 0.05^{bA}	23	0.41 ± 0.08^{bA}	07	0.10
A2	0.53 ± 0.12^{aA}	19	0.35 ± 0.06^{bA}	18	0.28 ± 0.05^{bB}	18	0.09
A3	0.43 ± 0.07^{aB}	10	0.26 ± 0.05^{bB}	23	0.26 ± 0.07^{bB}	11	0.07
LSD	0.08		0.07		0.09		

- Legend as in table (3-7)

3.3.5.2. Serum Selenium Concentration:

Table (3–16) shows a significant decrease in the concentration of serum selenium in all patients age groups in comparison with the controls age groups ($p \leq 0.05$).

In the controls age groups there is a significant decrease in the concentration of serum selenium in the Cont-A3 group in comparison with the Cont-A2 and Cont-A1 groups ($p \leq 0.05$). This results show no significant difference in the concentration of serum selenium between Cont-A2 group and Cont-A1 group ($p \leq 0.05$).

In the DM age groups there is a significant decrease in the concentration of serum selenium in the DM-A3 group in comparison with the DM-A2 and DM-A1 groups ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum selenium between DM-A2 group and DM-A1 group ($p \leq 0.05$).

In the DMMS age groups there is a significant decrease in the concentration of serum selenium in the DMMS-A3 and DMMS-A2 groups in comparison with the DMMS-A1 group ($p \leq 0.05$). Results of the present study show no significant difference in the concentration of serum selenium between DMMS-A3 group and DMMS-A2 group ($p \leq 0.05$).

Table (3–16): Serum selenium concentrations for all age groups.

Selenium concentrations ($\mu\text{g /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
A1	140.12 $\pm$ 15.25 ^{aA}	21	118.57 $\pm$ 10.34 ^{bA}	23	122.17 $\pm$ 9.52 ^{bA}	07	13.96
A2	137.43 $\pm$ 15.88 ^{aA}	19	111.32 $\pm$ 11.89 ^{bA}	18	110.86 $\pm$ 10.72 ^{bB}	18	9.44
A3	119.63 $\pm$ 13.83 ^{aB}	10	93.30 $\pm$ 13.54 ^{cB}	23	107.40 $\pm$ 11.21 ^{bB}	11	7.23
LSD	14.13		15.71		10.33		

3.4. Effect of BMI on Studied Parameters:

3.4.1. Fasting Blood Glucose Concentration:

Table (3–17) shows a significant increase in the concentration of FBG in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant increase in the concentration of FBG in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show a significant increase in the concentration of FBG in the Cont-Obese group in comparison with the Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant increase in the concentration of FBG in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show a significant increase in the concentration of FBG in the DM-Obese group in comparison with the DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant increase in the concentration of FBG in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$). In the DMMS BMI groups the comparison occur between Overweight and Obese groups because there is no any patient with type 2 diabetes mellitus and metabolic syndrome (DMMS) in the first group (Normal range: 18.5-24.99) and this is expected because the metabolic syndrome is characterized by elevated BMI.

The results show that overweight and obesity are common in type 2 diabetic patients. Obesity is a major potentially modifiable risk factor for type 2 diabetes (Pinkney, 2002). The present study are matched with the results of study of (Kumar *et al.*, 2008). A variety of studies show that patients with type 2 diabetes who succeed in losing weight often enjoy modest improvements in glycemic control and cardiovascular risk profiles, as long as the weight loss is maintained (Williamson *et al.*, 2000). In this work, we focus on BMI effect in type 2 diabetic patients with and without metabolic syndrome this is important because the obesity is an independent risk factor for cardiovascular disease, and effect likely to be mediated, at least in part through its known associations with the metabolic syndrome (Rimm *et al.*, 1995).

Table (3–17): FBG concentrations for all BMI groups.

FBG concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	87.18 $\pm$ 10.28 ^{bC}	23	181.10 $\pm$ 42.48 ^{aC}	13	0.00	0.0	15.73
Overweight	90.32 $\pm$ 11.36 ^{cB}	19	189.93 $\pm$ 50.31 ^{bB}	27	200.53 $\pm$ 58.21 ^{aB}	17	10.21
Obese	93.46 $\pm$ 8.54 ^{cA}	08	201.12 $\pm$ 59.67 ^{bA}	24	214.21 $\pm$ 42.54 ^{aA}	19	12.67
LSD	1.13		8.36		10.42		

Normal range: First BMI group range from (18.5-24.99)

Overweight: Second BMI group range from (25-29.99)

Obese: Third BMI group range from ($\text{BMI} \geq 30$)

3.4.2. Hemoglobin A_{1c} Ratio:

Table (3–18) shows a significant increase in the ratio of HbA_{1c} in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant increase in the ratio of HbA_{1c} in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show a significant increase in the ratio of HbA_{1c} in the Cont-Obese group in comparison with the Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant increase in the ratio of HbA_{1c} in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show no significant difference in the ratio of HbA_{1c} between DM-Obese group and DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant increase in the ratio of HbA_{1c} in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

Table (3–18): HbA_{1c} ratio for all BMI groups.

HbA _{1c} (%) Mean ± SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	5.35±0.52 ^{bC}	22	7.34±1.32 ^{aB}	13	0.00	0.0	1.14
Overweight	5.71±0.41 ^{cB}	18	9.13±1.45 ^{bA}	27	11.67±1.75 ^{aB}	17	0.88
Obese	6.10±0.46 ^{cA}	10	9.35±1.82 ^{bA}	24	12.48±1.43 ^{aA}	19	1.62
LSD	0.32		1.12		0.68		

- Legend as in table (3-17)

3.4.3. Serum Lipid Profile Concentrations:

3.4.3.1. Serum Triglyceride Concentration:

Table (3–19) shows a significant increase in the concentration of serum TG in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant increase in the concentration of serum TG in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show a significant increase in the concentration of serum TG in the Cont-Obese group in comparison with the Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant increase in the concentration of serum TG in the DM-Obese group in comparison with the DM-Overweight and DM-Normal range groups ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum TG between DM-Overweight group and DM-Normal range group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant increase in the concentration of serum TG in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

(Vidar *et al.*, 2012) the reported BMI was the strongest predictor of type 2 diabetes. At defined levels of BMI, the incidence of DM2 varied substantially with triglyceride levels and blood pressure. Thus, controlling triglycerides in middle-aged individuals should be targeted to prevent later onset of DM2. Hypertriglyceridemia is associated with an increased risk of cardiovascular events and acute pancreatitis (Robert *et al.*, 2007).

Table (3–19): Serum TG concentrations for all BMI groups.

TG concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	116.28 $\pm$ 30.15 ^{bC}	22	133.87 $\pm$ 38.19 ^{aB}	13	0.00	0.0	11.31
Overweight	123.66 $\pm$ 28.66 ^{cB}	18	134.66 $\pm$ 41.08 ^{bB}	27	167.44 $\pm$ 48.84 ^{aB}	17	10.16
Obese	134.21 $\pm$ 33.74 ^{cA}	10	143.11 $\pm$ 40.25 ^{bA}	24	210.45 $\pm$ 41.92 ^{aA}	19	7.93
LSD	5.36		7.05		10.31		

3.4.3.2. Serum Total Cholesterol Concentration:

Table (3–20) shows a significant increase in the concentration of serum TC in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant increase in the concentration of serum TC in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show no significant difference in the concentration of serum TC between Cont-Obese group and Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant increase in the concentration of serum TC in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum TC between DM-Obese group and DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant increase in the concentration of serum TC in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

Table (3–20): Serum TC concentrations for all BMI groups.

TC concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	158.71 $\pm$ 45.36 ^{bB}	22	171.91 $\pm$ 52.14 ^{aB}	13	0.00	0.0	10.13
Overweight	174.26 $\pm$ 39.42 ^{cA}	18	187.54 $\pm$ 33.25 ^{bA}	27	201.18 $\pm$ 52.26 ^{aB}	17	11.61
Obese	177.81 $\pm$ 35.26 ^{cA}	10	196.30 $\pm$ 41.12 ^{bA}	24	224.45 $\pm$ 41.65 ^{aA}	19	14.72
LSD	12.14		13.52		15.71		

- Legend as in table (3-17)

3.4.3.3. Serum HDL-c Concentration:

Table (3–21) shows a significant decrease in the concentration of serum HDL-c in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant decrease in the concentration of serum HDL-c in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show no significant difference in the concentration of serum HDL-c between Cont-Obese group and Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant decrease in the concentration of serum HDL-c in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show a significant decrease in the concentration of serum HDL-c in the DM-Obese group in comparison with the DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant decrease in the concentration of serum HDL-c in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

Table (3–21): Serum HDL-c concentrations for all BMI groups.

HDL-c concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	55.20 $\pm$ 4.31 ^{aA}	22	49.21 $\pm$ 4.71 ^{bA}	13	0.00	0.0	4.15
Overweight	48.29 $\pm$ 5.16 ^{aB}	18	44.10 $\pm$ 4.63 ^{bB}	27	37.76 $\pm$ 3.79 ^{cA}	17	3.10
Obese	47.23 $\pm$ 3.25 ^{aB}	10	40.00 $\pm$ 5.42 ^{bC}	24	31.13 $\pm$ 3.21 ^{cB}	19	5.33
LSD	5.13		3.16		3.89		

- Legend as in table (3-17)

3.4.4. Oxidative Stress:

3.4.4.1. Lipid Peroxidation Status (Malondialdehyde):

Table (3–22) shows a significant increase in the concentration of serum MDA in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant increase in the concentration of serum MDA in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show no significant difference in the concentration of serum MDA between Cont-Obese group and Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant increase in the concentration of serum MDA in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum MDA between DM-Obese group and DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant increase the concentration of serum MDA in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

Obesity is reported to be a risk factor for a number of diseases including Diabetes Mellitus. Type 2 diabetes is associated with increased lipid peroxidation and decreased antioxidant status (Kharb, 2007 ; Hisalkar *et al.*, 2012). In patients with type 2 diabetes, an end product of year of metabolic stress is accompanied with an increase in obesity (Hussain *et al.*, 2010). The diabetic condition contributes to initiation and progression of micro and macrovascular complications in individuals with diabetes (Mahapure *et al.*, 2008).

Table (3–22): Serum MDA concentrations for all BMI groups.

MDA concentrations ($\mu\text{mol /mL}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	1.53 ± 0.43^{bB}	22	2.66 ± 0.59^{aB}	13	0.00	0.0	0.89
Overweight	1.83 ± 0.51^{bA}	18	3.14 ± 0.81^{aA}	27	3.92 ± 0.65^{aB}	17	0.94
Obese	2.08 ± 0.55^{cA}	10	3.32 ± 0.63^{bA}	24	4.48 ± 0.84^{aA}	19	1.10
LSD	0.27		0.39		0.44		

- Legend as in table (3-17)

3.4.4.2. Antioxidant System:

3.4.4.2.1. Serum Albumin Concentration:

Table (3–23) shows a significant decrease in the concentration of serum Alb in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant decrease in the concentration of serum Alb in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show no significant difference

in the concentration of serum Alb between Cont-Obese group and Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant decrease in the concentration of serum Alb in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum Alb between DM-Obese group and DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant decrease the concentration of serum Alb in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

Obesity is reported to be a risk factor for a number of diseases including Diabetes Mellitus. Type 2 diabetes is associated with increased lipid peroxidation and decreased antioxidant status (Kharb, 2007 ; Hisalkar *et al.*, 2012).

Table (3–23): Serum Alb concentrations for all BMI groups.

Alb concentrations (g/L) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	4.61 $\pm$ 0.41 ^{aA}	22	4.35 $\pm$ 0.21 ^{bA}	13	0.00	0.0	0.17
Overweight	4.33 $\pm$ 0.45 ^{aB}	18	4.10 $\pm$ 0.25 ^{bB}	27	3.83 $\pm$ 0.36 ^{cA}	17	0.19
Obese	4.17 $\pm$ 0.33 ^{aB}	10	3.96 $\pm$ 0.38 ^{bB}	24	3.46 $\pm$ 0.31 ^{cB}	19	0.15
LSD	0.19		0.22		0.11		

- Legend as in table (3-17)

3.4.4.2.2. Serum Glutathione Concentration:

Table (3–24) shows a significant decrease in the concentration of serum GSH in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is a significant decrease in the concentration of serum GSH in the Cont-Obese and Cont-Overweight groups in comparison with the Cont-Normal range group ($p \leq 0.05$). This results show no significant difference in the concentration of serum GSH between Cont-Obese group and Cont-Overweight group ($p \leq 0.05$).

In the DM BMI groups there is a significant decrease in the concentration of serum GSH in the DM-Obese and DM-Overweight groups in comparison with the DM-Normal range group ($p \leq 0.05$). The results obtained in this study show no significant difference in the concentration of serum GSH between DM-Obese group and DM-Overweight group ($p \leq 0.05$).

In the DMMS BMI groups there is a significant decrease in the concentration of serum GSH in the DMMS-Obese group in comparison with the DMMS-Overweight group ($p \leq 0.05$).

Antioxidants in non-diabetic individuals can mitigate free radical-mediated oxidative stress, but in the chronic hyperglycemia state, increased free radical production may lead to the elevated lipid peroxidation, enhanced oxidative stress and overconsumption of chain-breaking antioxidants (Whiting *et al.*, 2008).

Table (3–24): Serum GSH concentrations for all BMI groups.

GSH concentrations ($\mu\text{mol/L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	362.53 $\pm$ 35.24 ^{aA}	22	262.50 $\pm$ 17.96 ^{bA}	13	0.00	0.0	16.38
Overweight	327.82 $\pm$ 38.78 ^{aB}	18	220.35 $\pm$ 22.71 ^{bB}	27	213.91 $\pm$ 20.72 ^{bA}	17	18.71
Obese	323.14 $\pm$ 31.53 ^{aB}	10	217.71 $\pm$ 19.29 ^{bB}	24	189.88 $\pm$ 15.31 ^{cB}	19	16.26
LSD	17.94		14.76		15.32		

- Legend as in table (3-17)

3.4.5. Serum Trace Elements Concentrations:

3.4.5.1. Serum Chromium Concentration:

Table (3–25) shows a significant decrease in the concentration of serum chromium in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is no significant difference in the concentration of serum chromium between Cont-Obese, Cont-Overweight and Cont-Normal range groups ($p \leq 0.05$).

In the DM BMI groups there is no significant difference in the concentration of serum chromium between DM-Obese, DM-Overweight and DM-Normal range groups ($p \leq 0.05$).

In the DMMS BMI groups there is no significant difference in the concentration of serum chromium between DMMS-Obese group and DMMS-Overweight group ($p \leq 0.05$).

Table (3–25): Serum chromium concentrations for all BMI groups.

Chromium concentrations ($\mu\text{g/L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	0.55 ± 0.13^{aA}	22	0.37 ± 0.06^{bA}	13	0.00	0.0	0.13
Overweight	0.51 ± 0.08^{aA}	18	0.33 ± 0.07^{bA}	27	0.32 ± 0.06^{bA}	17	0.06
Obese	0.47 ± 0.09^{aA}	10	0.31 ± 0.07^{bA}	24	0.29 ± 0.10^{bA}	19	0.10
LSD	0.09		0.10		0.07		

- Legend as in table (3-17)

3.4.5.2. Serum selenium Concentration:

Table (3–26) shows a significant decrease in the concentration of serum selenium in all patients BMI groups in comparison with the controls BMI groups ($p \leq 0.05$).

In the controls BMI groups there is no significant difference in the concentration of serum selenium between Cont-Obese, Cont-Overweight and Cont-Normal range groups ($p \leq 0.05$).

In the DM BMI groups there is no significant difference in the concentration of serum selenium between DM-Obese, DM-Overweight and DM-Normal range groups ($p \leq 0.05$).

In the DMMS BMI groups there is no significant difference in the concentration of serum selenium between DMMS-Obese group and DMMS-Overweight group ($p \leq 0.05$).

Table (3–26): Serum selenium concentrations for all BMI groups.

Selenium concentrations ($\mu\text{g /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Normal range	139.91 $\pm$ 14.76 ^{aA}	22	115.23 $\pm$ 8.92 ^{bA}	13	0.00	0.0	15.47
Overweight	132.43 $\pm$ 14.14 ^{aA}	18	107.36 $\pm$ 10.45 ^{bA}	27	117.90 $\pm$ 12.32 ^{bA}	17	10.94
Obese	128.80 $\pm$ 11.24 ^{aA}	10	104.80 $\pm$ 9.67 ^{bA}	24	106.72 $\pm$ 9.88 ^{bA}	19	7.67
LSD	17.62		13.77		13.11		

- Legend as in table in (3-17)

3.5. Effect of Sex on Studied Parameters:

3.5.1. Fasting Blood Glucose Concentration:

Table (3-27) shows a significant increase in the concentration of FBG in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of FBG between Cont-male group and Cont-Female group ($P \leq 0.05$). There is a significant increase in the concentration of FBG in the DM-Male group in comparison with the DM-Female group ($P \leq 0.05$). This result matched with the results of study of (Abdoljalal *et al.*, 2015). The results show no significant difference in the concentration of FBG between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3-27): FBG concentrations for all sex groups.

FBG concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	88.95 $\pm$ 10.17 ^{cA}	20	198.71 $\pm$ 55.96 ^{bA}	34	213.53 $\pm$ 30.92 ^{aA}	12	13.11
Female	89.67 $\pm$ 7.44 ^{cA}	30	185.10 $\pm$ 58.14 ^{bB}	30	204.86 $\pm$ 58.70 ^{aA}	24	15.32
LSD	0.93		8.92		11.32		

Note: Each value represents mean $\pm$ S.D values with non-identical superscript (a, b or c ...etc.), were considered significantly differences ($P \leq 0.05$) to compare horizontally, and with non-identical superscript (A, B or C ...etc.), were considered significantly differences ($P \leq 0.05$) to compare vertically.

3.5.2. Hemoglobin A_{1c} Ratio:

Table (3-28) shows a significant increase in the ratio of HbA_{1c} in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the ratio of HbA_{1c} between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is a significant increase in the ratio of HbA_{1c} in the DM-Male group in comparison with the DM-Female group ($P \leq 0.05$). The results show no significant difference in the ratio of HbA_{1c} between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–28): HbA_{1c} ratio for all sex groups.

HbA _{1c} (%) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	5.76 $\pm$ 0.38 ^{bA}	20	9.62 $\pm$ 1.90 ^{aA}	34	12.42 $\pm$ 1.75 ^{aA}	12	2.89
Female	5.52 $\pm$ 0.34 ^{cA}	30	7.97 $\pm$ 1.49 ^{bB}	30	11.94 $\pm$ 1.41 ^{aA}	24	2.21
LSD	0.42		1.12		0.87		

3.5.3. Serum Lipid Profile Concentrations:

3.5.3.1. Serum Triglyceride Concentration:

Table (3-29) shows a significant increase in the concentration of serum TG in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum TG between Cont-male group and Cont-Female group ($P \leq 0.05$). There is a significant increase in the concentration of serum TG in the DM-Male group in comparison with the DM-Female group ($P \leq 0.05$). This result matched with the results of study of (Abdoljalal *et al.*, 2015). The results show no significant difference in the concentration of serum TG between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–29): Serum TG concentrations for all sex groups.

TG concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	123.41 $\pm$ 28.26 ^{cA}	20	143.36 $\pm$ 45.35 ^{bA}	34	192.21 $\pm$ 42.51 ^{aA}	12	8.55
Female	121.93 $\pm$ 31.73 ^{cA}	30	131.22 $\pm$ 40.10 ^{bB}	30	189.10 $\pm$ 49.26 ^{aA}	24	8.27
LSD	5.16		6.32		6.17		

- Legend as in table (3-27)

3.5.3.2. Serum Total Cholesterol Concentration:

Table (3-30) shows a significant increase in the concentration of serum TC in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum TC between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is a significant increase in the concentration of serum TC in the DM-Male group in comparison with the DM-Female group ($P \leq 0.05$). The results show no significant difference in the concentration of serum TC between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–30): Serum TC concentrations for all sex groups.

TC concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	167.21 $\pm$ 39.10 ^{cA}	20	198.63 $\pm$ 51.58 ^{bA}	34	211.73 $\pm$ 50.41 ^{aA}	12	10.3
Female	168.74 $\pm$ 36.46 ^{cA}	30	177.96 $\pm$ 45.77 ^{bB}	30	214.32 $\pm$ 38.18 ^{aA}	24	13.8
LSD	12.52		16.31		10.94		

- Legend as in table (3-27)

3.5.3.3. Serum HDL-c Concentration:

Table (3-31) shows a significant decrease in the concentration of serum HDL-c in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum HDL-c between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is a significant decrease in the concentration of serum HDL-c in the DM-Male group in comparison with the DM-Female group ($P \leq 0.05$). The results show no significant difference in the concentration of serum HDL-c between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–31): Serum HDL-c concentrations for all sex groups.

HDL-c concentrations (mg/dL) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	50.27 $\pm$ 4.29 ^{aA}	20	40.47 $\pm$ 4.81 ^{bB}	34	35.72 $\pm$ 4.80 ^{cA}	12	3.53
Female	51.68 $\pm$ 5.33 ^{aA}	30	46.38 $\pm$ 4.20 ^{bA}	30	33.53 $\pm$ 4.18 ^{cA}	24	4.78
LSD	3.14		4.15		3.88		

- Legend as in table (3-27)

3.5.4. Oxidative Stress:

3.5.4.1. Lipid Peroxidation Status (Malondialdehyde):

Table (3-32) shows a significant increase in the concentration of serum MDA in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum MDA between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is no significant difference in the concentration of serum MDA between DM-Male group and DM-Female group ($P \leq 0.05$). The results show no significant difference

in the concentration of serum MDA between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–32): Serum MDA concentrations for all sex groups.

MDA concentrations ($\mu\text{mol /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	1.62 $\pm$ 0.50 ^{cA}	20	2.98 $\pm$ 0.57 ^{bA}	34	4.13 $\pm$ 0.69 ^{aA}	12	0.37
Female	1.84 $\pm$ 0.58 ^{cA}	30	3.25 $\pm$ 0.68 ^{bA}	30	4.27 $\pm$ 0.55 ^{aA}	24	0.29
LSD	0.31		0.28		0.21		

- Legend as in table (3-27)

3.5.4.2. Antioxidant System:

3.5.4.2.1. Serum Albumin Concentration:

Table (3-33) shows a significant decrease in the concentration of serum Alb in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum Alb between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is no significant difference in the concentration of serum Alb between DM-Male group and DM-Female group ($P \leq 0.05$). The results show no significant difference in the concentration of serum Alb between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–33): Serum Alb concentrations for all sex groups.

Alb concentrations (g/L) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	4.65 $\pm$ 0.32 ^{aA}	20	4.27 $\pm$ 0.28 ^{bA}	34	3.71 $\pm$ 0.41 ^{cA}	12	0.32
Female	4.27 $\pm$ 0.43 ^{aA}	30	3.91 $\pm$ 0.23 ^{bA}	30	3.60 $\pm$ 0.36 ^{cA}	24	0.28
LSD	0.42		0.45		0.23		

- Legend as in table (3-27)

3.5.4.2.2. Serum Glutathione Concentration:

Table (3-34) shows a significant decrease in the concentration of serum GSH in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum GSH between Cont-male group and Cont-Female group ($P \leq 0.05$) this result matched with the results of study of (Lang *et al.*, 1992). There is no significant difference in the concentration of serum GSH between DM-Male group and DM-Female group ($P \leq 0.05$). The results show no significant difference in the concentration of serum GSH between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–34): Serum GSH concentrations for all sex groups.

GSH concentrations ($\mu\text{mol /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	339.22 $\pm$ 37.12 ^{aA}	20	230.82 $\pm$ 22.36 ^{bA}	34	198.14 $\pm$ 18.65 ^{cA}	12	21.56
Female	344.12 $\pm$ 33.56 ^{aA}	30	224.63 $\pm$ 16.78 ^{bA}	30	202.78 $\pm$ 21.34 ^{cA}	24	19.33
LSD	15.34		13.76		12.53		

- Legend as in table (3-27)

3.5.5. Serum Trace Elements Concentrations:

3.5.5.1. Serum Chromium Concentration:

Table (3-35) shows a significant decrease in the concentration of serum chromium in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum chromium between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is a significant increase in the concentration of serum chromium in the DM-Male

group in comparison with the DM-Female group ($P \leq 0.05$). The results show no significant difference in the concentration of serum chromium between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Chromium had a significant improvements in insulin sensitivity (Glinsmann and Mertz, 1966). Insulin resistance affects about 50% to 70% of women so that the serum chromium was found lower in female diabetes. Our finding was matched with the results of study of (Gunton *et al.*, 2005).

Table (3–35): Serum chromium concentrations for all sex groups.

Chromium concentration ($\mu\text{g/L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	0.55 ± 0.11^{aA}	20	0.38 ± 0.08^{bA}	34	0.28 ± 0.05^{bA}	12	0.12
Female	0.50 ± 0.09^{aA}	30	0.27 ± 0.06^{bB}	30	0.31 ± 0.07^{bA}	24	0.10
LSD	0.09		0.07		0.06		

- Legend as in table (3-27)

3.5.5.2. Serum Selenium Concentration:

Table (3-36) shows a significant decrease in the concentration of serum selenium in all patients sex groups in comparison with the controls sex groups ($P \leq 0.05$).

The present study shows no significant difference in the concentration of serum selenium between Cont-male group and Cont-Female group ($P \leq 0.05$) and there is no significant difference in the concentration of serum selenium between DM-Male group and DM-Female group ($P \leq 0.05$). The results show no significant difference in the concentration of serum selenium between DMMS-Male group and DMMS-Female group ($P \leq 0.05$).

Table (3–36): Serum selenium concentrations for all sex groups.

Selenium concentrations ($\mu\text{g /L}$) Mean $\pm$ SD							
Groups	Control	No.	DM	No.	DMMS	No.	LSD
Male	139.13 $\pm$ 10.35 ^{aA}	20	104.14 $\pm$ 8.54 ^{bA}	34	116.12 $\pm$ 13.65 ^{bA}	12	15.57
Female	132.24 $\pm$ 14.34 ^{aA}	30	112.37 $\pm$ 10.76 ^{bA}	30	109.94 $\pm$ 11.71 ^{bA}	24	12.41
LSD	13.45		11.62		11.83		

- Legend as in table (3-27)

Conclusions and Future Works

Conclusions

From the data in this study, it was conclude the following points:

- 1- The presence of metabolic syndrome in type 2 diabetic patients lead to disturbances in FBG, thereby HbA_{1c} ratio.
- 2- Dyslipidemia can occur in patients with type 2 diabetes and it is clear in presence of metabolic syndrome.
- 3- Metabolic syndrome accompanied with type 2 diabetes increases oxidative stress.
- 4- Type 2 diabetes decreases the levels of both chromium and selenium, However there is no significant effect of metabolic syndrome on these trace elements.
- 5- Aging has a negative role on the studied parameters in diabetic patients with and without metabolic syndrome.
- 6- BMI has a negative role on the studied parameters in diabetic patients with and without metabolic syndrome.
- 7- There is a significant impact for sex on concentrations of FBG, HbA_{1c}, TG, TC, HDL-c, and chromium.

Future Works

It is important to design, further studies relevant as indicated below:

- 1-Study of the effects of physical activity and exercise on the levels of oxidants and anti-oxidant parameters in diabetic obese and diabetic non obese patients.
- 2-The effect of hypolipidemic drugs used by diabetic patients with metabolic syndrome.
- 3- Studying the effect of the metabolic syndrome components on the levels of some steroid hormones.

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الخلاصة

السكري النوع الثاني يشكل خطرا كبيرا على الصحة العامة، وعدم السيطرة المثالية عليه يؤدي إلى ارتفاع مزمن في مستوى الكلوكرز في الدم. سبب حدوث هذا النوع يعود اما إلى مقاومة خلايا الجسم لعمل هرمون الانسولين أو قد يعود إلى عدم إنتاج كمية كافية من الانسولين من قبل البنكرياس وذلك سببه عوامل متعددة أبرزها زيادة الوزن وقلة النشاط البدني .

المتلازمة الايضية هي مجموعة معقدة من الاضطرابات التي تزيد بشكل كبير من خطر الإصابة بأمراض القلب. استخدمت معايير المنظمة الامريكية للسكري في تشخيص المتلازمة الايضية .

صممت هذه الدراسة لتحديد مستويات HDL-c ,TC ,TG ,HbA_{1c} ,FBG حالة الإجهاد التأكسدي (المالونديهيد، الألبومين و الكلوتاتايون) و بعض العناصر النزرة (الكروم والسيلينيوم) في مرضى السكري من النوع الثاني مع و بدون المتلازمة الأيضية.

درست المعايير المقاسة على أساس أربعة متغيرات: مقارنة عامة، العمر، معامل كتلة الجسم و الجنس.

قسموا المرضى و الأصحاء في المقارنة العامة إلى ثلاث مجاميع:

- 1- مجموعة السيطرة: شملت 50 شخص من المفترض أصحاء تتراوح أعمارهم بين (41- 70).
- 2- مجموعة DM: شملت 64 من مرضى السكري النوع الثاني تتراوح اعمارهم بين (41-70).
- 3- مجموعة DMMS: شملت 36 من مرضى السكري النوع الثاني مع المتلازمة الايضية تتراوح أعمارهم بين (41- 70 سنة).

قسموا المرضى والأصحاء على أساس اعمارهم إلى ثلاث مجاميع عمرية :

A1 (41- 50 سنة)، A2 (51- 60 سنة) و A3 (61- 70 سنة).

قسموا المرضى و الأصحاء على أساس معامل كتلة الجسم إلى ثلاث مجاميع :

[(18.5- 24.99) الحد الطبيعي, (25-29.99) الوزن الزائد , (≥30.00) المصابين بالسمنة].

و بالنسبة للجنس قسموا المرضى و الأصحاء إلى (ذكر و انثى) .

اظهرت النتائج الحالية وجود زيادة كبيرة في تراكيز MDA ,TC ,TG , HbA_{1c} , FBG في كل من مجاميع المرضى بالمقارنة مع مجموعة السيطرة ($p \leq 0.05$).

و زيادة كبيرة ايضا في تراكيز MDA ,TC ,TG , HbA_{1c} , FBG في مجموعة مرضى السكري النوع الثاني مع المتلازمة الايضية بالمقارنة مع مجموعة مرضى السكري النوع الثاني بدون المتلازمة الايضية ($p \leq 0.05$).

و انخفاضاً كبيراً في تراكيز Se , Cr , GSH , Alb, HDL-c في كل مجاميع المرضى بالمقارنة مع مجموعة السيطرة ($p \leq 0.05$).

زيادة العمر له تأثير سلبي على المعايير المقاسة في مرضى السكري النوع الثاني مع وبدون المتلازمة الايضية.

كذلك معامل كتلة الجسم له تأثير سلبي على المعايير المقاسة في مرضى السكري النوع الثاني مع وبدون المتلازمة الايضية.

هناك تأثير كبير للجنس على تراكيز Cr, HDL-c ,TC ,TG , HbA_{1c} , FBG.



جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة ذي قار
كلية العلوم

دراسة سريرية لبعض المتغيرات الكيموحيوية في مرضى السكري النوع الثاني مع و بدون المتلازمة الأيضية

رسالة

مقدمة إلى مجلس كلية العلوم / جامعة ذي قار

كجزء من متطلبات نيل درجة الماجستير في الكيمياء الحياتية

من قبل

عبدالله فاخر يوسف

بكالوريوس علوم كيمياء (جامعة ذي قار)

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باشراف

أ.د. رائد معلق حنون الصالح

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