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Department of Chemistry

Effect of Obesity on Angiopoitetin-Like4(Angptl4) Protein and Omentin-1 Levels on Indiction for Patients of Diabetes Mellitus (Type II) in Females

A Thesis
Submitted to the Council of the College of Science, University of Babylon
In Partial Fulfillment of the Requirements for the Degree
of Master of Science in Chemistry

By

Amjed Hussein Ali Hayder

B.Sc.- Al-Mustansiriyah University -2007

Supervised By

Prof. Dr. Lamia Abdul-Majeed Al-Mashhedy

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بسم الله الرحمن الرحيم

﴿اللَّهُ لَا إِلَهَ إِلَّا هُوَ الْحَيُّ الْقَيُّومُ لَا تَأْخُذُهُ سِنَةٌ وَلَا نَوْمٌ لَهُ مَا فِي السَّمَاوَاتِ وَمَا فِي الْأَرْضِ مَنْ ذَا الَّذِي يَشْفَعُ عِنْدَهُ إِلَّا بِإِذْنِهِ يَعْلَمُ مَا بَيْنَ أَيْدِيهِمْ وَمَا خَلْفَهُمْ وَلَا يُحِيطُونَ بِشَيْءٍ مِنْ عِلْمِهِ إِلَّا بِمَا شَاءَ وَسِعَ كُرْسِيُّهُ السَّمَاوَاتِ وَالْأَرْضَ وَلَا يَئُودُهُ حِفْظُهُمَا وَهُوَ الْعَلِيُّ الْعَظِيمُ﴾

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I certify that this thesis entitled **(Effect of Obesity on Angiopoitetin-Like4(Angptl4) Protein and Omentin-1 Levels on Indiction For Patients of Diabetes Mellitus (Type II) in Females)** was prepared under my supervision at the Department of Chemistry/ College of Science, in University of Babylon, as a partial requirement for the Degree of Master of Science in Biochemistry and this work has never been published anywhere.

Signature :

Name: **Prof.Dr. Lamia Abdul-Majeed Al-Mashhedy**

Title: Professor
Address: Department of Chemistry – College of Science – University of Babylon
Date: / /2023

Given the available recommendation, I foreword this thesis for debate by the Examining Committee.

Signature :

Name : **Prof.Dr. Abbas Jasim Atiyah**

Title: Professor
Address: Head of Department of Chemistry – College of Science – University of Babylon
Date: / /2023

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We chairman and members of the examination committee, certify that we have studied this thesis **" Effect of Obesity on Angiopoitetin-Like4(Angptl4) Protein and Omentin-1 Levels on Indiction For Patients of Diabetes Mellitus (Type II) in Females**" presented by the student " **Amjed Hussein Ali** " and examined him in its contents and found it worthy to be accepted for the Degree of Master of Science - Chemistry/ Biochemistry with degree.

Signature
Name: Prof.Dr. Oda Mizil Yasser Al-Zamely
(Chairman)
Title: Professor
College of Science - University of Babylon
Date : / /2023

Signature
Name: Dr. Ban Mohammed Hussain Ali
(member)
Title: Assistant Professor
College of Agriculture- Al-Qasim Green University
Date : / /2023

Signature
Name: Dr. Qasim Jawad Al-Daami
(member)
Title: Assistant Professor
College of Pharmacy- University of Babylon
Date: / / 2023

Signature:
Name: Prof.Dr. Lamia Abdul-Majeed Al-Mashhedy
(Supervisor)
Title: Professor
College of Science- University of Babylon
Date: / /2023

Approved by the dean of the College of Science- Babylon University.

Signature:
Name: Prof.Dr. Mohammed Hadi Shinen Alshammari
Title: Professor
Address: Dean of College of Science -University of Babylon
Date: / /2023

DEDICATION

To

My friend and teacher… my father

To

The fountain of love… My precious mother

To

My brothers….Guide to my life

To

My sisters…Diamonds of my family

Amjcd

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I thank God Almighty for His grace, as He enabled me to accomplish this work thanks to Him.

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Amjed H. Ali

Summary

Background: Preface The prevalence rates of obesity, as well as type 2 diabetes, have increased greatly, and this has become a pandemic that affects societies and their economies, including Iraqi society. Obesity is considered one of the common risk factors that can lead to prediabetes, especially type 2 diabetes. The mechanisms linking obesity and type 2 diabetes are complex and still poorly understood, but likely involve a combination of adipose tissue release of excess circulating fatty acids, glycerol, and proinflammatory hormones and cytokines. These agents impair cellular insulin signaling and increase insulin resistance. Chronically high fat levels can also lead to poor pancreatic beta cell function and low levels of insulin production.

There are many proteins involved in the process of angiogenesis, including angiobiotin-4, a protein that regulates the breakdown of fats by inhibiting blood circulation and tissues.

The protein omentin-1 is synthesized by adipose tissue. It has been found to be significantly associated with both type 2 diabetes and obesity. The omentin-1 gene shows decreased expression in people who are obese, and some studies indicate an increase in the ratio when taking anti-diabetic drugs type 2, especially metformin. The development of type 2 diabetes is greatly influenced by insulin resistance, which is also associated with this protein.

Methods: The study consisted of 120 volunteers (60 patients and 60 control groups) and every sixty people were distributed into two groups of thirty people, so they were divided into four groups, Gp1 are the group with diabetes (type 2) but not obese, while the second group is Gp2. Of the people with diabetes and obesity as well, the healthy control group without diabetes was distributed into two groups, the Gc1 group, and they are the healthy non-obese ones, while the Gc2 group, they are the healthy control group with obesity, and each group also consisted of 30 volunteers for the study

Summary

I measured clinical biomarkers in the blood and anthropometric parameters. including age, sex, hip circumference, waist circumference, basic measurements of height, weight, and body mass index (BMI). demographic characteristics, urban or rural setting, blood pressure biomarkers (systolic SBP and diastolic DBP) as well as serum biochemical measures (Omentin-1, Angipopoietin-4, Fasting Blood Glucose FBS, Cumulative HbA1c, Serum Calcium Levels). Antioxidants such as GSH-reduced glutathione and Vit-C, lipid assays (HDL, LDL, VLDL, T.G, T.Cholesterol).

Result: There are significant differences between both omentin-1 and Angplt-4 and studied individuals (P = 0.011 and P = 0.0001, respectively). Both levels of omentin-1 and significantly related to a higher HbA1c index (P = 0.030 and P = 0.046, respectively). However, omentin-1 was only related to individuals who were overweight/obese. Additionally, both omentin-1 and ANGPLT-4 were significantly positively correlated to familial history of diabetes (P = 0.046 and P = 0.024, respectively Conclusions: Omentin-1 & ANGPLT-4.

The estimation of biochemical data pointed out significant differences in, omentin-1 (0.0001)for(Gp1,Gp2) and (0.09) to(Gp1,Gc1) and (0.0001) for (Gp2,Gc1), (0.09)for(Gp2,Gc2), it can be seen HbA1c for(Gp1,Gc2)was (0.001) and(0.043) to(Gp1, Gp2) and(0.043) to(Gp1, Gp2) and(0.0001) to(Gp2, Gc2), ANGPTL4 (0.0001) for(Gc2, Gp2), (0.001) to(Gp1,Gc2), (0.0001)for(Gp2,Gc1), HDL(0.002) for (Gc1,Gp2) and(0.000) to (Gc1,Gc2), and (0.217) of LDL to (Gc2, Gp2), serum Calcium (0.01) between (Gp1,Gc1) & (0.003) between (Gp2, Gc1) & (0.05) between (Gp1, Gc2), Serum Reduced Glutathion GSH (0.0001) for (Gp1, Gc1) and (0.0001) to (Gp1, Gc2) and (0,0001) between (Gp2, Gc1) Gc2) (0,0001) for (Gp2, Gc2), and Fasting Blood Suger FBS (0.0001) between (Gp1, Gc1), (0.0001) between (Gp1, Gc2) (0.001) between (Gp2, Gc1) (0.001) between (Gp2, Gc2), GSH (0.001) of (Gc1,Gp2) (

0.000) to (Gc2,Gp1), T.cholsterol(0.022) of (Gc1,Gc2), and it can be seen LDL (0.0007) to (Gp2,Gc1) and (0.0004) for (Gp1,Gc1), (0.004) to (Gp1,Gc2),

And A strong statistical correlation can be observed in Ascorbic acid (VIT-C) the results were statistical are (0.0001)between(Gp1,Gc1) and (0.003) for(Gp2,Gc2) and (0.001) between (Gp2,Gc1) it can be seen (0.0001) for (Gp1,Gc2), in VLDL(0.006) of (Gp1,Gc1), (0.004) between (Gp1,Gc2) and (0.0001) of (Gp2,Gc1) and (0.002) to (Gp2,Gc2) in patients with type 2 DM with and without obesity when compared with those of the control group. The distribution and allele frequencies of the ANGPTL-4 (Gc1>Gp1) adipose chemokine and interlicin1 (omentin-1 Gp2>Gc2) in all patients control, and the healthy controls were done (Gc1>Gp1).

The result showed significant differences in the concentration of Vitamin C there was a significant decrease ($p \leq 0.05$) in group Gp1(0.9+0.4) Gp2 (0.7+0.6) No statistical differences were observed for Angptl-4 with DBP, Ca

Conclusion: Diabetic associated with increment activity and decrement may alter insulin metabolism and play a significant role in the development of T2D resulting from insulin resistance activity. Diabetic nephropathy was associated with increment reactive oxygen species levels and decreased total antioxidant levels, which was associated with Increased omentin-1 concentrations might be a good diagnosis of diabetes mellitus and type 2 diabetes. More research is needed to confirm this theory and determine the relevance of omentin-1 concentrations in type 2 diabetes. decrement VIT-C and reduce glutathione activity.

Table of Contents

Table of Contents

Table of Contents

List of Figures

List of Figures

LIST OF Tables

LIST OF ABBREVIATIONS

TERM	MEANING
ARPs	Angiopoietins & Angiopoietin-Related Proteins
ATM	Adipose Tissue Macrophage
ADA	American Diabetes Association
BAT	Brown Adipose Tissue
BMP	Bone Morphogenetic Protein
CETP	Cholesteryl Ester Transfer Protein
CM	Chylo Microns
DAA	Diabetes Auto Antibody
DTNB	5,5- Di Thiobis (2-NitroBenzoic acid)
EC	Endothelial Cell
ELISA	Enzyme Linked Immuno Sorbent Assay
eNOS	endothelial Nitric oxide Synthase
EP tubes	Eppendorf tubes
FFA	Free Fatty Acids
FAD	Flavin Adenine Dinucleotide
FMN	Flavin Mono Nucleotide
GDA	Glutamic Acid Decarboxylase
GDF	Growth Differentiation Factor
GDM	Gestational Diabetes Mellitus
GIGT	Gestational Impaired Glucose Tolerance
GPx	Glutathione Peroxidase
GR	Glutathione Reductase
GSH	Glutathione
GSSG	Oxidized Glutathione
H_2O_2	Hydrogen Peroxide
HALS	Highly Active antiretroviral treatment–associated lipodystrophy syndrome
HEX	Hexachlorofluorescein
hGrx	Human Gluta redoxin
$HO^{\bullet}$	Hydroxyl Radical
HPV	Human papillomavirus
HRP	Horse Radish Peroxidase
HSL	Hormone-Sensitive Lipase
IA-2	Islet Autoantigen -2
IDL	Intermediate Density Lipoprotein

LIST OF ABBREVIATIONS

IDDM	Insulin Dependent Diabetes Mellitus
IGT	Impaired Glucose Tolerance
IL	Interleukin
iNOS	Inducible NO Synthase
IP3R	Inositol trisPhosphate Receptor
$L^{\bullet}$	Lipid Alkyl Radical
LPL	Lipoprotein Lipase
LRP	LDL-Receptor–related Protein
MDA	Malondialdehyde
Me-TP	Methanolic Extract Of Teucrium Polium
NADH	Necotine Amide Adenine Dinecleutide
NADPH	Reduced Nicotinamide Adenine Dinucleutide Phosphate
NEFA	Non-Esterified Fatty Acid
NIDDM	Non-Insulin-Dependent Diabetes mellitus
NOSs	Nitric Oxide Synthases
NK	Neutral Killer Cells
NKT	Neutral Killer T-Cells
$O_2^{-\bullet}$	Superoxide Anion
OS	Oxtidative stress
PBS	Phosphate buffer solution
PDGFRβ	platelet-derived growth factor receptor beta
PCOS	Poly Cystic Ovary Syndrome
PPARγ	Peroxisome Proliferator-Activated Receptor(α),(γ),(δ)
PUFA	Poly Unsaturated Fatty Acids
RNS	Reactive Nitrogen Species
ROS	Reactive Oxygen Species
RyR	Ryanodine Receptor
SER	Sarco-Endoplasmic Reticulum
SAT	Subcutaneous Adipose Tissue
SOD	Super Oxide Dismutase
TAP	Total Antioxidant Power
TAG	Tri Acyl Glycerol
TBA	Thio Barbituric Acid (4,6- Dihydroxy -2 Mercaptopyridine)
TCA	Tri ChloroAcetic acid
TGF	Transforming Growth Factor

LIST OF ABBREVIATIONS

TNF	Tumor Necrosis Factor α
Tris	Tris-(hydroxymethyl) amino methane
TSH	Total Thiol Groups
UCP1	Un Coupling Protein 1
VEGF	Vascular Endothelial Growth Factor
WAT	White Adipose Tissue

Chapter One

INTRODUCTION & LITERATURE REVIEW

1. INTRODUCTION

1.1 DIABETES MELLITUS

Diabetes Mellitus (D.M.) is one of the common diseases chronic or lifelong syndrome and chronic metabolic disorder that has become a major worldwide epidemic for the large number of people infected with it, T2DM is becoming more common with each passing year. In 2013, about 400 million people worldwide were estimated to have diabetes, with the figure expected to rise to 600 million by 2035(1), this metabolic syndrome one of the most important reasons for its occurrence is a hormonal imbalance in the endocrine glands that causes and is associated with an characterized by an increase in the level of (glucose), Note that glucose is essential for health and metabolic functions as it is an important the main energy source of generation in muscle cells and tissues(2).in the brain glucose is an essential source of energy for it, The primary cause of diabetes varies by type. However, regardless of the type of diabetes a patient has, it can lead to an increase in blood sugar. Having too Increased glucose in blood plasma can lead to problems to health for all parts of the body especially the organs with many blood vessels, Diabetic retinopathy (DR) causes worsening developing retinal detachment, and Advanced retinopathy with hemorrhage in vitreous, cataracts, or background retinopathy if not control glycemia(3)(4).

1.2. Classification of Diabetes Mellitus

1.2.1 Diabetes Mellitus TypeI(T1DM)

an immune disease It is classified as autoimmune-mediated Insulin-producing pancreatic beta cells are destroyed as a result of an autoimmune reaction with βcell and annihilation of ~3.2 million islets (> 90% Destruction)(5). Insulin is a necessary anabolic hormone that controls glucose, protein and lipid, mineral absorption, and metabolism as well as growth. Insulin is important because it allows glucose to enter muscle and adipose cells, encourages the liver to deposit glucose as glycogen and synthesize fatty acids,

accelerates amino acid uptake, inhibits fat breakdown in adipose tissue, and accelerates potassium absorption into cells. Type 1 Diabetes Mellitus (T1DM) necessitates the use of insulin replacement treatment for the rest of one's life. (DKA) or Diabetics-ketoacidosis occurs without insulin and is life-threatening(6). This activity reviews the evaluation and management of type 1 diabetes mellitus. It highlights the role of interprofessional team members in collaborating to provide well-coordinated care and enhance outcomes for affected patients. Gestational diabetes occurs during pregnancy, but women may cure it after childbirth(7).

It is divided into two types.

A- Immune-Mediated Diabetes

This type of diabetes, which has already been covered in the terms insulin-dependent diabetes, juvenile-onset diabetes, or Type I diabetes, is caused by cellular-mediated autoimmune destruction of the pancreatic -cells and affects only 5-10% of patients with diabetes. The pace of -cell destruction in this kind of diabetes is extremely diverse, being fast in some people (mostly infants and children) and sluggish in others (mainly adults)(8).

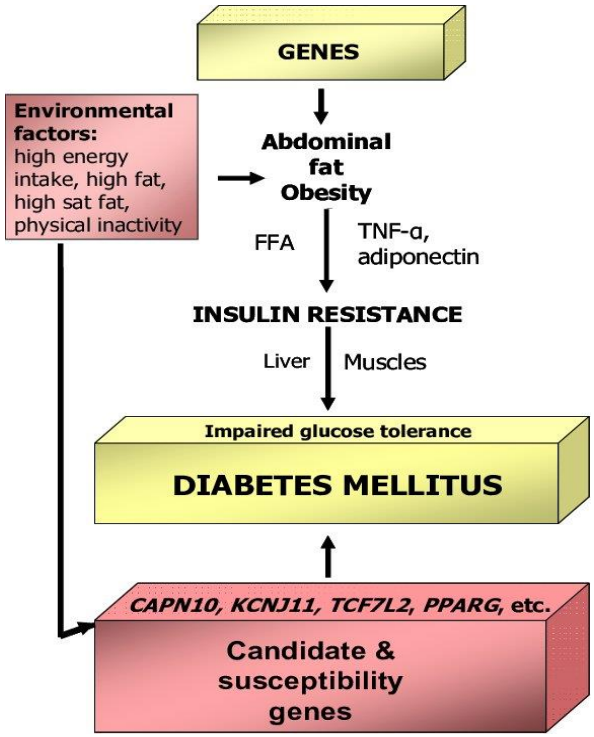
B- Idiopathic Diabetes

There are no recognized causes for some of the first types of diabetes's characteristics. Some of these patients have chronic insulin insufficiency and are exposed to ketone acid, but they show no signs of autoimmunity. Episodic ketoacidosis occurs in people with this kind of diabetes, and they have different degrees of insulin shortage between episodes. The cause of variable autoantibody status is unknown, however, anti-idiotypic antibodies may impact DAA assays over time. Both kinds of DMT1 are produced when -cells are damaged(9).

1.2.2 Diabetes Mellitus TypeII(T2DM)

Adult-onset diabetes, More common than type 1, non-insulin-dependent diabetes mellitus (NIDDM), Epidemiological data show that Diabetes is currently also one of the

main health problems in all countries of the world and is placed by the World Health Organization in the top ten in the ranking of causes of death(10), 90% Of the total number of diabetics in the United States are type 2, is a complex disease in which both genetic and environmental factors interact in determining impaired β-cell insulin secretion and peripheral insulin resistance, Insulin resistance in muscle, liver, and severely obese is common in T2DM and obesity patients, resulting in a reduced reaction of these insulin hormone receptors Figure(1-1).



Figure(1-1) In type 2 diabetes, there is a link between genes and environmental variables. Obesity, insulin resistance, and eventually diabetes may be caused by a combination of genes and environmental factors. Environmental variables may work in tandem with diabetes candidate and susceptibility genes to directly initiate type 2 diabetes pathogenesis(11).

When blood sugar levels are higher than normal but not high enough to be categorized as diabetes, the condition is known as impaired glucose tolerance (IGT) Figure(1-1). IGT is regarded as a pre-diabetic condition, and those who have it are more likely to acquire diabetes, On the other side, insulin resistance is an illness where the body

does not react to insulin, a hormone generated by the pancreas that controls blood sugar levels, as it should. This may cause high blood sugar levels Table(1-1), which eventually may cause type 2 diabetes and prediabetes.

Table (1-1) Diagnostic reference values(12) ,**Iraqi consensus**(13)

Parameters	Normal*	Prediabetes	T2DM
Haemoglobin A1c	<5.7%* <6.0%**	5.7-6.4%* 6.0-6.4%**	≥6.5%
Fasting plasma glucose	<100mg/dl* <110mg/dl**	100-125mg/dl * 110-125mg/dl **	≥126mg/dl
Two-hour plasma OGTT	<140mg/dl	140-199mg/dl	≥200mg/dl

OGTT:Oral Glucose Tolerance Test, T2DM:Type II Diabetes Mellitus, *Normal glucose metabolism, ‡American Diabetes Association, §World Health Organization.

Obesity, a sedentary lifestyle, and a diet heavy in carbs are some lifestyle and genetic variables that might cause insulin resistance. Similar to type 2 diabetes, IGT can be brought on by being overweight or obese and can be a sign of type 2 diabetes(14).

Insulin resistance is portrayed as a straightforward explanation. Insulin's inhibitory effect on lipolysis is waning, or Lipid FFA levels rise in adipocytes as a result of metabolism. The production and secretion of VLDL are stimulated by an improvement in FFA fluctuation in the liver, which results in hyper-tri-glyceride mia. Through the action of cholesteryl ester transfer protein, TG from VLDL is transferred to both HDL and LDL (CETP). This procedure produces triglyceride-enriched HDL and LDL particles. The kidney clears triglyceride-enriched HDL from accumulation more quickly, leaving fewer HDL particles to accept cholesterol from the vasculature. Insulin resistance causes a decrease in the metabolism of glucose in the liver glycogen synthesis, as a result of reduced glycogen synthase stimulation, improved hepatic gluconeogenesis, and glucose transfer by the hepatic(15).

1.2.3 Gestational Diabetes Mellitus

a condition characterized by abnormal glucose tolerance during pregnancy (GIGT), Gestational Diabetes mellitus is the most common pregnancy medical complication.

thought to be an exaggeration of pregnant women's physiologic changes in energy metabolism. Pregnancy, Gestational diabetes mellitus (GDM) affects 5 to 20% of pregnant women(16), on the other hand, may conceal an underlying proclivity for glucose intolerance, which will become apparent in the non-pregnant state at some point in the future, if not in the early stages of pregnancy Indeed, at least half of all women with gestational diabetes develop overt diabetes at some point in their lives(17). The primary concern in women diagnosed with gestational diabetes during pregnancy is increased fetal development, which may also lead to an increase in maternal and infant mortality. Shoulder dystocia is more common in diabetic mothers' infants due to fetal overgrowth and increase body deposition on the shoulders. Cesarean deliveries and preeclampsia are also on the rise(18).

1.2.4 Maturity Onset Diabetes of Young(MODY)

Maturity-onset diabetes of the young (MODY) is a dominantly inherited non-insulin-dependent diabetic condition that is frequently diagnosed before the age of 25 and was originally recognized by Tattersall. MODY is the most prevalent kind of monogenic diabetes, accounting for 1–2% of all diabetes cases in Europe, yet it is frequently misinterpreted as type 1 or type 2(19).

To comprehend maturity-onset diabetes of young (MODY), we must first comprehend the overall categorization of diabetes mellitus. Type 1 diabetes (T1DM), Type 2 diabetes (T2DM), other varieties of diabetes, and gestational diabetes are the different types of diabetes (GDM). Type 1 diabetes is the most common form of insulinoma, and it is divided into two types:(autoimmune,Islet autoantibody-positive;TIADM) and (idiopathic,Islet autoantibodies) are immune system-produced proteins that have been connected to type 1 diabetes. These autoantibodies are hostile to the islets of Langerhans or, in certain cases, are especially hostile to the autoantigens of the cells that secrete insulin. The diagnosis of type 1 diabetes is made when an individual has islet autoantibodies, which point to an autoimmune etiology(20).

1.3 History of Disease

the ancient Egyptians 3000 years ago described similar diabetes mellitus Clinical features(21), from the ancient city Cappodocia first time coined the term “diabetes” by Aratus (81-133AD)(22), (honey-sweet) was the literal translation to the word Mellitus Later it was added by Thomas Willis in 1675 (Britain) after he discovered what the ancient Indians discovered that the blood and urine of patient was so sweet, in 1776 (Britain) physician Matthew Dobson confirmed that the cause of sweetness in urine and blood is the high sugar content in them and is considered he is the first one confirmed this, In 1857 the French physician Claude Bernard concluded that diabetes was due to an increase in glucose production and the role of the pancreas in it, Von Meiring reported in 1889 with fellow physician Minkowski that acute diabetes mellitus occurred after total pancreatectomy in dogs This important qualitative discovery in the medical world was called (THE ROLE OF OSCAR MINKOWSKI)(23).

1.4 Treatment of Diabetes Mellitus

There are many modern methods for treating patient DM after active management of a patient with physical activity and nutrition care, use of oral hypoglycemic agents & injection or complication, use of an insulin pump to control blood glucose

Table(1-2) Oral and Injection anti-DM Drugs(24)**.**

Glasses of anti diabetic drugs	Antidiabetic drugs
Biguanide	Metformin
Insulins	
	Regular insulin
	NPH insulin
	Aspart insulin
	Protamine aspart insulin
	Degludec
	Detemir insulin
Dipeptidyl peptidase 4 inhibitors	Sitagliptin
	Linagliptin
	Vildaglptin
Alpha glucosidase inhibitors	Voglibose
Thiazolidinediones	Pioglitazone
Sulphonylureas	
	Glimepiride
	Gliclazide
	Glibenclamide
PPAPα+γ agonists	Saroglitazar
GLP-1receptor agonists	Liroglutide

1.5 Obesity

Obesity is the most important health problem a multifactorial chronic disease caused by the interaction of social, behavioral, environmental factors, psychological(25), energy metabolism, cellular, and molecular indicators(26), We can compare obesity from the first thermodynamic rule and explain obesity(27), that the body's consumption of energy leaving it is less than the energy that enters it, and it is the condition wherein the adipose tissue increases and can be characterized as an increase in weight that leads to an increase in adipose tissue(28). fat accumulation that is excessive Obesity is defined by the World Health Organization (WHO) as an increase in body mass index (BMI)(29).

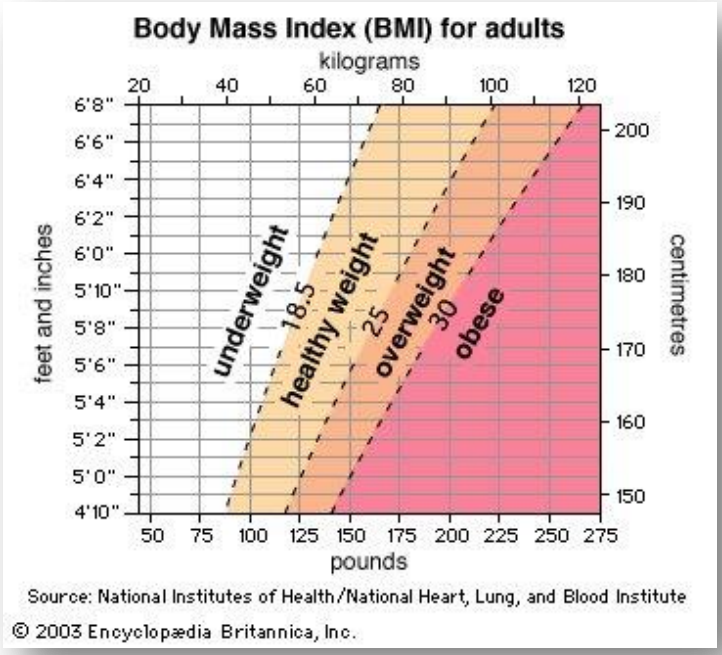
Table(1-3) International Definitions & Classification of Nutritional Status for Adults based on underweight, overweight, and Obesity, according to BMI(kg/m^2)(30)

Weight Status Classification	BMI(kg/m^2)WHO	BMI(kg/m^2)Asia-Pacific
Under weight	<18.5	<18.5
Normal or Healthy Weight	18.5-24.9	18.5-22.9
OverWeight&	25.0-29.9	23-24.9
Pre-Obese	---	25-29.9
Obese	≥&30.0	≥25
Class(I)Moderate-Obese	30.00-34.99	
Class(II)Morbid-Obese	35.00-39.99	
Class(III)Super-Obese	≥40.00	

(WHO: World Health Organization)

Widely believed assumption among the general public is that having a body mass index (weight/height^2) (BMI) greater than 30 and underweight having a BMI less than 25 or 25-20 kg/m^2(31). Obesity prevalence has risen dramatically in recent decades. In the United States, 69 percent of Americans are either overweight or obese, with 35 percent adiposity(32). Obesity is implicated in the pathogenesis of a variety of cardiovascular diseases, including T2DM& nonalcoholic fatty liver disease. Obesity is a cause of heart disease because it is associated with a significantly higher prevalence of chronic

conditions such as high blood pressure, high cholesterol, and metabolic syndrome, all of which increase the risk of stroke, and cardiovascular complications. Insulin resistance(IR) and increased inflammation in adiponectin are major contributors to the development of type 2 diabetes(T2D) on the other hand(33), Even as an adjunct to polycystic ovaries PCOS following weight gain(34).



Figure(1-2) body mass index for adults

1.6 Adipose Tissues

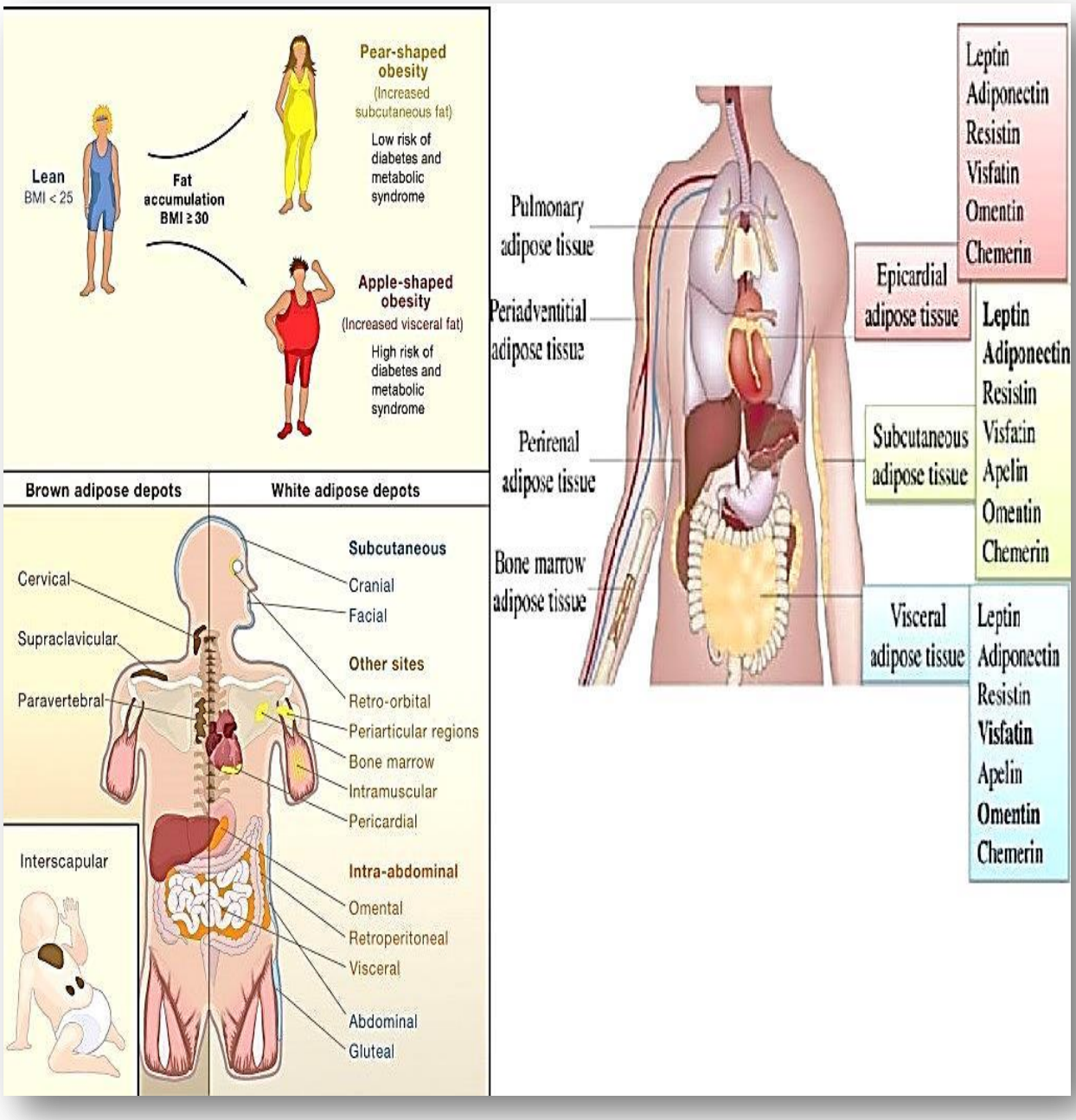
The major energy collection and protection organ is adipose tissue. It's found under the skin and surrounding the internal organs. By accumulating and expelling fatty acids and cells that secrete adipokines, it controls metabolism. Adipocyte enlargement and proliferation are caused by excessive dietary intake, resulting in local ischemia in fatty tissue and alterations in adipokine secretion. More immunological cells are recruited into adipose tissue as a result, and inflammatory signaling factors are released. Intracellular insulin signaling is hampered by excess free fatty acids and inflammatory factors(35).

Obesity may be an independent risk factor for the development of cardiovascular disease The nature of an independent relationship between elevated body mass index (BMI) levels, cardiovascular (CV) risk, stroke, heart attack, and mortality has long been debated. Furthermore, despite being shown to be an independent risk factor for several cardiovascular diseases, insulin resistance has been diagnosed, giving rise to the term "obesity paradox"(36). Several pathways have been identified that link obesity to cardiovascular disease. We attempt to summarize the complex relationship between obesity and cardiovascular disorders, specifically coronary atherosclerosis, heart failure, and atrial fibrillation(37). In addition to overweight women, obesity is a risk factor for thromboembolic complications this issue is crucial(38).

1.6.1 AdiposeTissue & Adipokines

White Adipose(WAT)& Bruin Adipose Tissue(BAT)is no longer regarded as passive tissue only used for energy storage but are increasingly becoming recognized as key regulator of physiologic and pathologic processes such as immunology and inflammation like pathophysiological cues. Macrophages are a component of adipose tissue that plays an active role in its functions. Cross-talk between lymphocytes and adipocytes can also regulate the immune system. TNF-alpha, IL-6, monocyte chemoattractant protein 1, Adipokines, also comprehended as adipocytokines, are cytokines (cell signaling proteins) secreted by adipose tissue. Some adipokines contribute to an obesity-related low-grade state of inflammation or the development of metabolic syndrome, a constellation of diseases including, but not limited to, type 2 diabetes, cardiovascular disease, and atherosclerosis. The first adipokine to be discovered was leptin in 1994. Since that time, hundreds of adipokines have been discovered(39). and other pro-inflammatory and anti-inflammatory substances are produced and released by adipose tissue, including Omentin-1(Intelectin-1) the adipokines leptin, Cardiophin-1, adiponectin, resistin, and visfatin, as well as cytokines and chemokines like TNF-alpha, IL-6, and others. A mole that causes inflammation& due to reduced T-cell responses.

molecular links between obesity and several pathologies Adipokine levels are altered in a range of inflammatory diseases, while its pathogenic significance has yet to be determined(40).

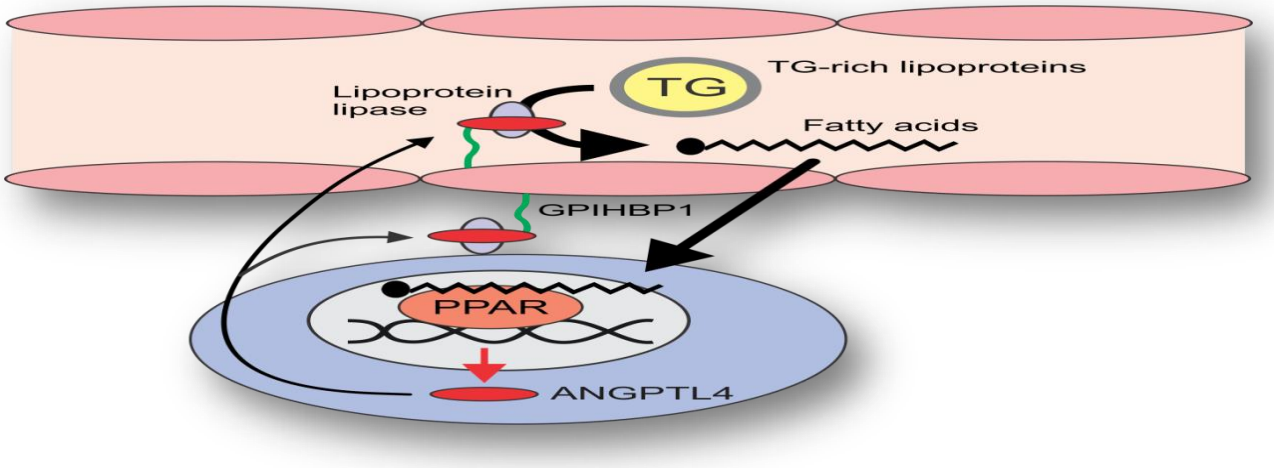


Figure(1-3) Human Obesity Risks Are Influenced by Fat Distribution.

Figure(1-3) it distribution of (WAT)&(BAT) with adipokine synthesis in subcutaneous(SAT), visceral(VAT), and epicardial large adipocytes tissues. The subcutaneous and visceral fat are the main regions of white adipose tissue, which includes multiple discrete anatomical depots. Numerous smaller adipose depots, such as epicardial, pulmonary, or bone marrow fat, may perform specialized activities in their surrounding tissues. Heterogeneous adipokine production by each adipose tissue deposit could influence organ function and systemic metabolism in different ways. Adipokines in bold indicate higher levels of production(40)(41).

1.7 lipid profile

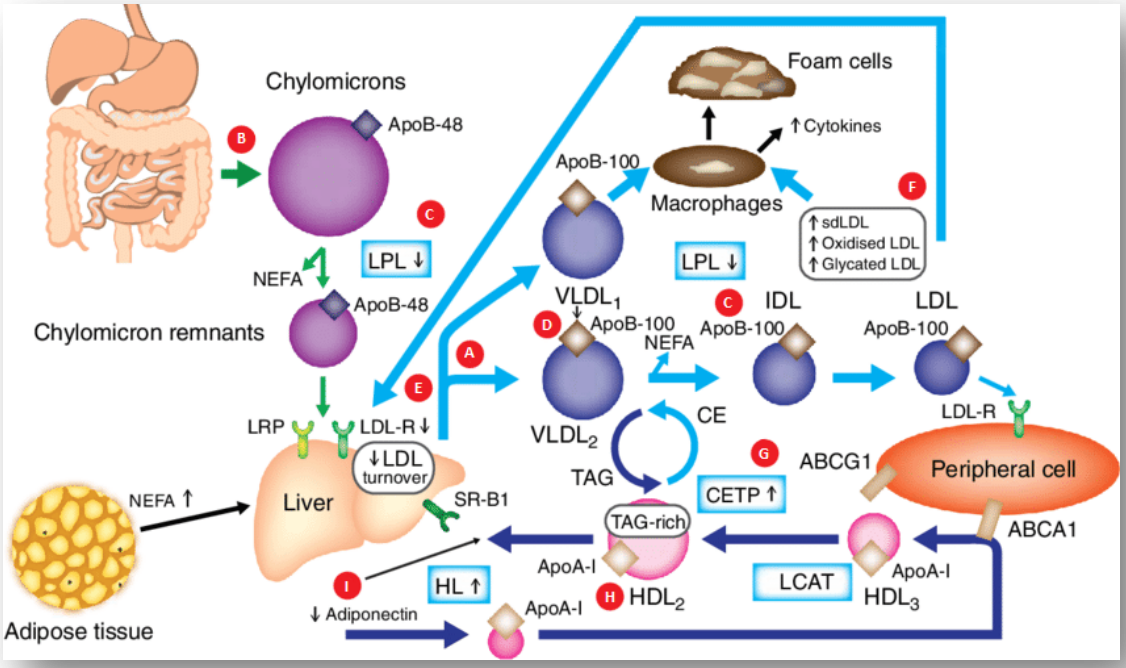
Free Fatty Acids(FFA) are important to energy production and are generated during hydrolysis of 1-glyceride, or mono-glycerides, 2-di-glycerides, or lipolysis triglycerides in the adipocyte by HSL(41) (in vivo& inhibits by insulin) and lipoprotein lipase the primary enzymes(extracellular& activates by insulin) a regulatory network of lipid and energy homeostasis(42), Lipolysis in vivo is mediated by different intracellular enzymes in the adipocyte, endothelial lipases, adipocyte cell size, and blood flow in adipose tissue.



Figure(1-4) The image shows the function of ANGPTL4 as an endogenous inhibitor oflipoprotein lipase and how fatty acids regulate it through PPA receptors.lipoprotein metabolism(Chylomicron,VLDL, IDL, LDL, HDL)and the effects of insulin on lipoprotein

Initially, these lipoproteins contain different aggregates in their outer shell that give each biomolecule a specific function in cellular metabolism**,** the major Apo. in these lipoprotein particles is, Chylomicron contain(ApolipoproteinA, B-48, E) VLDL(Apo.B-100, C, E) and IDL(Apo.B-100, E) LDL contain(Apo.B-100) HDL(Apo.A&C).

Insulin inhibits hepatic VLDL synthesis directly. Insulin has been demonstrated to cause a 66 percent drop in VLDL triacylglycerol formation and a 53 percent decline in VLDL-ApoB synthesis in people with normal lipoprotein metabolism. Insulin lowers VLDL production via lowering circulating levels of NEFA, which are VLDL substrates, and by directly inhibiting VLDL production in hepatocytes(43).



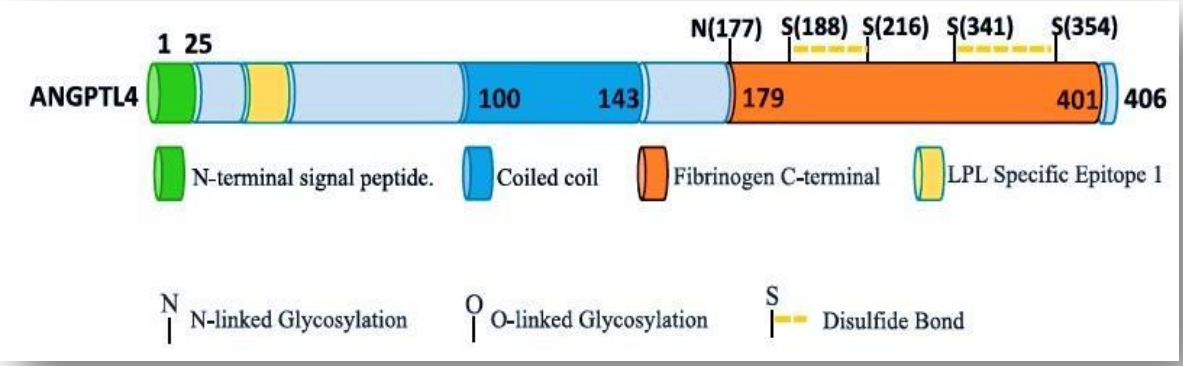
Figure(1-5) The most common lipid abnormalities in people with type 2 diabetes.

Figure(1-5) shows hypertriglyceridemia, and qualitative and kinetic abnormalities in triacylglycerols: (A)increasedVLDL (mainly LDL 1), (B)increasedChylomicronproduction,(C)decreasedChylomicron and VLDL catabolism (diminished LPL activity). (D)increased synthesis of big LDL(VLDL 1), which is

preferentially taken up by Macrophages; LDL(qualitative&kinetic abnormalities): (E)decreased LDL turnover (decreased LDL B/E receptor), (F)an increase in glycated LDLs, small, dense LDLs(TAG-rich), and oxidized LDLs, which also are selectively taken up HDL (low HDL-cholesterol, qualitative and kinetic abnormalities):(G) increased CETP activity (increased transfer of triacylglycerols from TAG-rich lipoproteins to LDLs and HDLs), (H)increased TAG content of HDLs, promoting HL activity and HDL catabolism, (I)low Adiponectin", favoringHDL catabolism CETP, cholesteryl ester transfer protein; dLDL, dense small LDL; HDLn, NascentHDL; HL, hepatic lipase; HSL, hormone-sensitive lipase; SR-B1, scavenger receptorB1; (45).

1.8 Angiopoietin-like proteins. ANGPTL-4

The ANGPTL4 gene in humans produces the protein angiopoietin-like protein 4 (ANGPTL4). The gene formerly known as ANGPTL2, HFARP, PGAR, or FIAF is now known as ANGPTL4. The encoded protein functions as a serum hormone that directly affects the regulation of lipid metabolism. By regulating vascular permeability, cancer cell motility, and invasiveness, ANGPTL4 is implicated in the metastatic process and plays a significant role in many malignancies. Human organs such as the liver, adipose tissue, and gut express ANGPTL4, a lipoprotein lipase inhibitor that controls lipid metabolism and storage.Recommended name(Angiopoietin related protein-4) and Alternative name; Angiopoietin like protein-4 & Gene name(ANGPTL4) Protein also known as; HepaticFibrinogen/or/Angiopoietin-RelatedProtein (HFARP)(44).



Figure(1-6) Schematic representation of ANGPTL proteins structure(45).

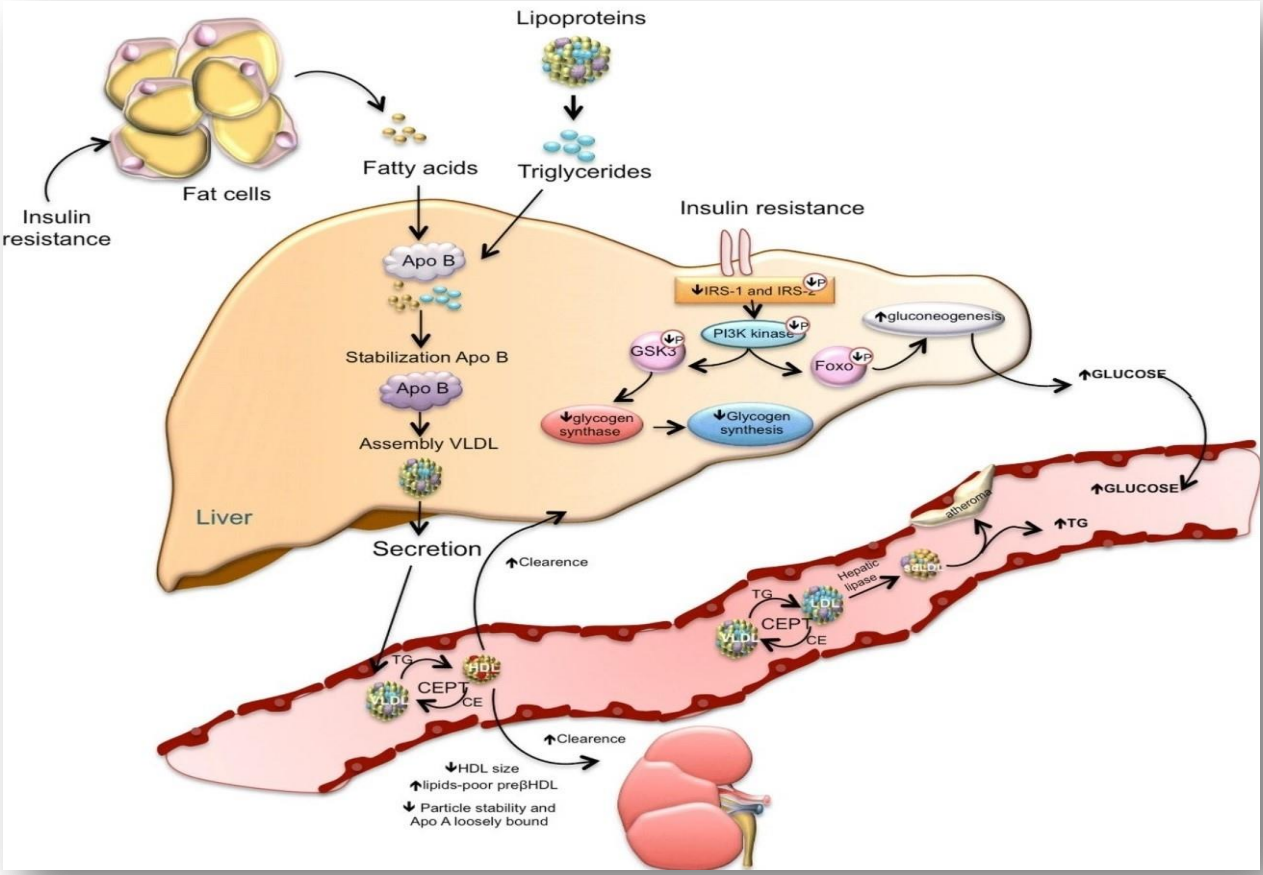
angiopoietin-like 4 gene family member a ~45-65 kDa secreted and glycosylated protein(46), has emerged as a remarkable multifaceted protein involved in a wide range of metabolic and non-metabolic conditions over the last decade. The physiological role of ANGPTL4 has been identified as a key player in numerous different areas such as energy homeostasis, at least in part, due to its inhibitory function, the interplay between LPL (lipoprotein lipase) or adipocyte lipolysis and ANGPTL4's coiled-coil domain.

Table(1.4)International Definitions & Classification of ANGPTl- PROTEINS

ANG.	Other common names	Main tissue expression	hum.	mou.
1	ARP1,angioarrestin,ANG3,AngY,ANGPT3, UNQ162,dJ595C2.2,2810039D03Ri	Liver, muscle	1	1
2	ARP2,AI593246,AW260363,HARP	Heart,vessels,adiposetissue	9	2
3	ANL3,ANG-5,FHBL2,ANGPT5	Liver	1	4
4	ARP4,PGAR,HFARP,FIAF	Liver,Adiposetissue,brain,in test thyroid,kidney,heart	19	7
5	ANGL5_HUMAN,A_14_P125422, NP835228.1	Heart	11	-
6	AGF,ARP5,ARP3	Liver	19	9

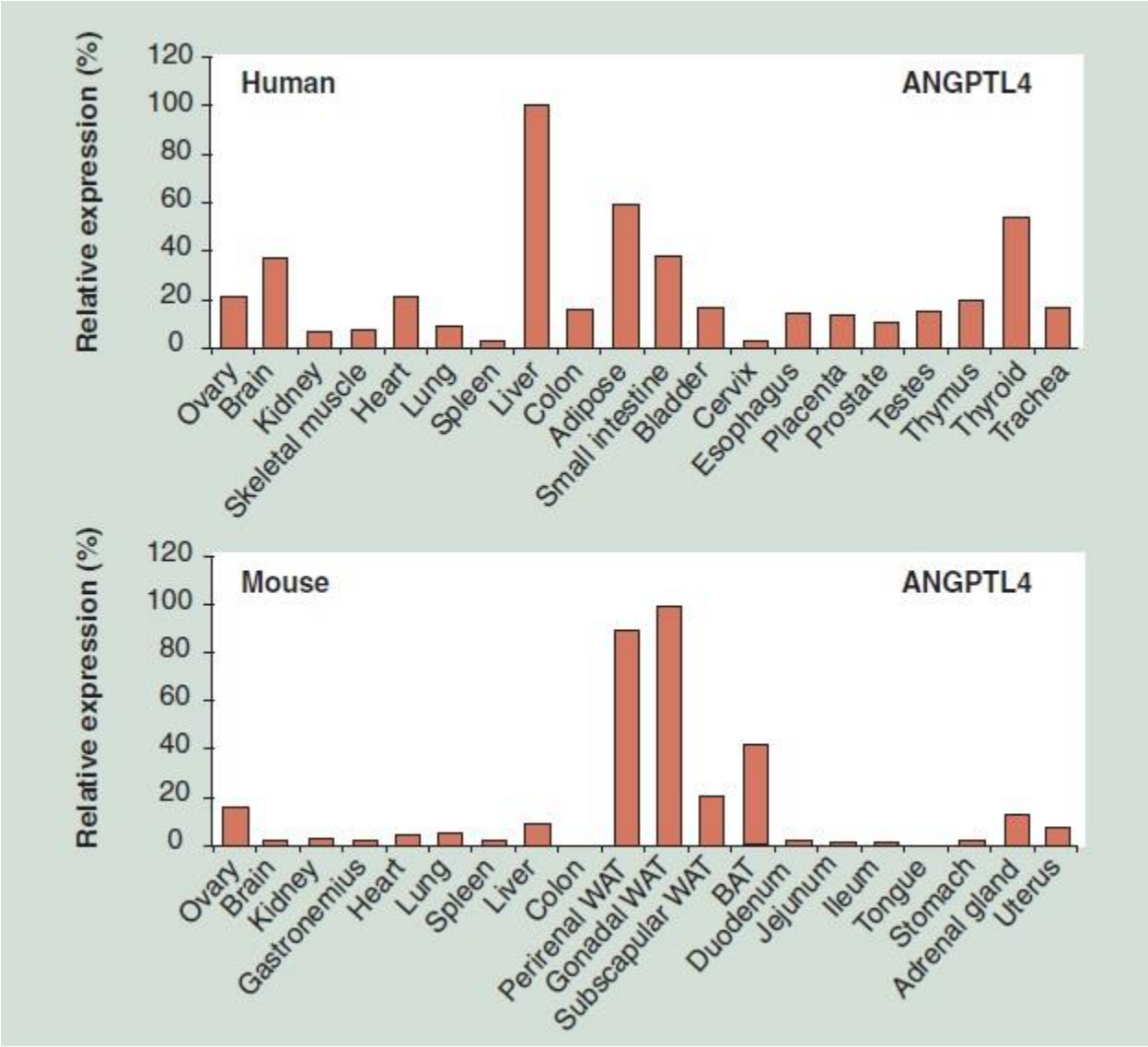
The fibrinogen-like domain of fibrinogen, ANGPTL4 interacts with and motivation to aid in tissue repair, as well as modulating vascular permeability& vasculogenesis or growth of blood vessels, Endothelial cells regulation quiescent states by competitive interaction(47), VEGF-A and Angiopoieteins is identified like first and second growth

factors family for vascular endothelium tyrosine receptor Tie1&Tie2(49) and regulates the level of ROS (reactive oxygen species) to enhance tumor growth(50).



Figure(1-7) The current state of knowledge about ANGPTL proteins in angiogenesis, inflammation, and tumorigenesis is reviewed here. Schematic diagram of the sequence of ANGPTL proteins. A fibrinogen-like domain, an N-terminal signal peptide, a coiled-coil domain, and are all correlated domains in the ANGPTL group(45)**.**

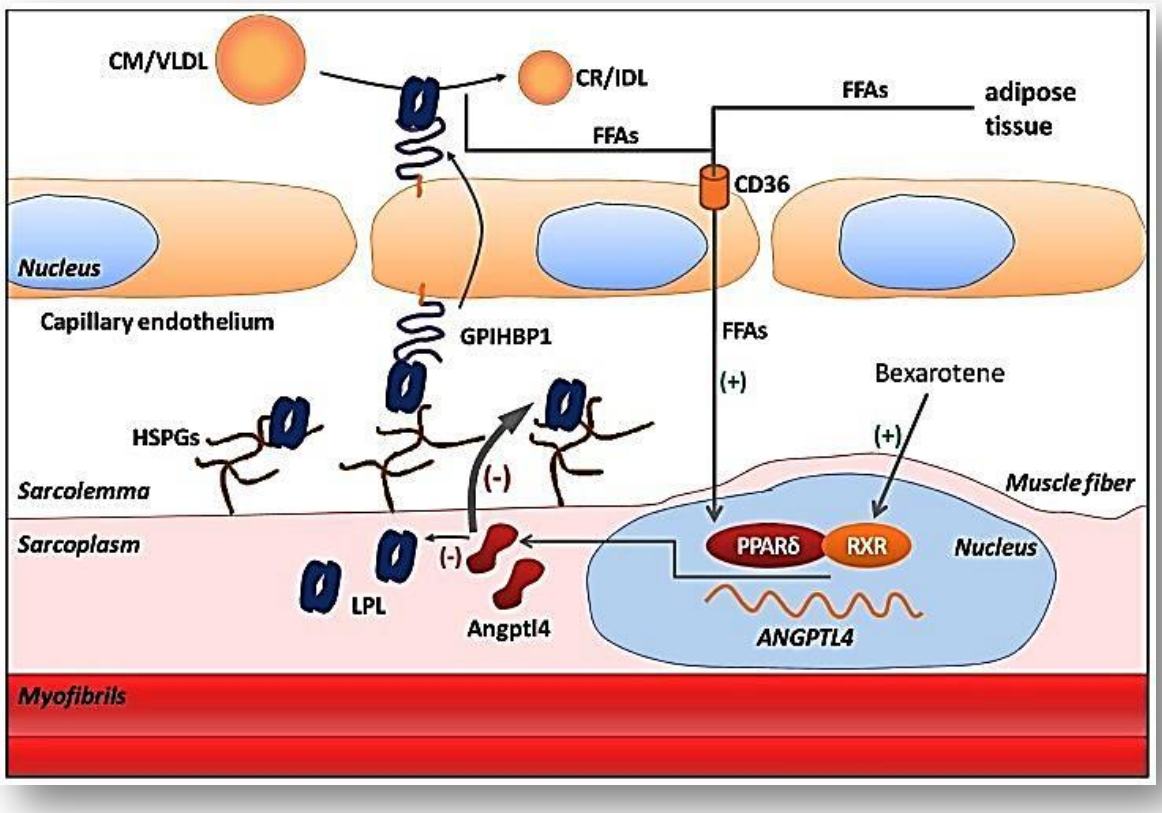
By preventing lipoprotein lipase (LPL) activity, ANGPTL4 is an essential regulator of lipid metabolism and energy balance. The function of ANGPTL4 in controlling lipid metabolism, however, varies depending on the tissue. In the heart, skeletal muscle, and small intestine, ANGPTL4 inhibits the local release of LPL, whereas ANGPTL4 produced from liver and adipose tissue primarily functions as an endocrine factor that controls systemic lipid metabolism. As a multipurpose protein, ANGPTL4 also prevents foam cell development in macrophages, acting as an anti-atherogenic agent(48).



Figure(1-8) Relative expression ANGPTL4 IN Human & Mouse

Angiopoietin-like proteins (ANGPTLs) are a protein family with structural similarities to angiopoietins. So far, eight ANGPTLs have been identified, namely ANGPTL1 through ANGPTL8. Emerging evidence suggests that ANGPTLs play an important role in regulating a wide range of physiological and pathophysiological processes. The majority of ANGPTLs have multi-biological properties, such as established functional roles in lipid and glucose metabolism, inflammatory processes, hematopoiesis, and cancer(49).

Figure(1-9) Hypertriglyceridemia raises the risk of several diseases, including diabetes, including nonalcoholic hyperlipidemia, and is associated with an increased risk of cardiovascular disease (CVD)(50). The angiopoietin-like proteins (ANGPTLs) family, particularly ANGPTL4, and 3,8, which control lipoprotein lipase (LPL) inhibiting stimulation, play critical roles in TG metabolic processes or non-esterified fatty acid (NEFA) concentrations(51), and pathogens that are associated, Many transcriptional and remark Factors that control triglyceride metabolism are implicated in the normal and pathophysiological regulation of ANGPTLs(52).



Figure(1-9) FAs produced domestically by LPL-mediated hydrolysis of VLDL and chylomicrons (CM) in combination with FAs originating from adipose tissue (FA-albumin) can activate the PPAR/RXR heterodimer, which in turn upregulates Angptl4 gene expression, according to the working hypothesis. Angptl4 suppresses LPL activity primarily at the sarcolemma's surface, resulting in less LPL accessible for transport at luminal locations via GPIHBP1. LPL inhibition by Angptl4 occurs intracellularly to a lower extent. This method may protect muscle tissue from lipid excess and insulin resistance, but it could also increase systemic hypertriglyceridemia caused by bexarotene(53)**.**

1.8.1 The Pharmacological Regulation of ANGPTL FAMILY

Hypertriglyceridemia is treated with a pharmacological objective. Loss-of-function mutations in ANGPTL3 are linked to significant reductions in plasma levels of VLDL, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) in humans (HDL). Instead, people with ANGPTL4 loss-of-function mutations have TG-rich lipoproteins and a small but considerable increase in HDL. By acting as powerful

inhibitors of the enzyme lipoprotein lipase, the angiopoietin-like proteins (ANGPTLs) 3, 4, and 8 have emerged as essential regulators of plasma lipid metabolism (LPL). In this study, we focus on the impact of ANGPTL3(54), ANGPTL4, and ANGPTL8 on LPL activity and plasma triglyceride clearance throughout physiological situations such as fasting, refeeding, exercise, and cold exposure to present an integrated picture of their function in lipid metabolism. ANGPTL4 induces LPL activation and a considerable reduction of TG-rich lipoproteins in plasma in animal models, including non-human primates, with no apparent side effects. It also decreases the inhibition of both targets to some extent(55). The LDL-C molecule is not dependent on the LDL receptor. A similar piece of evidence was found.

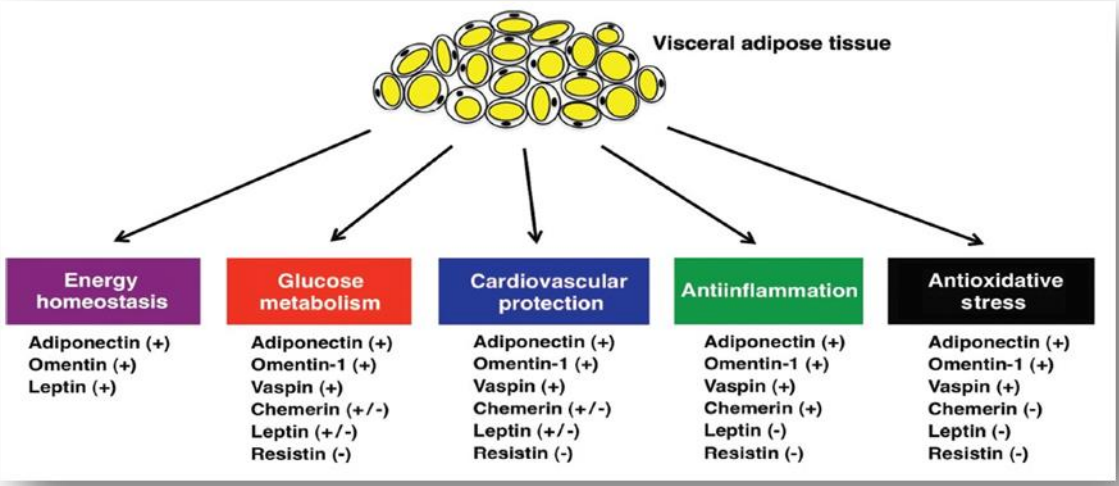
1.9 Omentin-1

Omentin-1 or Intelectin-1 a new adipokine, an anti-inflammation protein, intestinal lactoferrin receptor, a peptide secreted& released by visceral adipose tissues fat, appears to be synthesized to a greater extent in vascular stromal cells within the lipid than in the adipose tissues themselves, in contrast to visfatin. It operates as insulin and, like visfatin, has favorable effects on glucose absorption(56).

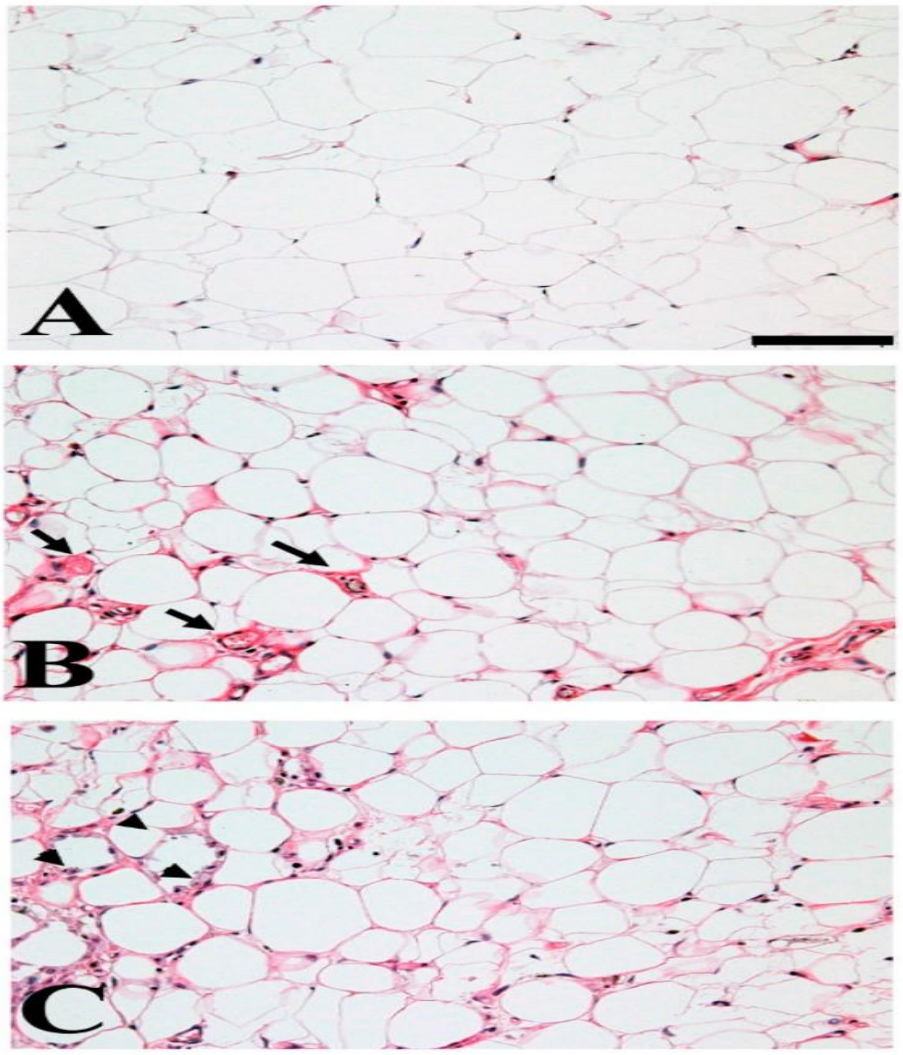
Intelectin-1 It's a sensitizer with insulin-mimicking characteristics In terms of glycemic management, Yang et al. (2006) found that boosting protein kinase b (Akt) phosphorylation (and hence activation) in human adipocytes increased insulin-stimulated glucose transport, indicating that omentin could increase insulin sensitivity.. initially described in intestinal Paneth of bacterial cells in carbohydrate moieties associates with galactofuranose It is believed to have a role in the intestinal defense mechanisms against enteric pathogenic Escherichia coli bacteria, implicated in cardiovascular disease the visceral fatty tissue a major sources of secreted anti-inflammatory protein Omentin-1. Insulin resistance (IR) and increased inflammation in visceral adipose tissue are major contributors to the development of type 2 diabetes (T2D) Altered levels of Omentin-1 are associated with obesity and Type 2 Diabetes (T2D)(57). Although Omentin-1 is

implicated in the insulin signaling pathway, the relationship between the genetic variants of Omentin-1 and T2D is not yet explored. There are many opinions in previous research about its effect on increasing complications of diabetes, and opinions are contradictory Signaling Mechanisms Involved in Omentin's Metabolic Activities, Interestingly, the chromosomal region in which the omentin-1 gene is located has been linked to type 2 diabetes in a number of different populations. As a result, changes in this gene may have an impact on how insulin is metabolized and contribute significantly to the onset of insulin resistance and type 2 diabetes(57).

Scientific data supports the significance of omentin in obesity and glucose metabolism regulation, as evidenced by the studies mentioned above. However, information on the systems involved is limited at this time. Omentin may play a role in appetite regulation, according to Brunetti et al(58).



Figure(1-10) Effects of new adipocytokines on inflammation, oxidative stress, glucose metabolism, the cardiovascular system, and energy balance. As new adipocytokines, adiponectin, omentin-1, vaspin, chemerin, resistin, and leptin have been chosen. Regarding energy balance, glucose metabolism, cardiovascular protection, the anti-inflammatory response, and oxidative stress, (+) denotes a good impact and (-), a negative effect(59).



Figure(1-11) The morphology of human adipose tissue is altered by inflammation. Excessive calorie consumption, as well as being overweight or obese, induces a dynamic change in adipose tissue. The vascularity of healthy adipose tissue (A) may be increased (B) The vascular arteries, which may also harbor inflammation during the hypertrophy phase, are indicated by an arrow (C) The arrowhead denotes the macrophage infiltration. Adipocytes and adipose stromal cells secrete less adiponectin and intelectin-1 as a result of hypertrophy, but they secrete more pro-inflammatory adipokines such as Leptin. Archival pathological tissue slices were formalin-fixed, paraffin-embedded, and stained with hematoxylin and eosin after getting approval from the Gifu University Graduate School of Medicine's Institutional Review Board (Specific approval No. 24-256). A distance of 100 meters is indicated by the scale bar.

1.9.1 The Pharmacological Regulation of Omentin-1

Following metformin medication, testosterone levels were found to be significantly lower. Treatments of omental adipose tissue explants with gonadal and adrenal steroids, on the other hand, had no discernible effect on omentin-1 levels. As a result, the effects of metformin on serum omentin-1 levels found in this study seem implausible(60).

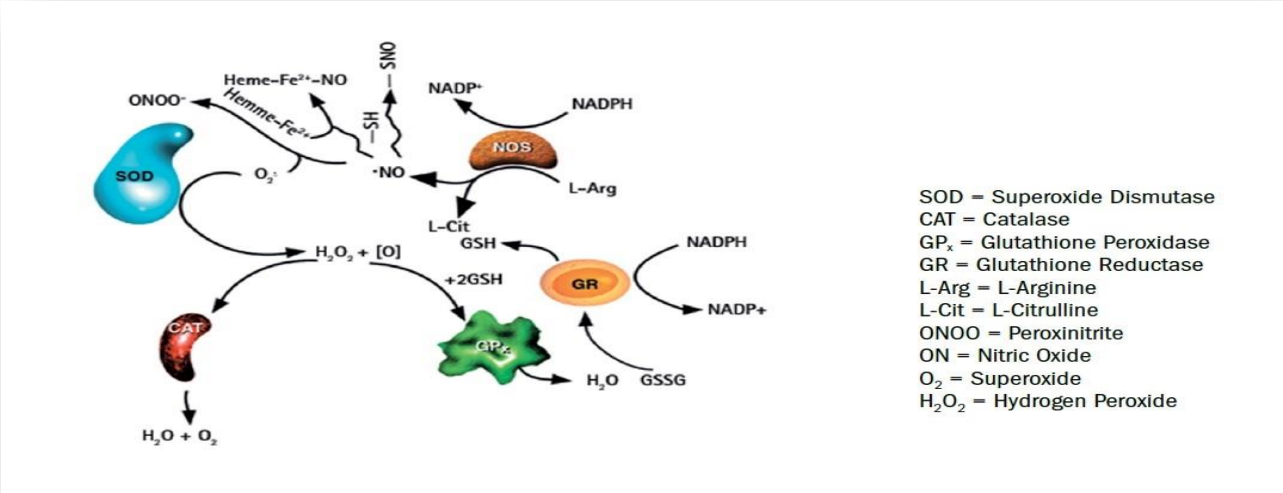
1.10 Oxidative Stress& Antioxidants

Free radicals are highly reactive and destructive molecules created naturally in the human body as a consequence of metabolism (oxidation)(61) or as a result of exposure to chemicals and toxins such as regular cigarettes, alcoholism, and UV light. Free radicals only last a fraction of a second, yet throughout that time they can damage DNA, leading to abnormalities that can lead to cancer. Antioxidants in our meals can neutralize unstable chemicals, lowering the chance of harm (62). The increase in the percentage of free radicals resulting from the imbalance between the level of free radicals that generate oxidants and the level of antioxidants leads to harmful damage that causes tissue damage. This imbalance in the biological balance is called oxidative stress.

Mitochondria are the primary source of free oxygen radicals, which would induce organ dysfunction by oxidizing biological molecules like carbohydrates(63), proteins, and lipids. Oxidative stress can be caused by either an excess of these species or a malfunction of the antioxidant defense mechanisms(64).

There is various nutritionally induced oxidative stress main source that causes inflammation. Much evidence suggests that high nutritional intakes can advertise oxidative stress and, as a result, contribute to inflammatory response via nuclear factor-kappa B- (NF-B-) modulated cellular pathways Nutritional carbohydrates(65), animal-based proteins, and lipids are worth mentioning because they may contribute to the long-term effects of nutrient content assisted inflammation. Oxidative stress is a major contributor to metabolic disorders associated with high-carbohydrate and animal-based

protein diets, as well as too much-saturated fat or obesity and it is frequently associated with improved survival once the cardiovascular disease. Obesity has now become an endemic problem, and it is a leading cause of a wide range of medical conditions, including coronary heart disease (CVD), DM`S, and cancer. The molecular pathways of nutritional quality characterized by oxidative stress, on the other hand, are complex and inconsistently acknowledged(66).



Figure(1-12) The main antioxidant enzymes directly involved in the neutralization of ROS and RNS. SOD, (67)

1.11 Sources of free radicals in people with obesity and type 2 diabetes.

Obese patients have reported a higher density of β_3-Adrenergically receptors in their adipose tissues and a lower density of insulin receptors, increasing lipolysis and FFA release, a condition which has many metabolic implications, including results in the production of oxygen-derived free-radical, induction of insulin resistance, and synergism in the action of IL- In distinct cell lines, lipotoxicity induces both morphological and functional damage(68). Adipose tissue dysfunction, as well as lipotoxicity, comprise two

mechanisms that explain the pro-inflammatory condition, altered adipokine secretion and insulin resistance (IR)(69).

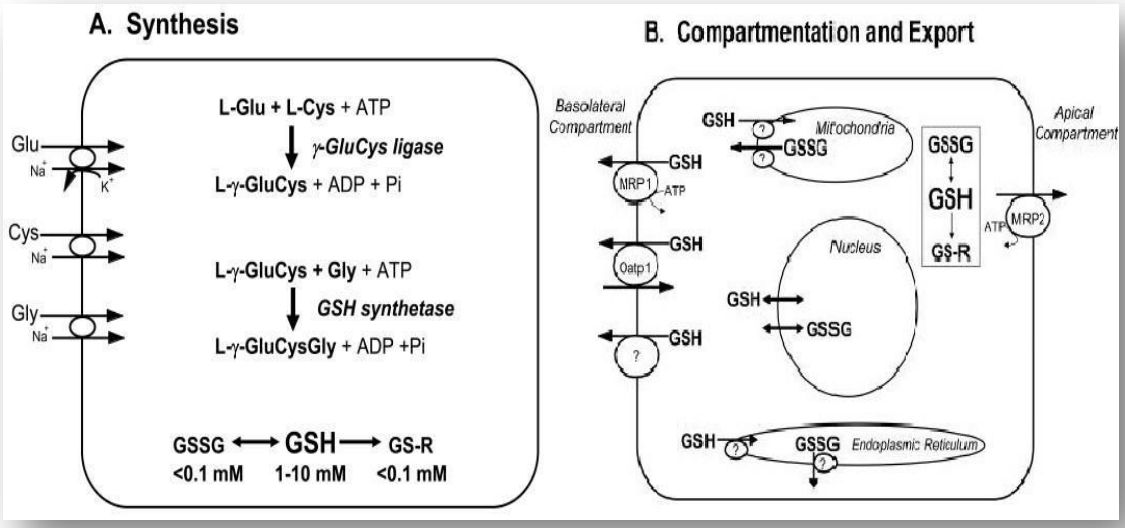
The non-enzymatic source of ROS is the mitochondrial respiratory chain. Brownlee's hypothesis of the primary function of mitochondrial superoxide generation in the etiology of diabetes problems has been around for about 20 years. The vicious cycle of oxidative stress in diabetes is assumed to be driven by hyperglycemia-induced production of free radicals at the mitochondrial level(70)**.**

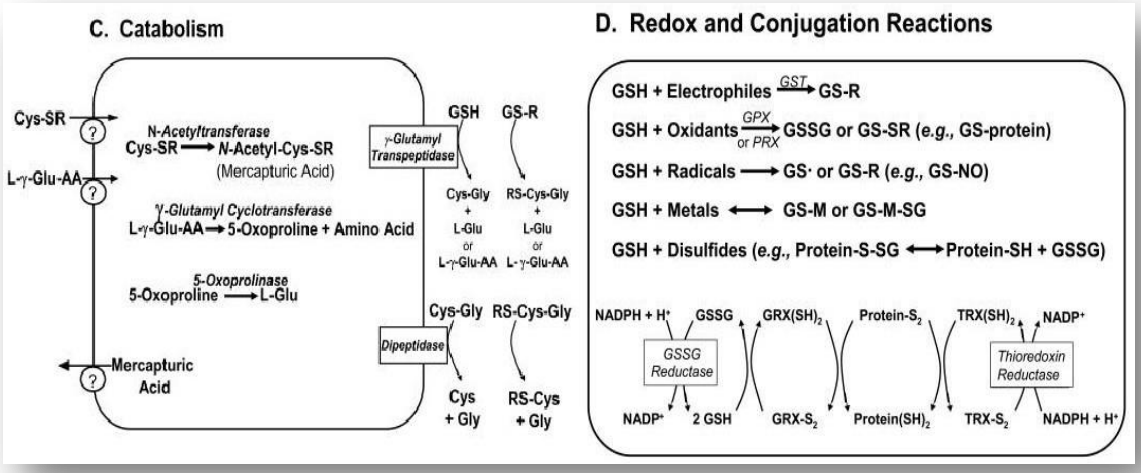
In summary, researchers believe that increased intracellular glucose causes the formation of an abundant amount of electron donors during the Krebs cycle Like the following redox cofactor particles $FADH_2$ or $NADH_2$(71), which causes the interior mitochondrial membrane potential to rise, resulting in mitochondrial malfunction like ion concentration gradients by cations+inward with anion-outward and increased ROS production(72). Under hyperglycemic circumstances, the increased production of pyruvate via faster glycolysis is hypothesized to flood the mitochondria, resulting in ROS creation at the level of complex II in the respiratory chain. Reactive oxygen species cause LDL to be oxidized; ox-LDL is not detected by the LDL receptor and is thus taken up by scavenger receptors in macrophages, resulting in foam cells and so atherosclerosis, and last apoptosis(73).

1.12 Glutathione or reduced Glutathione (GSH)

Reduced Glutathione as an Endogenous antioxidant (L-glycine, L-cysteine, and L-glutamic acid) tripeptide is reduced because it's an electron donor that acts as a free radical scavenger Every cell in the body contains the antioxidant glutathione, often known as GSH. It has a reputation for reducing free radicals. Important cellular components can be damaged by reactive oxygen species, free radicals, peroxides, lipid peroxides, and heavy metals, however glutathione can stop this from happening. The carboxyl group of the glutamate side

chain and cysteine are linked by a gamma peptide in this tripeptide. By means of typical peptide linkage, the cysteine residue's carboxyl group is joined to glycine.





Figure(1-13) In human cells, there are several major routes for glutathione homeostasis(74)**.**

Because it is an electron donor and a free radical scavenger, reduced glutathione, an endogenous antioxidant (L-glycine, L-cysteine, and L-glutamic acid tripeptide), is decreased. This indicates that it can contribute one electron to scavenge free radicals and stop them from causing harm to tissues and cells. As a result, GSH is crucial for protecting cells from oxidative damage and preserving their reducing environment(75).

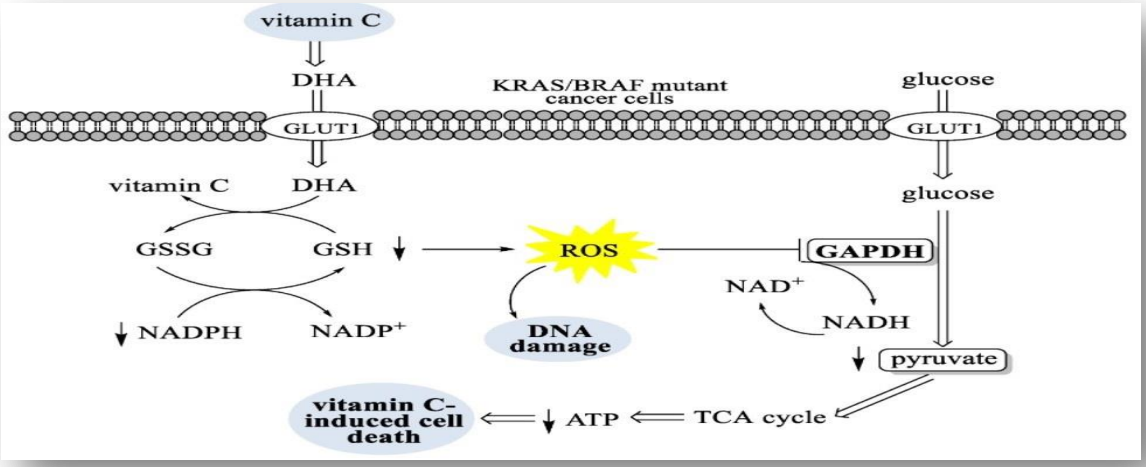
1.13 Ascorbic acid (VIT-C)

water-soluble vitamin & essential antioxidant that decreases other chemicals (for example, reactive oxygen species) while also being transformed to its oxidized form, dehydroascorbic acid(DHA)(76). Although humans are unable to produce ascorbic acid, some other species can, which is considered necessary for the hydroxylation of proline residues in collagen, as well as for the protein's normal structure and function (77).

It is a potent antioxidant that works by keeping iron in the hydroxylating enzyme in a reduced (Fe^{2+}) state(78), ascorbic acid reversibly oxidized with(DHA), also aids in the absorption of dietary non-heme iron in the intestine(79).

The dominant VitC species at physiological pH (7.0-7.4) is ascorbate mono-anion is a Donor Antioxidant [($AscH^-$) = 99.95% -99.9%)]donates an H^+or $H^{\bullet+e^-}$ of vitamin C will be present as $AscH^-$ to an oxidizing radical see Figure(1-14), with low concentrations of Di-acid($AscH_2$) Ascorbic acid [= 0.004%-0.001%] and Di-anion(Asc^{2-})Ascorbate Radical [0.005%], Ascorbate ($AscH^-$) is a powerful reducing agent and antioxidant due to its capacity to transfer one or two electrons. AA becomes a ROS-generating compound at millimolar concentrations (pharmacologic concentrations). In actuality, a minor amount of AA is obtained from ascorbate(80).

Some research points to vitamin C supplementation as a viable treatment for type 2 diabetes. Further analysis is necessary to determine its efficacy and evidence quality. Systolic blood pressure, with moderate evidence certainty, and HbA1c and diastolic blood pressure, with very low evidence certainty, were the results that changed to a statistically and clinically important extent with Vitamin C, according to a meta-analysis and systemic review of randomized controlled studies(81).



Figure(1-14) In cancer cells with KRAS and BRAF mutations, vitamin C toxicity is mechanistically explained. TCA: citric acid cycle, commonly known as the tricarboxylic acid cycle or the Krebs cycle; GSSG: an oxidized form of glutathione; NADP+: nicotinamide adenine dinucleotide phosphate; NADH: reduced nicotinamide adenine dinucleotide; NAD+: oxidized nicotinamide adenine dinucleotide. Dehydroascorbic acid (DHA); GSH stands for reduced glutathione,GSSG for oxidized glutathione, NADPH for reduced nicotinamide adenine dinucleotide phosphate, NADP+ for nicotinamide adenine dinucleotide phosphate, ROS for reactive oxygen species, and BRAF for v-raf murine sarcoma viral oncogene homolog B. Glyceraldehyde 3-phosphate dehydrogenase, tricarboxylic acid cycle, or Krebs cycle; NADH, reduced nicotinamide adenine dinucleotide; NAD+, oxidized nicotinamide adenine dinucleotide; Adenosine triphosphate, or ATP (82).

Another comprehensive review and meta-analysis of clinical trials assessing the impact of vitamin C supplementation on diabetes patients' lipid profiles discovered that the levels of total cholesterol, LDL, and HDL were not significantly affected by vitamin C supplementation. However, it decreased HgA1C, fasting blood sugar, and triglycerides. Although evidence from short-term studies suggests that vitamin C supplementation may enhance blood pressure and glycemic control in people with type 2 diabetes, vitamin c supplementation cannot currently be advised as a therapy until larger, long-term, and high-quality trials confirm these results(83).

1.14 CALCIUM

The effect of calcium dynamics on blood glucose in the Endoplasmic reticulum depends on important markers of inflammation in diabetic Mellitus for overweight and obese women(84), it took a lot of research in a large area of research was taken by medical and research studies centers(85), Calcium homeostasis is required for insulin resistance and β-cell function& secretion(86). Elevated blood calcium levels have been linked to indications of poor glucose metabolism in cross-sectional studies. However, just one prospective cohort study has found that people with higher serum calcium concentrations have a higher risk of diabetes(87).

Hyperparathyroidism and glucose metabolism problems occur significantly more commonly together than previously thought. The number of people with diabetes mellitus in primary hyperparathyroidism has been reported to range between 8% and 22%, whereas the prevalence of primary hyperparathyroidism in diabetes mellitus is thought to be around 1%(88). Furthermore, patients with hyperparathyroidism have a substantially higher prevalence of impaired glucose tolerance and/or impaired fasting glucose than the general public. Changes in impaired insulin action, both of which are present in hyperparathyroidism, are the main causes of glucose metabolism disturbances. Hyperglycemic metabolism is caused by both primary and secondary hyperparathyroidism. Patients diagnosed with hyperparathyroidism have a higher prevalence of diabetes mellitus, and extracting the parathyroid glands improves glucose tolerance in these patients(89).

PTH increases calcium levels by releasing calcium from bones and boosting calcium absorption through your small intestine. The parathyroid glands release less PTH when blood calcium levels are too high. However, one or more of these glands can release too much hormone at times(90).

1.14.1 The Parathyroid Glands' Role in Calcium Regulation

The parathyroid glands' sole duty is to keep the calcium level in our body within a small range so that our neurological and musculoskeletal systems may function normally(91). They only do this. Every minute of each day, they measure the quantity of calcium in the blood. and if the calcium levels drop a little, the parathyroid is triggered, Overactivity of one or more of the parathyroid glands is the most common parathyroid illness(92).

The parathyroid glands detect this and produce parathyroid hormone (PTH), which travels to the bones and withdraws calcium from the calcium vault before releasing it into the bloodstream. PTH deploys calcium by enhancing calcium reabsorption in the proximal renal tubule and increasing calcium excretion from bone(93). Many studies indicate the existence of a relationship between aging and diseases of old age, with a decrease in muscle mass in old age, the percentage of fat formation in the body, disorders of the parathyroid glands, and the percentage of vitamin D, which is the active vitamin in controlling the percentage of calcium in the bloodstream, as well as bone cells in the elderly and the disturbance of these concentrations due to Oxidative stress, insulin tolerance, and other complications of aging (94).

1.14.2 Effect of calcium on insulin secretion pathway

A considerable positive effect of vitamin D and calcium supplements on insulin sensitivity was demonstrated in many studies limited to persons with pre-diabetes(95)**.** Figure (1-15) Pancreatic beta cells are responsible for secreting insulin at the proper time and in the right amount. Any change in their function disrupts glucose homeostasis, resulting in life-threatening hypoglycemia in the case of excessive insulin secretion and damaging hyperglycemia in the case of insufficient insulin secret.

It's hardly surprising, then, that beta cells are tightly controlled by a variety of stimulatory and inhibitory substances, with glucose playing a key role through mechanisms that are still unknown despite more than 40 years of research(96).

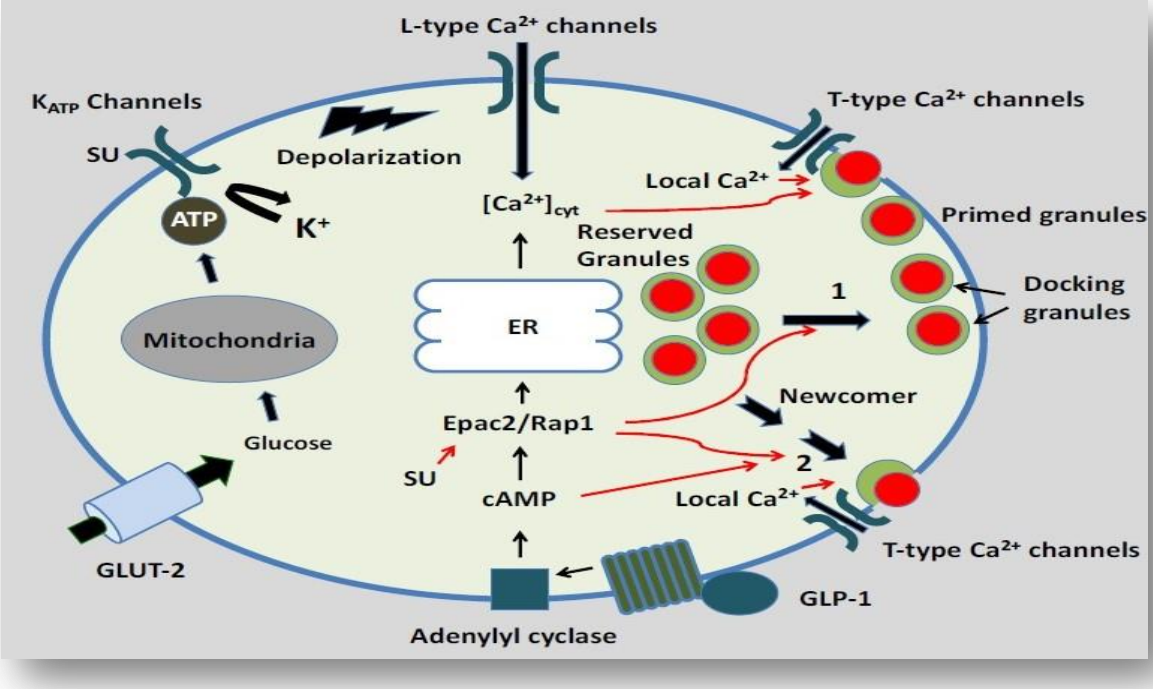


Figure (1-15) Pancreatic-cell regulation of insulin secretion pathways(96)**.**

An intricate interaction between metabolic and electrogenic processes controls the production of insulin from pancreatic beta cells. Figure (1-15) The ATP-sensitive K^+ (KATP) channel-dependent pathway is the term used to describe the electrogenic process controlling insulin production from beta cells(97). The only cell type in our bodies that can produce and secrete insulin to tell our bodies' tissues and cells to absorb nutrients after a meal are pancreatic beta cells. It is crucial to accurately regulate insulin release since too little insulin can lead to diabetes while too much insulin can result in potentially dangerous hypoglycemia(98).

1.14.3 The impact of calcium on insulin action

Insulin is a significant physiological target of striated muscles (skeletal and cardiac), and this hormone activates complicated signaling pathways that regulate cell development and energy consumption A key hormone, insulin controls several metabolic processes in the body, including the uptake of glucose by muscle cells. In order to increase glucose absorption, it accomplishes this by promoting the translocation of the glucose transporter (GLUT4) from internal compartments to the cell surface.(99). Insulin stimulates glucose transporter (GLUT4) translocation from internal compartments to the cell surface, which enhances glucose absorption in muscle cells. The well-mapped tyrosine, lipid, and serine/threonine phosphorylation events make up the classic insulin-triggered signaling cascade that controls this activity. Recent discoveries show insulin-dependent Ca^{2+} mobilization in skeletal muscle cells and cardiomyocytes, which runs parallel to these signals Insulin activity is significantly influenced by calcium. In addition to other signaling pathways that insulin activates, it also causes calcium mobilization in skeletal muscle cells and cardiomyocytes. Through Sarco-Endoplasmic Reticulum (SER) channels such the Ryanodine Receptor (RyR) and the inositol 1,4,5-triphosphate receptor (IP3R), insulin specifically increases the release of calcium into the cytosol. RyR controls the quick release of calcium brought on by insulin in skeletal muscle cells(100)(5). Insulin stimulates the Ryanodine Receptor (RyR) and the inositol 1,4,5-triphosphate receptor, which are Sarco-Endoplasmic Reticulum (SER) channels that release Ca^{2+} into the cytosol (IP3R). RyR(**Ry**anodineReceptor) causes a fast, insulin-induced Ca^{2+} release in skeletal muscle cells, which is initiated by S-glutathionylation of cysteine residues,macro-minerals Ca^{2+} are linked to obesity Additionally, calcium is necessary for the release of insulin. For insulin to be released, calcium must enter beta-islet cells via L-type calcium channels. Since insulin production and action are affected by calcium homeostasis, it is possible that this might result in diseases like type 2 diabetes(101).

It's interesting to note that calcium and obesity are related. Observational studies have revealed a link between the prevalence of type 2 diabetes or the metabolic syndrome with poor vitamin D status, calcium intake, or dairy consumption1. This implies that consuming enough calcium and vitamin D may help to improve glucose metabolism and maybe ward off type 2 diabetes.(102), However, it's important to note that most of these studies are observational and may not account for all confounding factors.

Aim of a study:

1. Elucidate the role of obesity-related parameters on the levels of Anti-inflammatory novel adipokine (omentin-1) in diabetic obese patients.
2. Estimate the prevalence of protein (ANGPTL-4) in diabetic obese patients.
3. Explore the correlation of Omeinten-1 and Angptl-4 with measures of obesity and insulin resistance.
4. Calculate the serum concentration of biomarker testing like FBS, HbA1c, lipid profile, Ca, and Non-enzymatic antioxidants like Vit-C, and GSH with diabetic obese patients and explore the correlation of them with biochemical parameters.
5. Recognizing the relationship between biochemical study and corresponding histological results to confirm the speculated results.

Chapter One

Materials & Methods

2.1-Chemicals:

Table (2-1) the list of chemical compounds that were used in this study.

Table (2-1) Chemicals and Kits

Chemicals	Symbol& Formula	Puri%	Company Supplied
Acetic Acid	CH_3COOH	97.5%	BDH
Angptl4-Human ELISA KIT	---	--	Bioassay_TechnologyLab
Ammonia	NH_3	99%	BDH
Ascorbic Acid	$C_6H_8O_6$	99.8%	Sigma- Aldrich
Benzene	C_6H_6	99.6%	Merck
Butanol	$CH_3(CH_2)_3OH$	99%	Labort
Calcium CPC determination kit	---	--	Gesellschaft-Germany
CopperSulfate(**An**hydrous)	$CuSO_4$	99.5%	BDH England
Diethyl Ether	$(C_2H_5)_2O$	99.5%	SDFCL Mumbai
5,5- Dithiobis -2-nitrobenzoic acid	$[-SC_6H_3(NO_2)CO_2H]_2$	98%	Sigma- Aldrich
Ethanol	CH_3CH_2OH	99.9%	Fluka
Ethyl Acetate	CH_3-COO-CH_2-CH_3	99.8%	Merck
EthylenDiaminTetraAceticAcid	EDTA-Na_2	98%	Sigma- Aldrich
Formal-2,4-dinitrophenlhydrazon	$H_2C=NNC_6H_3(NO_2)_2$	99%	BDH
HbA1c kit	---	--	StanBioU.S.A.EK com.
Glucose kit	---	--	Gesellschaft-Germany
Glacial Acetic Acid	CH_3COOH	99.5%	BDH
$_L$-Glutathione(reduced)-GSH	$C_{10}H_{17}N_3O_6S$	98%	Merck
Hydrochloric Acid	HCl	99%	BDH England
absoluteMethanol(Methyl alcohol)	CH_3OH	99.8%	Hayman(England)
Metaphosphoric acid	$(HPO_3)n$	36%	Sigma- Aldrich
Ninhydrin2,2-Dihydroxyindane-1,3-Dion	$C_9H_6O_4$	99%	Merck
Omentin1-Human ELISA KIT	---	--	Bioassay_Technologylab
1-Propanol	$CH_3(CH_2)_2OH$	99%	Sigma- Aldrich

Potassium**I**odide	KI	98%	Sigma- Aldrich
Sodium**C**arbonate	Na_2CO_3	98%	Sigma- Aldrich
Sodium**H**ydroxide	NaOH	99%	GMBH (Germany)
Sulfuric **a**cid **s**olution	H_2SO_4	99.9%	Gmbh
Potassium ferricyanide	$K_3Fe(CN)_6$	99%	Sigma- Aldrich
Trichloroacetic acid	Cl_3CCOOH	99%	Hopkin&Williams
Tris(hydroxymethyl)aminomethane	$NH_2C(CH_2OH)_3$	≥99.8%	Sigma- Aldrich
Thiourea	NH_2CSNH_2	99%	Aldrich
Sodium Dodecyl Sulphate	$CH_3(CH_2)_{11}OSO_3Na$	99%	Sigma- Aldrich
phenazine methosulfate	$C_{13}H_{11}N_2 . CH_3SO_4$	98%	Sigma- Aldrich

2.2 Instruments Analysis and Equipments:

The instruments and equipment used in this study are listed in Table (2-2).

Table (2-2) Instruments and Equipments

Instrument	Supplied company
Centrifuge	(Germany) Hettich
ELISA READER & WHSHER	BioTek
Micropipette (10-100)	Dragon Med
Scanning Electron Microscope Inspect S50	FEI (Netherlands)
Hot plate + Magnetic Stirrer	Gallin kamp (England)
Electric blender	Glassco (India)
Heater	IKA (Germany)
pH-meter	Inolab 740 WTW
Incubator	Memer Edelsta (Germany)
Oven	Memmert UNB (Germany)
Water Bath	Memmert WNB (Germany)
Cobas C311 Automated	Roche Diagnostics GmbH, USA
Sensitive Balance	Sartorius AG (Germany)
UV/VIS Spectrophotometer PG Instruments Ltd	T80 (UK)

2.3 Subjects and Samples

2.3.1 The Subject A total of 120 Femals Volunteers to conduct the study were divided into four groups Figure(2-2):

[(Gp1); 30 patients with T2DM and without Obesity] [**(Gp2);** 30 patients with T2DM and morbidly obese]

[(Gc1); 30 healthy control non T2DM & without Obesity][**(Gc2);**30 control without T2DM but morbidly obese]

The diabetic patients were diagnosed based on WHO criteria and the questionnaire form Figure (2-1).

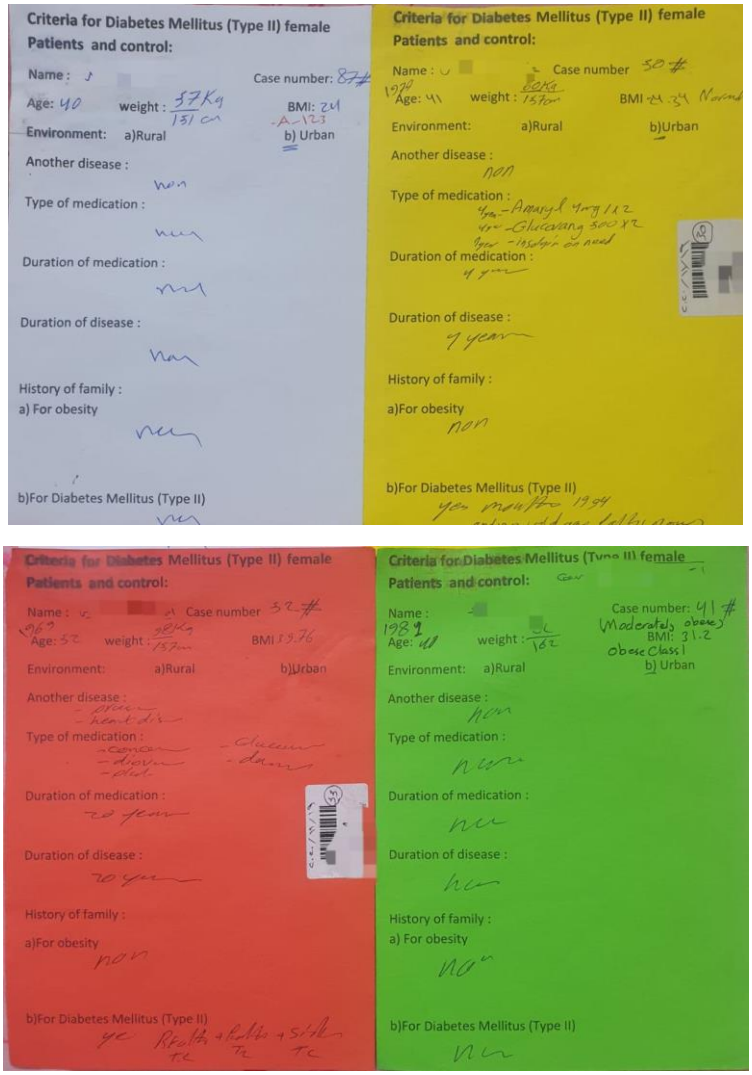


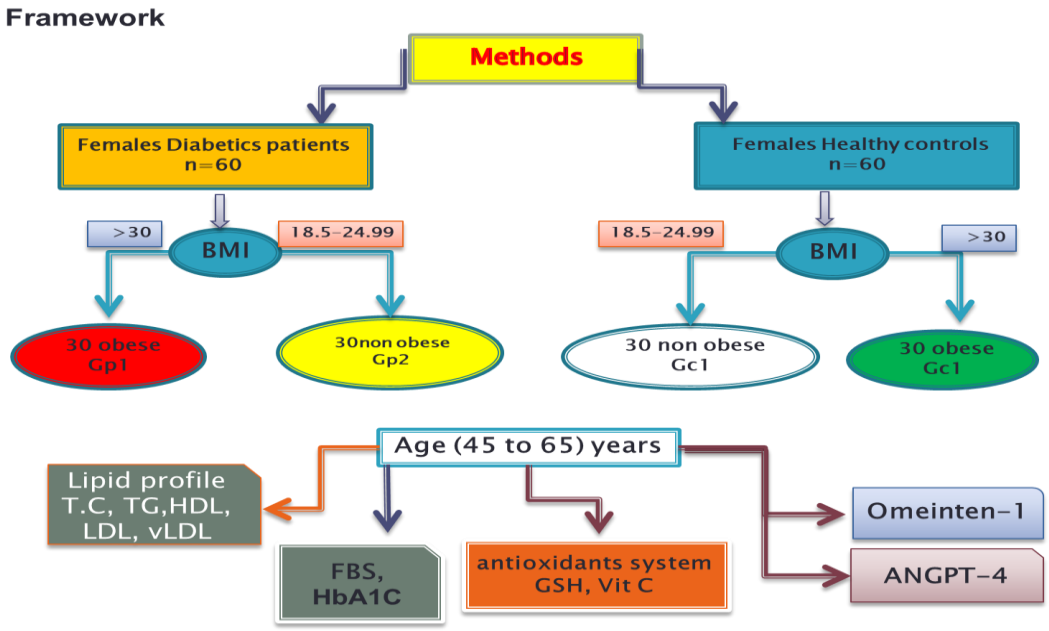
Figure (2-1) Information and medical history form

2.3.2 Collection of the Patients Samples:

Blood samples were collected by physicians. Physicians performed physical exams (weight, height, blood pressure(SBP-DPB), and Waist&Hip circumference,)BMI Body mass index (BMI) was calculated (weight in kilograms/height in meters squared) and took blood samples in gel tube and EDTA tube (native and EDTA-anticoagulated) for laboratory analysis.

2.3.3 Methodologies:

A clinical study was performed at The Center for Diabetes and Endocrinology, and Al-Kindi Teaching Hospital in cooperation with Central Public Health Laboratory (Baghdad, Iraq). All blood samples of patients were collected in a fasting state (9-11 A.m.), and inside the Specialized Endocrinology and Diabetes Center in Baghdad / Al-Rusafa from between the date of October 28, 2020, to February 28, 2021**,** The aim was to select 60 women, all of whom had type 2 diabetes,30 were obese and 30 were not obese. The average age was between forty five and sixty-five years, Figure (2-2).



Figure(2-2)Scheme of how to distribute study groups

2.4 Preparation of the Samples:

All measurements and blood collection (5 ml) were performed in the morning following fasting (10-14h) venous blood was withdrawn using a 5 ml syringe for a single use, then the blood was placed in tubes containing a special gel. The tube contains an anticoagulant substance. By keeping it vertically for a quarter of an hour, it helps to form two layers at the bottom, a stagnant layer, and the top, the serum with a color close to yellow and To separate the serum from the plasma after placing it for 15 minutes in a centrifuge at a speed of 3000 revolutions per minute to ensure obtaining the largest possible amount of serum and then withdrawing the serum using a micropipette and distributing the sample into several 1 ml micro-tubes or Eppendorf tubes (EP tubes) and keeping it at a temperature of 80 degrees below zero Celsius until use In laboratory tests for our research.

2.5 Biochemical measurement:

2.5.1 Determination of Antioxidant System

A standard method was used to organize the chemical tests of the aqueous extracts of the plant sample, Vitamin C is a powerful antioxidant having the ability to donate a hydrogen atom and form a relatively stable ascorbyl-free radical. Vitamin E, vitamin C, and β-carotene are known as antioxidant vitamins that are suggested to decrease oxidative damage and lower the risk of certain chronic diseases. Diseases, such as cardiovascular disorders, are associated with inadequate concentrations of l-ascorbic acid, tocopherol, and β-carotene.

2.5.1.1 Determination of Levels Serum Ascorbic Acid (Vitamin C) (µmol/L)(103)**:**

a method to determine ascorbic acid (Vitamin C) in blood serum by a reaction named hydrozone of oxidation ascorbic acid by 2,4,dinitro phenyl hydrazine (DNPH). However, there are other methods for determining ascorbic acid in blood serum. For example, a simple method for plasma total vitamin C analysis suitable for routine clinical laboratory use has

been developed. This method involves a constant-low-pH sample reduction procedure followed by isocratic reverse-phase HPLC separation using a purely aqueous low-pH non-buffered mobile phase. Another method for determining ascorbic acid and its compounds is by titration or polarography. The determination is based on the oxidation of ascorbic acid to dehydroascorbic acid(104)

Non-enzymatic antioxidants Vitamin C are determined by spectrophotometric method. Vitamin C was assessed for serum ascorbic acid by UV spectrophotometric method, Vitamin C is a potent reducing agent and scavenger of free radicals in biological systems. It is involved in the first line of antioxidant defense, protecting lipid membranes, and proteins from oxidative damage

Principle:

There is a simple challenge, but it is worth paying attention to. The concentration of vitamin C in the blood drops to 50 percent of the initial level after storing it in typical clinical conditions for about a month and a half(105).

Reagent:

The chemical methods which are available for assessment of ascorbic acid are depend on either the reducing properties of the 1.2-enediol group that lead to absorbance changes in indicator dyes or the formation of hydrazone, the 2,4 dinitrophenyl hydrazine (DNPH) methods, ascorbic acid (AA) is Oxidized by Cu^{+2} to dehydroascorbic acid (DHA) and diketogulonic acid (Tietz, 1995). When treated with DNPH, the 2,4-dehydrophenyl osazon product forms which in the presence of sulfuric acid (Burtis and Ashwood,1999) ,forms an orange-red complex that is absorbed in 520 nm.

1. Meta phosphoric acid m-HPO_3 (0.75 M) dissolve 3gm of m-HPO_3 in 50 ml DDW

2. Sulfuric acid 4.5M of H_2SO_4, concentrated was added to 30ml DDW and then brought to a final volume of 100 ml

3. Sulfuric acid (12M): 65mL of H_2SO_4, Conc. Was added to 30mL of cold DDW and then brought to a final volume of 100mL.

4. Thiourea (0.66M): 2.5 gm of thiourea was dissolved in 50ml DDW

5. 2,4 dinitrophenyl hydrazine (0.01 M): dissolve 5.0gm of 2,4 DNPH in 200mL 0f (4.5 M) of H_2SO_4 and bring to a final volume of 250 ml with 4.5 M of H_2SO_4 then refrigerated overnight and filtrated

6. Copper sulfate (0.027 M): dissolve O.6 mg of anhydrous copper sulfate in100ml DDW.

7. DTCS reagent contain the following:

5 mL of thiourea, 5 ml copper sulfate and 100 mL of 2,4-DNPH reigent.

8. Ascorbic acid standard stock solution (2,8mM) is prepared by dissolving 50mg of (AA) in a final volume of 100 ml of m-HPO_3, dilutions are made in m-HPO_3 to 2.5,5, 10, 15, and 20mg/L that equal (0.014, 0.028,0.056, 0.084 and 0.12mM) respectively Fig (2-3)

Procedure:

Duplicates of each standard and sample test tube are prepared, and then Pipetted into test tubes.

Reagents	Sample µl	Standard µl	Blank µl
m-HPO_3	800		
DW		1000	1000
Serum	200		
Mixed in vortex mixture, then centrifuged at 2500 rpm for 10 minutes			
Supernet	600	600	600
Standard		600	
m-HPO_3			600
DTCS reagent	200	200	200

Mixed and vortex mixture, then incubated in the water bath at 37C• for 3 hours, then the tubes were removed from the water bath and chilled for 10 minutes in an ice water bath while slowly mixing

Reagents	Sample µl	Standard µl	Blank µl
H_2SO_4	1000	1000	1000

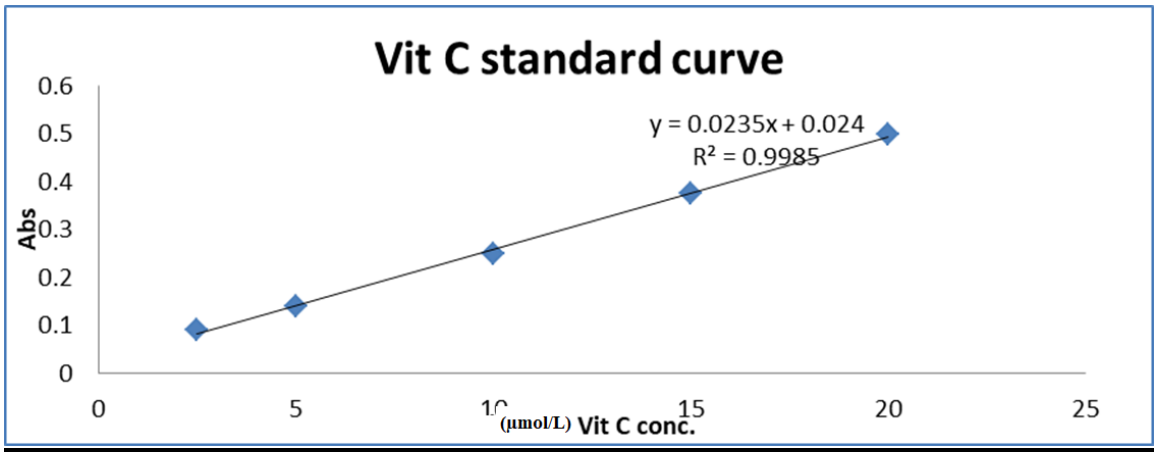


Figure (2-3) Standard curve for VIT-C (µmol/L)

2.5.1.2- Determination of Levels of Serum Reduced Glutathione (GSH) µmol/g(106):

Non-enzymatic antioxidants GSH are determined by The common name for this assay (Ellman`s test) protocol& it is a quantitative measuring of –(SH)sulfhydryl functional group in thiols, The colorimetric assay method has been using biochemical reagent(Ellman`s) abbreviated letters (DTNB) to measure reduced glutathione(GSH) Figure (2-4).

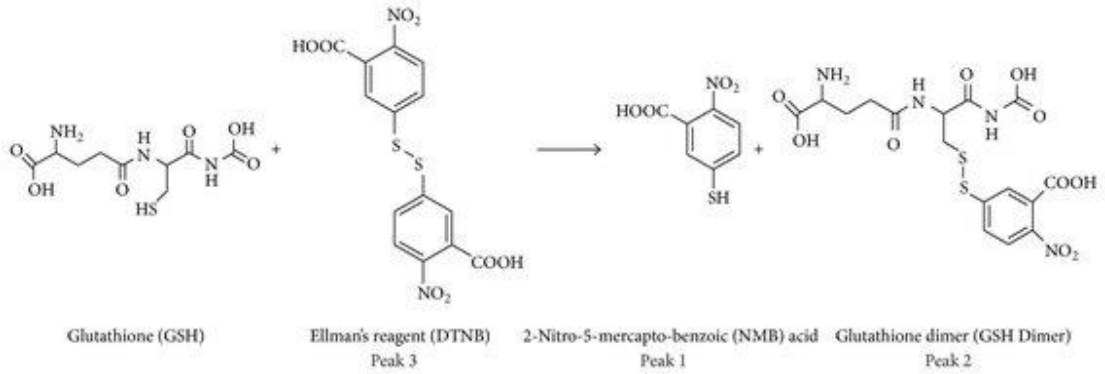


Figure (2-4) Reaction of Ellman's reagent with glutathione(107).

Principle:

(DTNB, Ellman's reagent)5,5′-dithiobis(2-nitrobenzoic acid)a disulfide chromogenic quickly reacts with the sulfhydryl group and causes it to be reduced As a result of this

interaction, a dull yellow pigment compound is generated Its concentration can be measured at wavelength 412, 5, 5- Dithiobis (2-nitrobenzoic acid) DTNB Ellmans Reagent is a disulfide chromogen that is readily reduced by sulfhydryl group of GSH to produce an intensely yellow Compound. The absorbance of the reduced chromogen is measured at 412 nm and is directly proportional to the GSH concentration but it must be read urgently (Burtis &Ashood, 1999). Figure (2-4).

Reagents:

1-Precipitating agents solution. Trichloroacetic-acid(TCA)(3.1mol/L) solution.50%, was prepared by dissolving 25g of TCA in 49 ml DW.

2-Free Sulfhydryl groups detection Reagent, DTNB, or Ellman`s Rea, was prepared by dissolving 0.095g of DTNB in 24 ml of CH_3OH(AbsoluteMethanol)(Methyl alcohol), DTNB reagent (0.01M). 0.0198 gm of DTNB Ellmans Reagent was dissolved in five ml of absolute methanol.

3-GSH Stock standard(0.001 mol/L), was prepared by dissolving 0.06 gm of GSH in 200 ml of EDTA solution.

4- EDTA-Na_2(2%)solution, thylene-diaminetetraacetic-acid-disodium (EDTA-Na2.2H20) 0.4 M. **was** adding 37g of EDTA-Na_2 to 500ml DW, It is well dissolved in distilled water.

5- Tris(hydroxymethyl)aminomethane-EDTA-Buffer.Tris-EDTA buffer (0.4 M) 4.82 gm of Tris bas were dissolved in 80 ml of DDW. Then 10 ml of EDTA solution (0.4M) was added and completed to the final volume of 100 ml with DDW. The pH was adjusted to 8.9 by the addition of 1N of HCI**.** At first, we prepared Tris solution at a concentration of 0.31 mol/L by adding 30g of Tris base to 800ml DW and dissolved well, Then we added the 2%EDTA buffered sodium solution prepared in the fourth step In the amount of 100 ml, and bring to 1 liter by adding DW. The pH is maintained at 8.9

Procedure:

Reagents	Sample µl	Standard µl	Blank µl
Serum	100 µl	-------	-----
Standard	-----	100 µl	-----
DDW	800 µl	800 µl	900 µl
TCA	100 µl	100 µl	100 µl

1-Duplicate of each sample tube was prepared then, 800 µl of DDW and 100 µl of TCA were added to 100 µl of the sample.

A blank tube was prepared by adding 100 ul of TCA to 900 µl of distilled water.

The tubes were mixed in the intermittently for (10-15) minutes and centrifuged for 15 minutes at 3000 rpm

Reagents	Sample µl	Blank µl
Supernat	400 µl	400 µl
Tris-EDTA buffer	800 µl	800 µl
DTNB	20 µl	20 µl

All tubes were mixed and the absorbance was read at 412 nm within 5 minutes after the addition of DTNB.

2-The standard curve of glutathione was prepared from dilution the

glutathione standard solution by DDW to the following concentrations: -5,10, 15, 20, 30, 40, 50, 100 µM.

Then the above steps were repeated and the absorbance was read at 412 nm for each concentration.

Calculation:

The standard curve of glutathione was drawn between absorbance and different concentrations of glutathione; the concentration of serum glutathione of the sample was calculated from it, Figure (2-5).

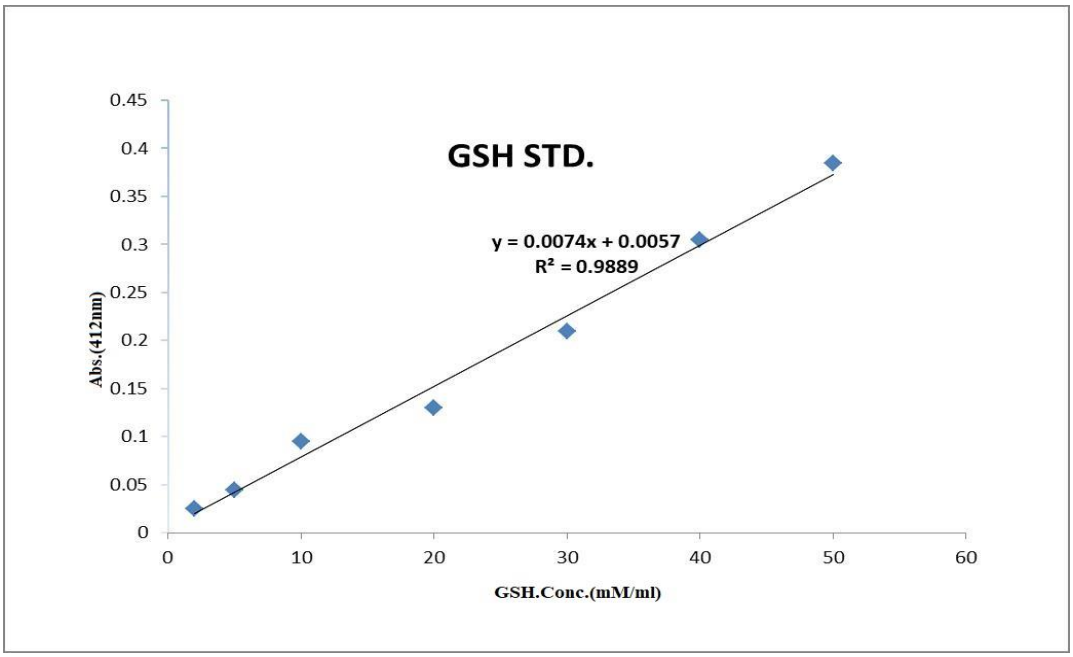


Figure (2-5) Standard curve for GSH

2.6 Determination of Fasting Blood Glucose Conc. level in serum (mmol/l):

The amount of glucose, a form of sugar, in your blood after going at least eight hours without eating is known as your fasting blood glucose concentration. It is often expressed in millimoles per liter (mmol/L) or milligrams per deciliter (mg/dL), which are sometimes converted to mmol/L for comparison. Normal fasting blood glucose levels are predicted to be between 70 mg/dL (3.9 mmol/L) and 100 mg/dL (5.6 mmol/L), or between these ranges. Changes in lifestyle and monitoring of glycemia are advised when fasting blood glucose levels are between 100 and 125 mg/dL (5.6 to 6.9 mmol/L). Diabetes is diagnosed if the fasting blood glucose level is 126 mg/dL (7 mmol/L) or greater on two different occasions.

Principle:

The Trinder method for glucose analysis utilizes the coupled enzyme reactions shown below:

$$Glucose + O_2 \rightarrow glucose\ oxidase glucuronic acid + H_2O_2$$

$$H_2O_2 + reduced dye \rightarrow horseradish\ peroxidase oxidized dye + H_2O$$

The reaction is linear to approximately 10,000 mg/L (1000 mg/dL) and reaches its endpoint in 15-20 minutes at 37°C.

1. Label sufficient 13 x 100 mm test tubes for each standard, control, and patient sample to be tested.
2. Pipet 2.0 mL of glucose reagent into each tube.
3. Add 10 µ L of standard, control, or serum to each appropriate tube.
4. Mix well.
5. Incubate each tube at 37°C for 20 minutes.
6. Using appropriate cuvettes, measure the absorbance of each reaction mixture at 525 nm against a water blank.
7. Calculate each glucose concentration using the absorbance and concentration of the standard by the proportion method
8. Record your results on the data sheet

2.7 Assessment of Glycosylated Hemoglobin (HbA1C) level (mmol/L):

The HbA1c test determines how much-glycosylated hemoglobin is present in the blood concerning total blood glucose. The glycosylated hemoglobin (Glycohemoglobin) formed when hemoglobin is coupled to glucose lasts during the life of the red blood cell, which is 120 days.

Hemolysis whole blood was used in this method, which was then eluted through a resin with a weakly binding cation (+) exchange capability, resulting in non-glycosylated hemoglobin (HbA0) being attached to the resin and free glycosylated hemoglobin (HbA1c) being separated in the supernatant. The (HbA1c) percent was determined by measuring absorbance at 415 nm of the (Hb This ratio to a glycohemoglobin was compared to a standard made using the same method.

2.8 Determination of Serum Calcium (Ca^{2+}) level (mmol/L):

A blood test to calculate the amount of calcium[Alternative Names: Ca^{2+}; Calcium-serum; Ca^{++} or Ca(II)] in the blood is known as serum calcium. Serum calcium is macro-minerals typically measured to detect or monitor bone illnesses or calcium-regulation abnormalities (parathyroid or renal diseases)

Principle:

Colorimetric determination of the Ca^{2+} human blood serum which reaction scheme is as follows:

1- oCPC o-cresolphthalein-complexone interacts with calcium ions Ca^{++}

2- This interaction must have an alkaline medium to form a complex show in a purple color

3- The absorbance of the reaction mixture from Calcium(II) concentration in the serum sample.

Reagents:

1-Reagent(1):SodiumAzide 0.095% & Calcium(II) 2 mmol/l (The Standard).

2-Reagent(2): oCPC/o-cresolphthalein-complexone 0.1 mmol/l and 8-Hydroxyquinoline 14 mmol/l & HydroChloricAcid 40 mmol/1 (TheColorReagent).

3-Reagent(3):Lysine-Buffer(pH11.1)0.2mol/l&Sodium-Azide0.095% (BufferSolution).

4-Reagent(4):mixed same volume from R2+R1(WorkingReagent)

Procedure:

All samples and STD&Blank tubes are set up as follows:

Contents	BlankTube	(STD)STANDARD	Sample
Standard	- -----	20 µl	-
(serum)Sample	-----	-----	20 µl
WorkingSolution	1000 µl	1000 µl	1000 µl
Mix all these additives, and measure the absorbance in Wavelength570nm			

Calculations:

Calcium(II)Concentration is Calculated by the following equation:

$$C=2 \times \frac{\Delta A\ Sample}{\Delta A\ STD.}\left(\frac{mmol}{l}\right)$$

$\Delta A\ STD.$ = *StandardAbs.- BlankAbs. (within 5to 30min)measure*

2.9 Lipid Profile(LP) Blood Serum Test:

A lipid profile, commonly referred to as a lipid panel, is a blood test that quantifies your blood's triglyceride and cholesterol levels. This test can help evaluate your risk of accumulating fatty deposits (plaques) in your arteries, which can cause atherosclerosis, which can result in congested or clogged arteries throughout your body. Low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, and total cholesterol values are frequently included in the lipid profile. While HDL is known as "good" cholesterol because it helps take away LDL cholesterol, keeping your arteries open and your blood flowing more easily, LDL is frequently referred to as "bad" cholesterol because it can lead to the formation of plaque in your arteries. Triglycerides are a kind of blood fat that have been linked to a number of things, A lipid profile, also known as a lipid panel, is a set of blood tests used to detect lipid abnormalities like cholesterol and triglycerides. [not confirmed in the body] The findings of this test can be used to diagnose specific hereditary illnesses as well as estimate the risk of cardiovascular disease, pancreatitis, and other ailments.

The Lipid Profile blood test determines how much cholesterol is present in the human body. Total Cholesterol, Triglycerides, High-Density Lipoproteins- Cholesterol (HDL-C, commonly known as "good cholesterol"), Low-Density Lipoproteins- Cholesterol (LDL=C, also known as "bad cholesterol"), a ratio of Total Cholesterol to HDL, and an estimated risk factor are all measured in the Lipid Profile typically the lipid profile includes cholesterol & TG & HDL, LDL, and VLDL.

2.9.1 Determination of Serum Total Cholesterol Level (mmol/L):

Cholesterol is a lipid molecule that is found in cell membranes and lipoproteins. Steroid hormones, bile acids, and vitamin D are all made up of cholesterol. Cholesterol or its precursors are abnormal in a variety of human disorders, including heart disease, stroke, type II diabetes, brain disease, and many more.

Principle:

The enzymatic method described by Allain and all, which reaction schemeis as follows:

1. Cholesterol Esters $\xrightarrow{CE}$ Cholesterol + Fatty Acids

2. Cholesterol + O_2 $\xrightarrow{CO}$ Cholest-4-en-3-one + H_2O_2

3. $2H_2O_2$ + HBA +4 AAP $\xrightarrow{POD}$ Quinoneimine Dye + $4H_2O$

Where:

CE	=	Cholesterol Esterase
CO	=	Cholesterol Oxidase
HBA	=	Hydroxybenzoic Acid
4AAP	=	4-aminoantipyrine
POD	=	Peroxidase

Reagents:

R1 CHOLESTEROL CHOD PAP Reagent(Phosphate buffer 100 mmol/L+ Chloro-4-phenol 5 mmol/L+ Sodium Cholate 2.3 mmol/L+ Triton x 100 1.5 mmol/L+ Cholesterol oxydase (CO) > 100 IU/L+ Cholesterol esterase (CE) > 170 IU/L+ Peroxydase (POD) > 1200 IU/L+ Amino – antipyrine (PAP) 0.25 mmol/L+ PEG 6000 167 µmol/L)

R2 CHOLESTEROL CHOD P Cholesterol(200AP)Standard mg/dL(5.17 mmol/L)

2.9.2 Determination of serum Triglueserad level (mmol/L):

It is an ester of three fatty acids with cholesterol. These fatty acids may be homogeneous or a mixture of fatty acids. Triglycerides are transported through the blood from adipose tissue to sites of vital metabolism in the liver

Principle:

The triglycerides (GPO) method is based on the enzymatic measurement of glycerol after hydrolysis by lipoprotein lipase that use the enzyme glycerol phosphate oxidase (GPO). Fossati1 described the basis of this method by combining it with the traditional Trinder2 reaction sequence Reagent kit for the quantitative detection of triglycerides levels in serum using an enzymatic colorimetric method (PAP). Glycerol and fatty acids are combined to produce triglycerides, which are either synthesized in the liver or taken from the serum.

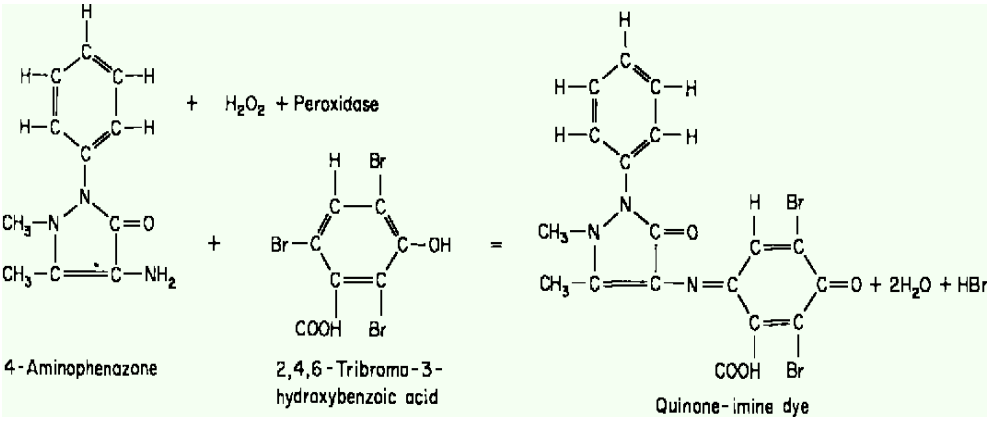
Reagents:

R1

250ml of monoreagent(PIPES-buffer,PH=7.5(50mmol/L)+ 4-chlolrophenol(5mmol/L)+4-aminophenenazone(0.25mmol/L)+ Mangnesium ions(4.5mmol/L)+ATP(2mmol/L)+Lipases

2.9.3 Determination of serum High-Density Lipoprotein Cholesterol HDL-C (mmol/L):

The addition of phosphotungstic acid magnesium chloride precipitates chylomicrons, VLDL (very low-density lipoproteins), and LDL (low-density lipoproteins). The HDL (high-density lipoproteins) fraction is extracted from the supernatant fluid and tested for HDL cholesterol using the CHOLESTEROL liquid color test kit Fiuger(2-6).



Fiuger(2-6) Determination of serum High-Density Lipoprotein (108)

2.9.4 Determination of serum Low Densty Lapoproten Cholesterol(LDL)-C(mmol/L):

Total cholesterol minus HDL cholesterol minus triglycerides divided by five is the conventional Friedewald calculation for calculating LDL cholesterol. The formula applies a one-size-fits-all factor of five to everyone for the sake of simplicity. However, Johns Hopkins researchers discovered that for some high-risk people, this causes LDL cholesterol to probably be lower than it is. The researchers wanted a more precise model that factored in specific facts about a person's cholesterol and triglyceride levels, Total cholesterol minus HDL cholesterol minus triglycerides divided by five is the conventional Friedewald calculation for calculating LDL cholesterol. The formula applies a one-size-fits-all factor of five to everyone for the sake of simplicity.

$$LDL\text{-}C = Total\ Cholesterol - (HDL\text{-}C + 0.38 \times Triglycerides)$$

2.9.5 Determination of Very Low Densty Lapoproten (Vldl) (mmol/L):

the process of determining the concentration of Very Low-Density Lipoprotein (VLDL) in blood samples. Fresh blood samples from overnight-fasted normal patients and people with various forms of Hyperlipoproteinemia (HLP) were kept at 4°C for no more than four days. Patients were divided into several phenotypes according to Fredrickson et

al's criteria, with threshold levels for serum cholesterol, triglycerides, and LDL cholesterol of 5.2 mmol/L. HLP is classified as type if the VLDL cholesterol/serum triglyceride ratio is greater than 0.69, there is a lack of apoproteins E-3 and E-4, and the isoelectric concentrating pattern of VLDL apoproteins is mixed with lipids. The precipitation techniques and the Friedewald formula are considered equally accurate or erroneous if they provide a precise criterion at the outset.

2.10 Determination of Human AngiopotenLikeProtein-4 by using sandwich ELISA Kit (ng/mL):

Principle:

kit developed by Ela science is an improvement of the traditional sandwich ELISA kit. It simplifies the operation process, saves at least 1h, and requires less sample volume for assays, greatly improving the detection efficiency.

The most frequent Elisa method is sandwich ELISA (or sandwich immunoassay). This format necessitates the use of two antibodies/antigens that are specific for different antigen/antibody epitopes. Matching antibody/antigen pairings are the name given to these two antibodies /antigens. To immobilize the tested analytic, one of the antibodies/antigens is coated on the surface of the microplate and employed as the capture antibody/antigen. To aid in the identification of the analytic, the other antibody/antigen is conjugated with biotin or other indicators. An Enzyme-Linked Immunosorbent Assay is included in this kit (ELISA). Human ANGPTL4 antibody has been pre-coated on the plate. ANGPTL4 from the sample is introduced to the wells and binds to antibodies coated on them. The biotinylated human ANGPTL4 Antibody is then added to the sample and binds to ANGPTL4. The biotinylated ANGPTL4 antibody is then bound by Streptavidin-HRP. During the washing phase after incubation, all unbound Streptavidin-HRP is rinsed away. The hue develops in proportion to

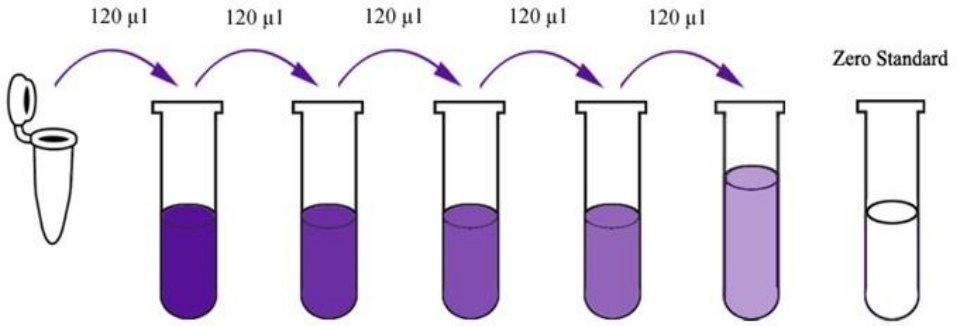
the amount of human ANGPTL4 in the substrate solution. The reaction is stopped by adding an acidic stop solution and measuring the absorbance at 450 nm .

Reagent Preparation:

Before using, all reagents should be brought to room temperature. Standard To make a 400ng/ml standard stock solution, combine 120l of the standard (800ng/ml) with 120l of standard diluent. Before producing dilutions, let the standard sit for 15 minutes with moderate agitation. Prepare duplicate standard points by diluting the standard stock solution (400ng/ml) 1:2 with standard diluent to get solutions of 200ng/ml, 100ng/ml, 50ng/ml, and 25ng/ml. The zero standard is standard diluent (0 ng/ml). Any leftover solution should be frozen at -20°C and utilized within one month of freezing. The following are proposed dilutions of standard solutions

Procedure:

	Reagent blank	Sample
400ng/ml	Standard No.5	120µl Original Standard + 120µl Standard Diluent
200ng/ml	Standard No.4	120µl Standard No.5 + 120µl Standard Diluent
100ng/ml	Standard No.3	120µl Standard No.4 + 120µl Standard Diluent
50ng/ml	Standard No.2	120µl Standard No.3 + 120µl Standard Diluent
25ng/ml	Standard No.1	120µl Standard No.2 + 120µl Standard Diluent



ANGPTL4 Standard Diluent

Standard Concentration	Standard No.5	Standard No.4	Standard No.3	Standard No.2	Standard No.1
800ng/ml	400ng/ml	200ng/ml	100ng/ml	50ng/ml	25ng/ml

Washing Buffer 20ml Wash Buffer, diluted To make 500 mL of 1x Wash Buffer, dilute 25 times in deionized or distilled water. If crystals have developed in the concentrate, gently stir until they have all dissolved.

Assay Procedure:

1. Follow the instructions for preparing all reagents, standard solutions, and samples. Before using, bring all reagents to room temperature. At room temperature, the test is carried out.
2. Determine how many strips are needed for the test. To utilize the strips, place them in the frames. The unused strips should be kept at a temperature of 2-8°C.
3. To a standard well, add 50 liters of standard. Because the standard solution contains biotinylated antibodies, do not add ntibodies to the standard well.
4. Place 40 mL sample in sample wells, followed by 10 mL anti-ANGPTL4 antibody, 50 mL streptavidin-HRP in sample wells, and 50 mL streptavidin-HRP in standard wells (Not blank control well). Mix thoroughly. Use a sealer to seal the plate. At 37°C, incubate for 60 minutes.
5. Remove the sealant and wash the plate with a wash buffer five times. For each wash, soak wells in at least 0.35 mL buffer were added for 30 seconds to 1 minute. Aspirate all wells and wash 5 times with wash buffer, over-pressurized wells with wash buffer for automatic washing. Using toilet tissue or another absorbent material, blot the plate.
6. Pour 50 liters of substrate solution A into each hole, followed by 50 liters of substrate solution B. Incubation at 37°C plate for ten min at 37°C in the darkness, covered with a fresh sealer.
7. Pour 50 l Stop Solution through each well; the blue color will become yellow almost instantly.

8. After 10 minutes after applying the stop solution, determine the optical density (OD value) of each well using an Elisa reader set to 450 nm.

Calculation of Result:

Draw a best-fit curve across the points on the graph by graphing the average OD for each standard on the vertical (Y) axis against the concentration on the horizontal (X) axis. These calculations are best done with computer-based curve-fitting tools, and regression analysis may be used to identify the optimal fit line Figure (2-7).

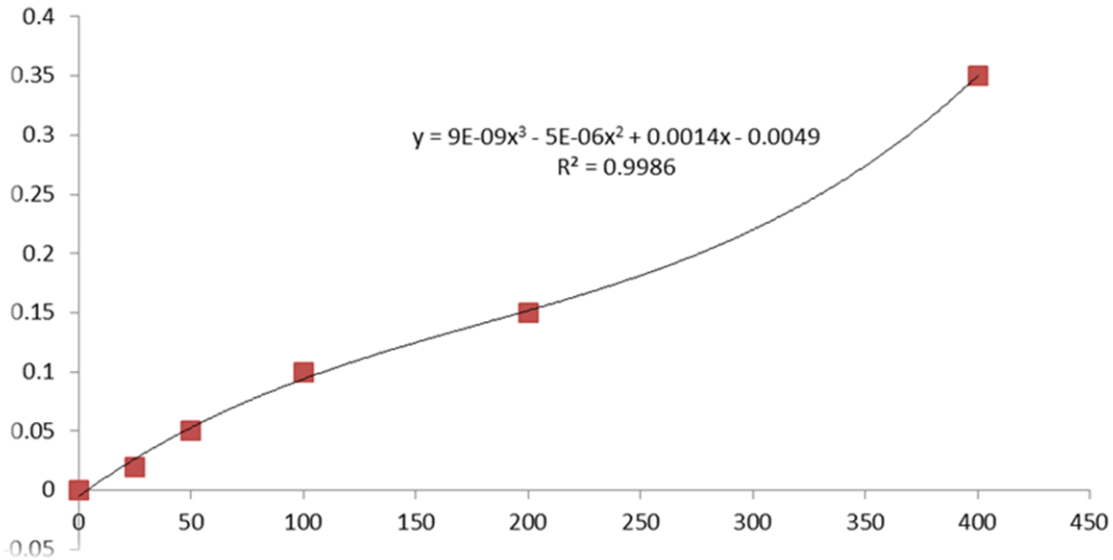


Figure (2-7) Standard curve for ANGPTL4

2.11 Determination of Human Omentin-1 by using sandwich ELISA Kit (U/L)

Principle:

An Enzyme-Linked Immunosorbent Assay is included in this kit (ELISA). Human Omentin-1 antibody has been pre-coated on the plate. Omentin-1, which is present in the sample, is introduced to the wells and binds to the antibodies. The biotinylated human Omentin-1 Antibody is then added to the sample and binds to Omentin-1. After that, Streptavidin-HRP is added, which binds to the biotinylated proteins,

This sandwich kit detects human Omentin-1 (also known as Omentin-1) in serum, cell culture supernates, CellLysates, plasma, and tissue homogenates in an accurate quantitative manner. An Enzyme-Linked Immunosorbent Assay is included in this kit (ELISA). Intelectin 1 (ITLN1) Human Antibody

has been pre-coated on the plate. ITLN1 is introduced to the sample and binds to antibodies that have been deposited on the wells. The biotinylated Human ITLN1 Antibody is then added to each tube and binds to ITLN1. The biotinylated ITLN1 antibody is then bound by Streptavidin-HRP. During the washing phase after incubation, all unbound Streptavidin-HRP is rinsed away. After that, the substrate is added, and the color appears in accordance to the amount of Human ITLN1 present. The process is stopped by adding an acidic stop solution and measuring the absorbance at 450 nm .

Reagents:

Reagent Provided		
Components	**Quantity (96T)**	**Quantity (48T)**
Standard solution (640ng/L)	0.5ml x1	0.5ml x1
Standard diluent	3ml x1	3ml x1
Streptavidin-HRP	6ml x1	3ml x1
Stop solution	6ml x1	3ml x1
Substrate solution A	6ml x1	3ml x1
Substrate solution B	6ml x1	3ml x1
Wash buffer Concentrate (25x)	20ml x1	20ml x1
Biotinylated Human ITLN1 antibody	1ml x1	1ml x1

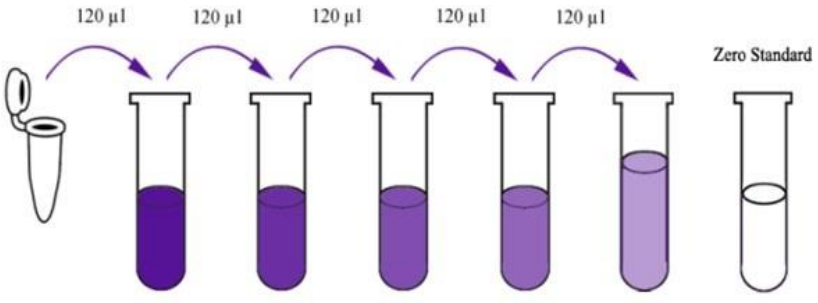
Procedure:

Before using any reagents, make sure they're at room temp. To make a 320ng/L standard stock solution, combine 120ul of the standard (640ng/L) with 120ul of standard

diluent. Before producing dilutions, let the standard sit for 15 minutes with moderate agitation. Create duplicated standard points by diluting the standard stock solution (320ng/L) 1:2 with standard diluent to obtain solutions in the following concentrations: 160ng/L, 80ng/L, 40ng/L, and 20ng/L. Any leftover solution should be frozen at -20°C and utilized within one month of freezing.

The following are proposed dilutions of standard solutions:

320ng/L	**Standard No.5**	**120ul Original standard + 120ul Standard diluent**
160ng/L	Standard No.4	120ul Standard No.5 + 120ul Standard diluent
80ng/L	Standard No.3	120ul Standard No.4 + 120ul Standard diluent
40ng/L	Standard No.2	120ul Standard No.3 + 120ul Standard diluent
20ng/L	Standard No.1	120ul Standard No.2 + 120ul Standard diluent



Dilution of standard solutions Omentin

Standard concentration	**Standard No.5**	**Standard No.4**	**Standard No.3**	**Standard No.2**	**Standard No.1**
640ng/L	320ng/L	160ng/L	80ng/L	40ng/L	20ng/L

Buffer for washing 20 Wash Buffer, diluted To make 500 mL of 1x Wash Buffer, dilute 25 times in deionized or distilled water. If crystals are developed in the concentration, gently stir until they have all dissolved Figure (2-8).

Draw a best fit curve across the points on the graph by graphing the average OD for each standard on the vertical (Y) axis against the concentration on the horizontal (X) axis. These calculations are best done with computer-based curve-fitting tools, and regression analysis may be used to identify the optimal fit line .

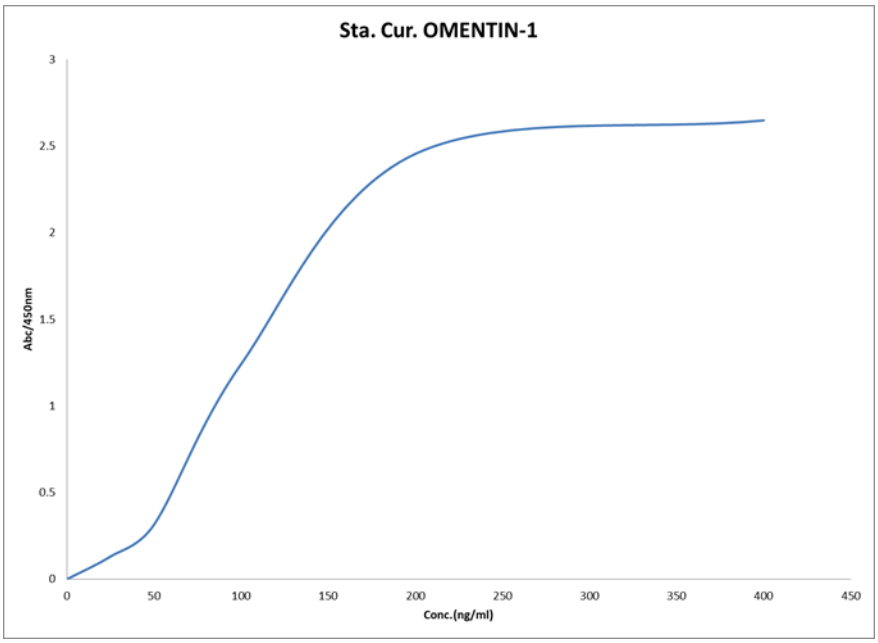


Figure (2-8) Standard curve for OMENTIN-1

2.12 Statistical analysis:

We use the IBM company Statistics program (SPSS) version 26 for Windows 10, Values are expressed as means ± standard deviation (S.D). The results were analyzed statistically by (ANOVA) followed by the LSD Multiple Comparison Test. Significance was accepted at a p-value of $P \leq 0.05$ and the (r) correlation was used between all 4grups.

Chapter One

Results and Discussion

Results and Discussion

3.1. Characteristics of Patients and Control Groups

Table (3-1) demonstrates the baseline characteristics of the study, which includes the data of Age for patient groups and control groups. It contains the results for the measurements of Age, Table (3-2) BMI ($Kg/M^{2)}$, And Tabel(3-3) Fasting blood sugar, and Table (3-4) HbA1c for patients non-obese (Gp1) aged 52±8.5 years, patients obese(Gp2) aged 52±7.6, healthy non-obese (Gc1) and healthy obese(Gc2)groups their age 46±5.3 and 43±4.6 respectively.

The results in Table (3-3) show that highly significant increase in glucose levels for patients than control due to the patients being diabetic obese and non-obese while the controls are obese and non-obese healthy and this result illustrates through the BMI levels that explain there are matching between the body mass index for patients and controls.

The high levels of HbA1c for patients give an indicator they are in unregulated control(GP1 and Gp2) compare with Gc1, while the result of Gc2 explains there is a risk factor to develop diabetes disease due to increased BMI.

Table (3-1) Clinical Measurements of Age (Year) Patients and Control Groups

				CI 95%		P-Value		r-Value
Age (Years)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.1	-0.14
	Gp1	30	52±8.5	49	55	**Gp1,Gc1**	0.004	0.001
	Gp2	30	52±7.6	48	54	**Gp1,Gc2**	0.000	0.12
	Gc1	30	46±5.3	44	49	**Gp2,Gc1**	0.004	0.07
	Gc2	30	43±4.6	41	45	**Gp2,Gc2**	0.000	0.35

Table (3-2) Clinical Measurements of BMI (Kg/M^2) Patients and Control Groups

				CI 95%		P-Value		r-Value
BMI (Kg/M^2)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.001	-0.05
	Gp1	30	26.7±2.7	25.7	27.7	**Gp1,Gc1**	0.1	0.03
	Gp2	30	37.6±5.5	35.6	39.6	**Gp1,Gc2**	0.001	0.25
	Gc1	30	25.7±3.2	24.2	27.4	**Gp2,Gc1**	0.001	-0.02
	Gc2	30	36.7±6.6	34.3	38.1	**Gp2,Gc2**	0.9	-0.15

Table (3-3) Clinical Measurements of FBS (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
FBS (mmol/L)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.9	-0.12
	Gp1	30	13.9±6.7	11.48	16.29	**Gp1,Gc1**	0.0001	-0.06
	Gp2	30	14.3±4.7	12.63	16.03	**Gp1,Gc2**	0.0001	-0.13
	Gc1	30	5.57±1.15	4.98	6.15	**Gp2,Gc1**	0.001	0.31
	Gc2	30	6.57±1.18	5.65	7.48	**Gp2,Gc2**	0.001	-0.002

Table (3-4) Clinical Measurements of HbA1c (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
HbA1c. (mmol/L)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.43	-0.06
	Gp1	30	9.7±3.1	8.58	12.82	**Gp1,Gc1**	0.001	-0.06
	Gp2	30	12.4±2.8	11.4	13.45	**Gp1,Gc2**	0.0001	0.05
	Gc1	30	5.6±0.5	5.29	5.8	**Gp2,Gc1**	0.0001	-0.02
	Gc2	30	6.1±0.7	5.76	6.46	**Gp2,Gc2**	0.0001	0.11

Table (3-5) Clinical Measurements of CHOL. (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
CHOL. (mmol/L)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.9	0.31
	Gp1	30	5.02±1.1	4.63	5.41	**Gp1,Gc1**	0.0001	-0.00
	Gp2	30	5.05±1.3	4.59	5.51	**Gp1,Gc2**	0.0004	0.3
	Gc1	30	3.9±0.5	3.75	4.24	**Gp2,Gc1**	0.001	0.12
	Gc2	30	4.1±1.1	3.54	4.63	**Gp2,Gc2**	0.006	-0.12

Table (3-6) Clinical Measurements of TG (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
TG (mmol/L)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.21	-0.27
	Gp1	30	1.95±0.5	1.74	2.16	**Gp1,Gc1**	0.006	-0.17
	Gp2	30	2.3±0.77	2.01	2.56	**Gp1,Gc2**	0.004	-0.09
	Gc1	30	1.62±0.3	1.45	1.78	**Gp2,Gc1**	0.0001	0.15
	Gc2	30	1.58±0.4	1.38	1.76	**Gp2,Gc2**	0.0002	0.01

Table (3-7) Clinical Measurements of HDL (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
HDL (mmol/L)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.09	-0.32
	Gp1	30	1.23±0.3	1.11	1.32	**Gp1,Gc1**	0.46	-0.48
	Gp2	30	1.08±0.2	0.99	1.18	**Gp1,Gc2**	0.77	-0.26
	Gc1	30	1.95±0.4	1.75	2.17	**Gp2,Gc1**	0.002	0.12
	Gc2	30	1.3±0.3	1.12	1.45	**Gp2,Gc2**	0.023	-0.003

Table (3-8) Clinical Measurements of LDL (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
LDL (mmol/L)	**groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.8	0.3
	Gp1	30	2.8±1.03	2.03	3.07	**Gp1,Gc1**	0.0004	0.01
	Gp2	30	2.9±1.01	2.54	4.1	**Gp1,Gc2**	0.004	0.2
	Gc1	30	1.9±0.4	1.75	2.27	**Gp2,Gc1**	0.0007	0.1
	Gc2	30	2.04±1.1	1.46	2.64	**Gp2,Gc2**	0.01	-0.02

Table (3-9) Clinical Measurements of VLDL (mmol/L) Patients and Control Groups

				CI 95%		P-Value		r-Value
VLDL (mmol/L)	**groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.72	-0.26
	Gp1	30	0.9±0.2	0.87	1.08	**Gp1,Gc1**	0.006	-0.17
	Gp2	30	1.14±0.3	0.92	1.17	**Gp1,Gc2**	0.004	-0.09
	Gc1	30	0.81±0.1	0.73	0.89	**Gp2,Gc1**	0.0001	0.15
	Gc2	30	0.85±0.1	0.77	0.93	**Gp2,Gc2**	0.002	0.01

Table (3-10) Clinical Measurements GSH (µmol/ml) of Patients and Control Groups

				CI 95%		P-Value		r-Value
GSH (µmol/ml)	**groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.76	0.32
	Gp1	30	1.01±0.2	0.92	1.09	**Gp1,Gc1**	0.0001	-0.28
	Gp2	30	0.9±0.3	0.88	1.15	**Gp1,Gc2**	0.0001	0.30
	Gc1	30	3.23±0.6	2.91	3.55	**Gp2,Gc1**	0.0001	-0.09
	Gc2	30	2.99±0.8	2.59	3.4	**Gp2,Gc2**	0.0001	-0.003

Calcium Concentration

Calcium levels were non-significant increased for Gp1 and Gp2 while the results illustrate there was a significant increase for the patients group compared with control groupsTable (3-9)

Table(3-11) Calcium(mmol/L) Levels of Patients and Control Groups

				CI 95%		P-Value		r-Value
Ca^{2+} (mmol/L)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.1	-0.005
	Gp1	30	1.8±0.5	1.38	1.94	**Gp1,Gc1**	0.01	-0.149
	Gp2	30	1.5±1.1	1.3	2.38	**Gp1,Gc2**	0.05	-0.106
	Gc1	30	2.3±1.01	1.95	2.69	**Gp2,Gc1**	0.003	-0.005
	Gc2	30	2.4±1.1	2.03	2.86	**Gp2,Gc2**	0.02	0.028

Obesity is a severe public health issue in the 21st century, and nutritional and behavioral strategies have not been able to stop its rise(109)(110).

Since calcium is the most prevalent nutrient in the human system, variables relating to internal and extracellular calcium may have a role in the physiological causes of obesity and concomitant disorders(111). Numerous biological processes, including skeletal mineralization, muscular contraction, cell division during glycogen consumption, and cell division, depend on calcium. Negative feedback processes such as absorption through the intestines, renal reabsorption, and bone storage can regulate calcium metabolism in the human body. Concerning the metabolic impact of calcium on adipose tissue in the treatment of obesity, several concepts have been put up(112).

Numerous theories have been put out to explain the results seen in investigations on the relationship between calcium consumption and obesity(113). The quantity of intracellular Ca^{2+} in the adipocyte cell is associated with one of calcium's anti-obesity effect mechanisms.

The vitamin D compound 1,25-dihydroxy vitamin D (1.25-(OH)2-D), which is involved in fat production and activating intracellular Ca^{2+} in adipocytes to cause lipolysis, control this pathway(114)(115).

While vitamin D is inhibited in a high calcium diet, the concentration of intracellular Ca^{2+} in adipose tissue drops Table (3-11), increasing lipolytic activity and decreasing lipogenesis, which explains the fat loss model in adipose tissue. The anti-obesity impact has been explained using this technique(116)(117).

Recent research suggests that the regulation of adipocyte cell function may be influenced by the activation of the calcium-sensitive receptor. Following a low calcium intake, the adipocyte cell experiences an increase in intracellular calcium. This model predicts a rise in serum vitamin D due to the activation of calcium-sensitive receptors in adipose tissue. This may be due to the combined impact of increased lipogenic marker activity and reduced lipolytic enzyme activation(118)(119).

Table (3-11) By reducing intestinal fat absorption and boosting fecal fat excretion, calcium may also help people lose weight. In the digestive system, calcium combines with fatty acids to produce insoluble calcium soaps, which increases the elimination of fecal fat and may have the capacity to control body weight(120)(121).

An key electrolyte for several vital biological processes is calcium. Numerous processes connected to glucose regulation may benefit greatly from the presence of calcium. In certain tissues that respond to insulin, calcium controls intracellular processes mediated by insulin, participates in the secretory activity of pancreatic beta cells, and phosphorylates the receptors for insulin. Additionally, several regulatory genes for pro-inflammatory cytokines linked to insulin resistance are downregulated by calcium(122)(123).

The production of insulin is a calcium-dependent process. For internal activities regulated by insulin in tissues responsive to insulin, such as fatty tissues and muscle, calcium is essential(124)(125).

For effective insulin-mediated actions, intracellular calcium concentration must fall within a certain range. A dysregulated insulin signal transduction cascade that results in decreased glucose transporter function occurs when intracellular calcium concentrations vary in insulin-responsive tissues. This contributes to peripheral insulin resistance(126)(127)(128).

3.2. Omentin-1 Levels for Patients and Control Groups

Table3-12. Serum omentin-1 levels were observed to be significantly higher in obese patients and overweight women control with mean SD Gp2 (76.0± 34.91ng/ml) compared to controls obese Gc2 (73.1± 21.08 ng/ml) (P<0.001). We also discovered strong significant

Table (3-12) Omentin-1(ng/ml) Levels of Patients and Control Groups

				CI 95%		P-Value		r-Value
Omentin-1 (ng/ml)	**Groups**	**N**	**Mean±SD**	**Lower**	**Upper**	**Gp1,Gp2**	0.0001	0.11
	Gp1	30	35.02±14.8	29.73	40.35	**Gp1,Gc1**	0.09	-0.02
	Gp2	30	76.02±34.9	63.54	88.91	**Gp1,Gc2**	0.0001	-0.3
	Gc1	30	40.6±13.9	33.53	47.68	**Gp2,Gc1**	0.0001	0.4
	Gc2	30	63.7±21.1	53.04	74.39	**Gp2,Gc2**	0.09	-0.17

Adipose tissue secretes adipokines such as leptin, adiponectin, and visfatin, just like an endocrine organ. These adipokines seem to play a key role in the pathophysiology of insulin resistance, diabetes, atherosclerotic, vascular endothelial dysfunction, and inflammation. Omentin is a newly discovered adipose tissue-derived protein(129)

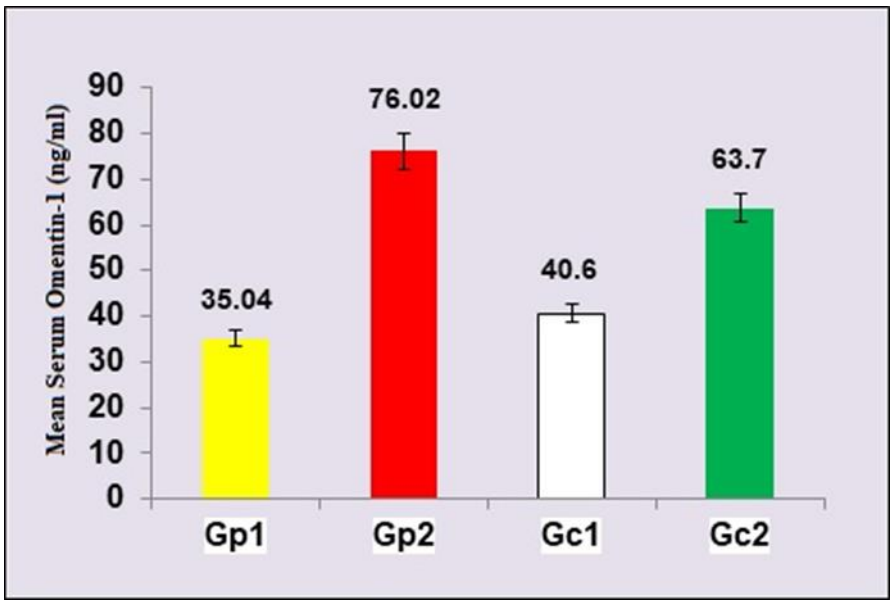


Figure (3-1) Omentin-1 levels with the severity of PAD. The median is shown by the center lines on the box plots, the interquartile range is represented by the length of the box, and the lines extend to the minimum and maximum values. Lower levels of circulating omentin are based on their functional status as defined by the classification.

associations between serum omentin-1 and (WEIGHT, BMI, WAST, HIP, SBP, DBP, FBG, HbA1C, CHOL, T.G, HDL, LDL, vLDL) (r = .520, .590, .733, .671, .436, .215, .663, .714, .737, .725, .737, .735, .741) and systolic blood pressure (r = 0.274, p = 0.031), Table(3-1,2.3) respectively (P< 0.001) In Gc2, there was a positive association with waist circumference, but no correlation in femalesGc1. Furthermore, some researchers found that males have greater omentin-1 levels than females. We found no evidence of sexual dimorphism or a link to visceral obesity. The intricate interactions between insulin levels and omentin-1 might explain these discrepancies in the research.

Table (3-13) Demographic Summarizes the Biochemical and omentin-1 Clinical Data for all research groups.

	Control			Patients		
	(Gc1)	**(Gc2)**	**Total**	**(Gp1)**	**(Gp2)**	**Total**
Number(n)	30	30	60	30	30	60
Age(years)	46.9±5.2	43.5±4.67	45.2±5.17	52.9±8.50	52.2± 7.69	52.5±7.1
Weight(kg)	**66± 7.46***	97.8± 22.59	81.9± 22.8	68.3± 9.55	94.2± 12.29	**81.26±16.9****
Height(cm)	156.8± 4.5	160.4± 5.93	158.6±5.5	159.4± 5.6	158.5± 6.08	158.9±5.78
BMI(kg/m^2)	25.8±3.1	37.7±6.67	**31.8±7.83***	26.7±2.74	37.6± 5.57	**32.2±6.94****
WAST(cm)	85.6± 4.36	130.1±9.1	**107.9±23.3****	89.1±8.37	132±10.22	**110.6±23.3****
HIP(cm)	87.2± 4.41	132.2±9.23	**109.7±23.6****	92.9±16.89	134.1±10.47	**113.5±24.8****
SBP(mmHg)	122.8± 4.3	128.6±4.22	125.7±5.12	126.2±5.26	131.6±4.1	128.9±5.38
DBP(mmHg)	77.7±3.48	85.3±5.05	81.5±5.78	83.7±6.36	84.7±5.1	84.2±5.73
FBG (mmol/l)	5.5±1.12	6.6±1.81	**6.1±1.55***	13.9±6.72	14.4± 4.75	14.1±5.72
HbA1C(mmol/l)	5.6± 0.48	6.1±0.7	5.8±0.65	11.7±3.13	12.4±2.9	12.1±2.97
T. chol(mmol/l)	3.1±0.47	4.1±1.08	4.0±0.81	5.1±1.08	5.1± 1.28	5.1±1.16
HDL (mmol/l)	1.3±0.29	1.3±0.32	1.3±0.3	1.2±0.31	1.1± 0.26	1.2±0.29
LDL-C(mmol/l)	1.1±0.40	2.1±1.16	2.0±0.84	2.9±1.03	2.9± 1.24	2.9±1.12
T.G (mmol/l)	1.6±0.32	1.1±0.36	1.6±0.33	1.9±0.58	2.3± 0.77	2.12±0.69
vLDL (mmol/l)	0.8±0.16	0.8±0.18	0.8±0.16	0.1±0.29	1.1± 0.35	1.0±0.32
Omentin(ng/ml	40.6±13.54	63.7± 21.08	52.2±20.84	35.1±14.84	76.0± 34.91	55.5±33.37

Values are expressed as means ± SD, SBP, systolic blood pressure, DBP, diastolic blood pressure, BMI, body mass index, WC, waist circumference, FBG, fasting blood glucose, HbA1C, glycated hemoglobin, TG, triglycerides, TC, total cholesterol, HDLC, high-density lipoprotein cholesterol, LDLC, low-density lipoprotein cholesterol.

3.3 Angiopoietin-like protein 4 (ANGPTL-4) levels for Patients and Control Groups

In patients with type 2 diabetes, serum levels of ANGPTL4 were significantly lower than those in healthy subjects as shown in Table, suggesting that the decreased ANGPTL4

could be a causative factor of this disease. These results collectively indicate that ANGPTL4 exerts distinct effects on glucose and lipid metabolism and that its beneficial effect on glucose homeostasis might be useful for the treatment of diabetes.

Table (3-14) Angiopoietin-like protein 4 (ANGPTL-4) (mcg/dl) levels for Patients and Control Groups

				CI 95%		P-Value		r-Value
ANGPTL-4 (mcg/dl)	Groups	N	Mean±SD	lower	Upper	Gp1,Gp2	0.001	0.05
	Gp1	30	8.9±3.5	7.64	10.13	Gp1,Gc1	0.001	0.02
	Gp2	30	2.6±1.8	1.93	3.25	Gp1,Gc2	0.001	-0.009
	Gc1	30	26.6±7.4	22.82	30.34	Gp2,Gc1	0.0001	0.27
	Gc2	30	13.4±3.8	11.47	15.34	Gp2,Gc2	0.0001	-0.05

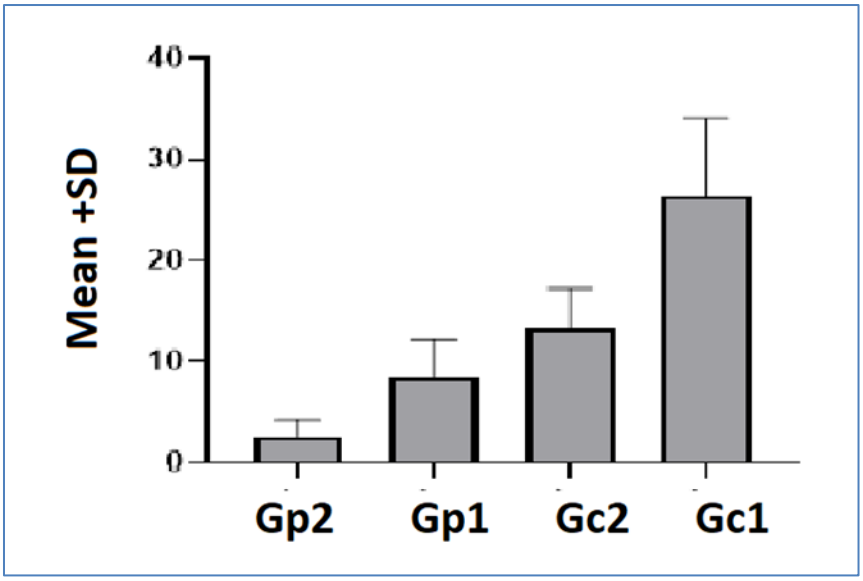


Figure (3-2) Angiopoietin-like protein 4 (ANGPTL-4) (mcg/dl) levels for Patients and Control Groups

ANGPTL-4 has been recently proposed as a key factor regulating lipid metabolism by its inhibitory role on LPL activity(130)(131).

Table (3-14) In addition, ANGPTL-4 controls lipoprotein metabolism in addition to modifying HDL metabolism and function. High-density lipoproteins (HDL) and triglyceride (TG) metabolism is a complex process that is currently poorly understood. Both postprandially and during fasting, their levels typically show a negative association with one another. Patients with type 2 diabetes are more likely to experience increased TG and lower HDL levels(132).

Plasma lipids are regulated by the angiopoietin-like proteins ANGPTL4 and ANGPTL8. explore the ANGPTL mechanisms that regulate human plasma lipid levels. studies in vitro and on animals reveal that LPL and Endothelial Lipase EL (EL, LIPG) are the principal targets of ANGPTLs. Pre-clinical research has shown that ANGPTL-4 treatment reduced dietary intake and body mass growth while increasing energy expenditure(133)(134).

Table (3-15) CorrelationGc1&Gp2 for Angptl4, Age,BMI,HbA1c,OMENTIN-1.

CorrelationGc1&Gp2		Age	BMI	HbA1c	OMENTIN-1
Angptl4(mcg/dl)	Pearson Correlation	-.553**	-0.445**	-.344**	-0.427**
	Sig. (2-tailed)	0.041	.000	0.007	0.0006
	N	60	60	60	60

****Correlation is significant at the 0.01 level (2-tailed).**

It has been shown that ANGPTL-4 generated from brown adipose tissue plays an important part in the control of the metabolism of lipids and glucose as well as the regulation of thermogenesis ,Table (3-15), or Several metabolic processes and actions of ANGPTL-4 were described, including the effect on adipose tissue lipolysis and glucose homeostasis regulation (135)(136).

3.5.Vitamin C Levels for Patients and Control Groups

Table(3-16) we discovered some details on the clinical evaluations of blood vitamin C levels (µmol/L) in both patient and control groups. According to one research, one-third of the patients had a vitamin C level of less than 11 mol/L, and the baseline plasma vitamin C level was 23 mol/L (hypovitaminosis C). Another research reported that the definition of "inadequate" vitamin C levels was defined as plasma levels of less than 50 µmol/L, while "moderate-to-severe" vitamin C insufficiency was classified as a plasma level of 11.91 µmol/L or less. One of the biggest health risks in the world today is obesity. Additionally, the disease's characteristic excessive body fat buildup may cause several concomitant clinical symptoms, including type 2 diabetes. These co-morbidity's emergence has frequently been linked to imbalanced oxidative stress. Antioxidant-based therapies might therefore be thought of as intriguing means of preventing the difficulties associated with obesity-related fat buildup(137).

Table (3-16) Clinical Measurements of Serum Vitamin C (µmol/L) for Patients and Control Groups

				CI 95%		P-Value		r-Value
Vit C (µmol/L)	groups	N	Mean±SD	Lower	Upper	Gp1,Gp2	0.24	-0.41
	Gp1	30	0.92±0.4	0.77	1.06	Gp1,Gc1	0.0001	0.24
	Gp2	30	0.7±0.5	0.54	0.94	Gp1,Gc2	0.0001	0.35
	Gc1	30	1.54±0.5	1.3	1.77	Gp2,Gc1	0.0001	-0.27
	Gc2	30	1.43±0.7	1.07	1.79	Gp2,Gc2	0.0003	-0.21

The findings revealed that obese patients with T2DM have lower levels of Serum vitamin C(µmol/L), and this finding was explained by variations in vitamin C levels when compared to obese and non-obese adults without diabetes. The lower levels of vitamin C and eventual diabetes development, as well as higher glucose levels, may be related(138).

Table (3-16) Due to a number of causes, including increased physiological needs from oxidative damage, people with type 2 diabetes are more likely to experience vitamin C deficiencies. According to one study, using vitamin C supplements may be able to treat type 2 diabetes. Further analysis is necessary to determine its efficacy and evidence quality. Although evidence from brief studies suggests that vitamin C supplementation may enhance glycemic control and blood pressure in individuals with type 2 diabetes, vitamin C supplementation cannot currently be advised as a therapy until larger, long-term, and high-quality trials confirm these results(81).

People who have Type 2 diabetes are at a higher risk of deficiency of vitamin C due to a variety of factors, including higher body requirements from oxidative harm, poorer acceptance into cells, excessive losses via the kidneys, and inadequate intake of food. Vitamin C is an antioxidant that is thought to have a protective role in diabetes by reducing the adverse effects caused by free radicals(139).

Diabetic persons are said to have good DM control if their fasting and postprandial blood glucose levels are as near to those of non-diabetics as possible. possible. This notion may be valid conceptually, but it is incorrect in practice. Actual practice is tough to come by, even with good intentions. Variations in blood glucose levels might complicate diabetes management. not just from day to day, but also from hour to hour. Because the goal of treatment isn't just to reduce symptoms, blood glucose levels while maintaining a healthy metabolic condition The research of hyperglycemia has been kept as normal as feasible. As a marker for appropriate diabetes management, it has certain drawbacks. As a result, several investigations have been recommended. looking for some

However, Fasting serum omentin-1 levels were greater in male individuals. There was no difference in male T2DM participants compared to female T2DM subjects. Between the sexes, there was statistical significance (20.2 3.5 mg/L vs. $P > 0.05$, 18.7 4.3 mg/L).

Obesity is a multifaceted disease with complicated pathophysiology involving biological, psychosocial, socioeconomic, and environmental, components, as well as variations in the routes and mechanisms that lead to negative health effects. Normal Weight Obese (NWO) women

The best indicator of the relationship between blood pressure and obesity is BMI. It also implies that obesity is probably more closely linked to home blood pressure than to office blood pressure. Finally, whereas obesity tends to affect SBP more than DBP, these findings show that the prevalence of systolic hypertension in children and adolescents may be related not just to fat but also to the measurement method used.

Table (3-17) Pearson Correlation Gp1&Gp2 for SBP,FBS,Weight,Vit.C.

Correlations Gp1,Gp2		FBS	Weight	Vit.C
SBP(mmHg)	Pearso Corre.	.343*	.644**	-0.396**
	Sig. (2-tailed)	0.001	0.0001	0.001
	N	60	60	60

***. Correlation is significant at the 0.05 level (2-tailed). SystolicBloodPressure(SBP),**

****. Correlation is significant at the 0.01 level (2-tailed).**

There is a significant nagitive relationship between weight and Vit.C in Gp1&Gp2 correiation with weight,r(58)=-.39, p≤ .001**

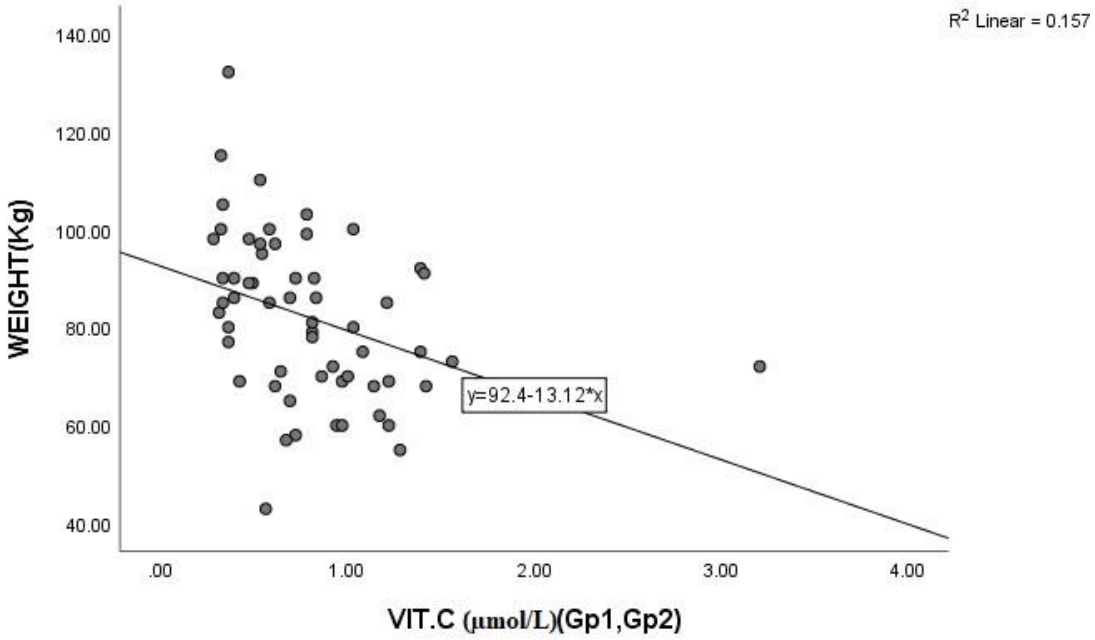


Figure (3-3) Ascorbic acid levels for Patients (Gp1,Gp2)and weight(Kg).

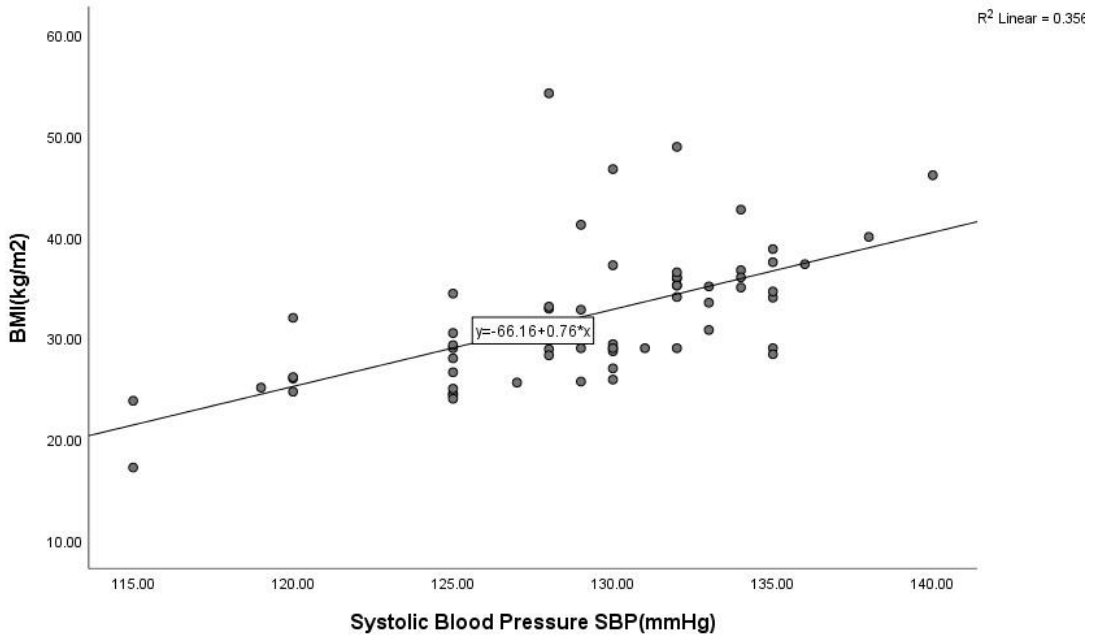


Figure (3-4) BMI(kg/m$^{2)}$/ and systolic blood pressure levels for Patients group (Gp1,Gp2)

There is a significant positive relationship Systolic Blood Pressure SBP(mmHg) and BMI(Kg/m2).in Gp1&Gp2 correiation BMI/SBP.. ,r(58)= .597** , p= .000**, An

increase in body mass inevitably leads to an increase in the main causes of high blood pressure Figure (3-4).

Invariable correlation showed a significant relationship between SBP& BMI The independent effects of the apnea-hypopnea index and body mass index were assessed using multivariable analysis, The degree of obesity is most closely connected with the connection between SBP and EBP in adults. More research is needed to determine the impact of obesity and the effect of therapy on blood pressure in adults .

Table (3-18) Pearson Correlation Gp1&Gp2 forBMI, SBP,OMENTIN-1, ANGPTL4.

Correlations Gp1,Gp2		SBP	OMENTIN-1	ANGPTL4
BMI (Kg/m^2)	**Pearso Corre.**	.597**	.559**	0.588**
	Sig. (2-tailed)	.000	.000	.000
	N	60	60	60

***. Correlation is significant at the 0.05 level (2-tailed).**

****. Correlation is significant at the 0.01 level (2-tailed).**

According to the data I uncovered,Table (3-18), there are some connections between BMI, SBP, and Omentin-1. Omentin-1 serum concentrations were shown to significantly correlate with body mass index (P 0.001) and systolic blood pressure (P 0.05) in a study of preeclampsia patients. Omentin-1 readings were shown to be correlated with BMI in children and teenagers with type 1 diabetes (r = -0.273; p 0.01) in another investigation. A Boston University School of Public Health study also discovered a substantial, statistically significant connection between BMI and systolic blood pressure(140).

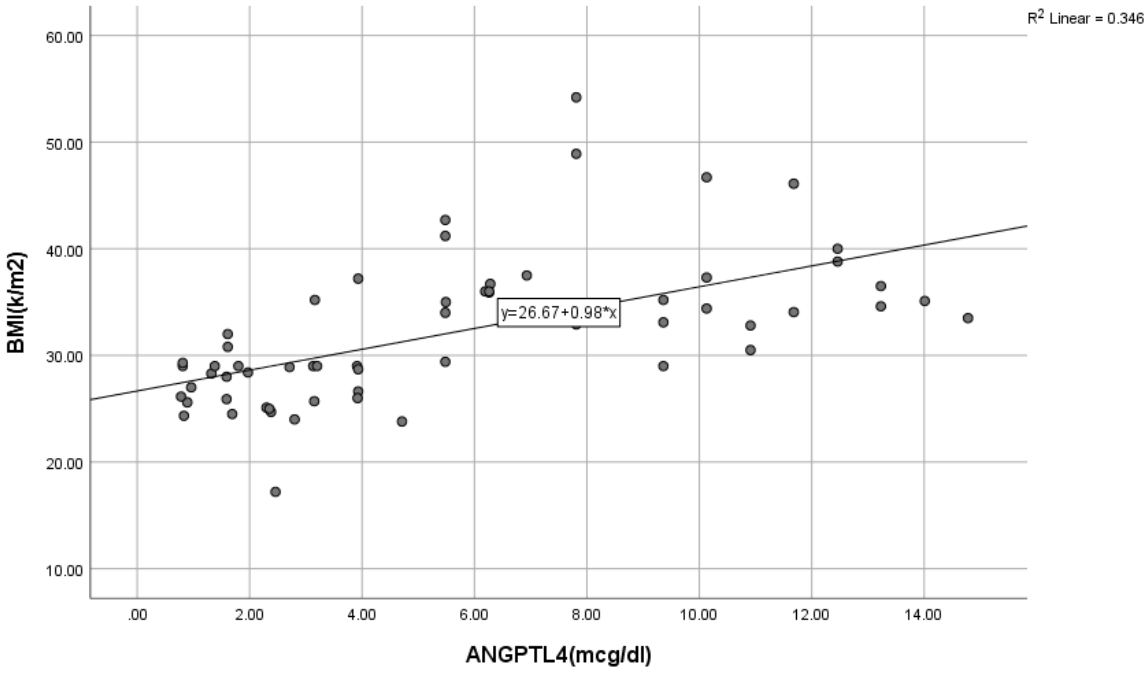


Figure (3-5) The Correlation between ANGPTL-4(mcg/dl) levels for Patients (Gp1,Gp2) and BMI(Kg/M^2).

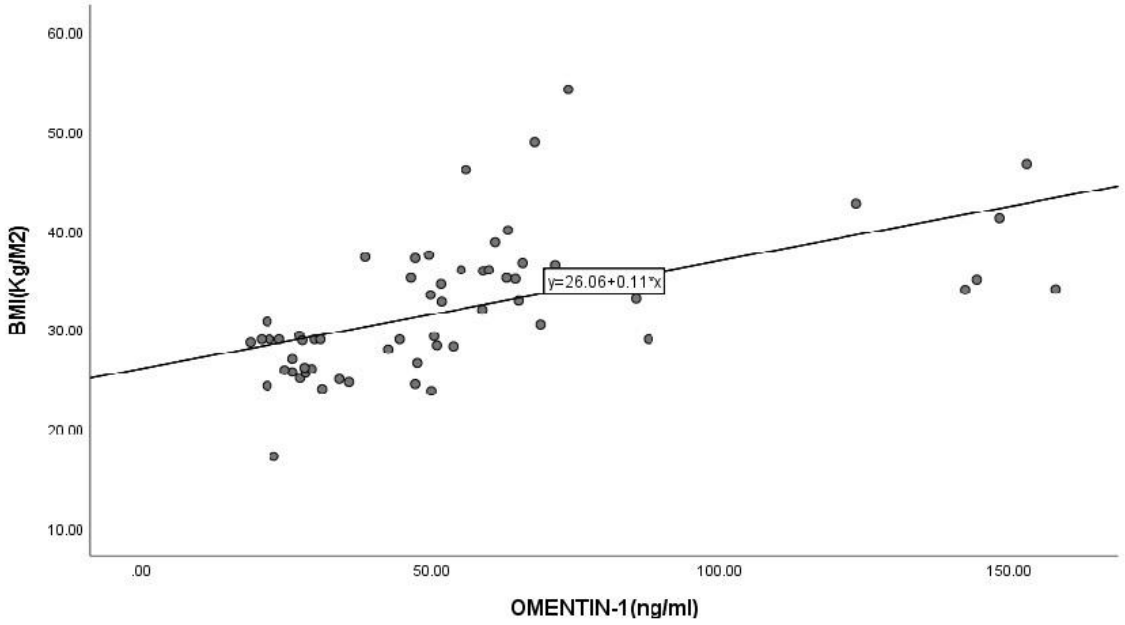


Figure (3-6) The Correlation between OMENTIN-1 levels for Patients (Gp1,Gp2)and BMI(Kg/M^2).

Figure(3-6)There is a significant positive relationship between OMENTIN-1 and BMI(Kg/m^2).in Gp1&Gp2 and increased in patients with DM2. correiation with weight,r(58)= .559**, p= .000**, it is possible that taking drugs for the treatmentof type 2 diabetes has a role in increasing omentin-1 in groups of thin patients and patients with obesity.

Our study has shown significantly high levels of serum omentin-1 in obese type 2 diabetic females in comparison to healthy subjects. Omentin-1 is inversely related to obesity, HbA1c, and SBP. No significant associations between glycemic control and fasting lipids. Serum omentin-1 can be used as a biomarker for obesity-related the purpose of this study was to see how well serum omentin-1 could differentiate patients from controls. P values of less than 0.05 were deemed statistically significant, whereas P values of less than 0.01 were deemed highly significant.

Table (3-19) Pearson Correlation Gc1,Gc2&Gp1,Gp2 FOR Vit.C,Age,Weight,BMI.

CorrelationsGc1,Gc2&Gp1,Gp2		Age	weight	BMI
VIT.C(mg/dl)	Pearson Corre.	-.256*	-.255*	-0.192*
	Sig. (2-tailed)	0.039	0.038	0.035
	N	120	120	120

***. Correlation is significant at the 0.05 level (2-tailed).**

****. Correlation is significant at the 0.01 level (2-tailed).**

This link between vitamin C and height is because height is positively correlated with body mass index In African Americans, ANGPTL4 40K carriers were extremely infrequent(141).

The importance of early diabetes diagnosis in reducing complications is critical. Although HbA1c is a reliable predictor of problems(142), there is little evidence of its accuracy in the diagnosis of diabetes. Cross-sectional demographical research was used to investigate the relationship between HbA1c and FBS in this study, Our findings revealed

that the link between HbA1c and FBS was quite robust, especially in diabetics. In general, FBS was a better predictor of HbA1c than HbA1c was a predictor of FBS.

Table (3-20) Pearson Correlation Gc1&Gp2

Pearson Correlations Gc1 & Gp2 (no obese control & obese patient)

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	AGE	1															
2	WEIGHT	0.219	1														
3	HEIGHT	-0.134	0.235	1													
4	BMI	.294*	.910**	-0.122	1												
5	WAIST	.316*	.862**	-0.063	.917**	1											
6	HIP	.324*	.863**	-0.067	.915**	.997**	1										
7	SBP	.304*	.665**	0.122	.661**	.724**	.734**	1									
8	DBP	.375*	.538**	0.214	.503**	.565**	.571**	.778**	1								
9	FBS	0.142	.636**	.310*	.556**	.657**	.647**	.656**	.475**	1							
10	HbA1c	0.15	.703**	0.161	.678**	.785**	.778**	.665**	.563**	.872**	1						
11	CHOL	.317*	0.241	0.164	0.199	.313*	.319*	.347*	.353*	.479**	.460**	1					
12	T.G	.306*	.362*	0.153	.338*	.411**	.412**	.336*	0.251	.387**	.351*	.399**	1				
13	HDL	-0.252	-0.275	-0.051	-.310*	-.328*	-.335*	-0.235	-0.191	-.326*	-.334*	-0.032	-0.200	1			
14	LDL	.303*	0.212	0.139	0.186	0.287	.295*	.327*	.348*	.465**	.462**	.939**	0.167	-0.235	1		
15	VLDL	0.283	0.291	0.139	0.2707	.326*	.327*	0.276	0.198	.321*	0.274	.370*	.995**	-0.163	0.129	1	
16	OMENTIN1	.390**	.441**	0.016	.469**	.499**	.498**	.339*	.338*	.335*	.492**	0.144	0.280	-0.281	0.142	0.233	1

Pearson Correlations Gc1 & Gp2 (no obese control & obese patient)

DiastolicBloodPressure(DBP), HemoglobinA1c(HbA1c),Fasting total CHOLesterol(CHOL), High-DensityLipoprotein-Cholesterol(HDL), LowDensityLipoprotein-cholesterol(LDL), TriGlyceride(TG),

There are many spiritual connections and their relationship with each other To measure the efficacy of specific therapy in the management of diabetes mellitus, a precise assessment of blood glucose control is required. For more than 25 years.

Table (3-21) Pearson Correlation Gp1&Gp2 for FBS,Ca^{2+},CHOL.

CorrelationGp1&Gp2		Ca^{2+}	HbA1c	CHOL
FBS (mmol/l)	Pearson Corr.(r)	-.315*	.805**	.322*
	Sig. (2-tailed)	0.018	0.0001	0.016
	N	60	60	60

***. Correlation is significant at the 0.05 level (2-tailed).**

****. Correlation is significant at the 0.01 level (2-tailed).**

For more than 25 years, whole blood hemoglobin A1c (HbA1c) tests have been used frequently in diabetes patients to evaluate long-term glycemic control. The A1C test is a routine blood examination used to determine if a patient has type 1 or type 2 diabetes and to assess how well they are controlling their blood sugar levels. The A1C test is often referred to as the HbA1c test, hemoglobin A1C test, or glycated hemoglobin test. The diagnostic threshold for diagnosing diabetes is a HbA1c level of 6.5%, prediabetes individuals have HbA1 values of 5.7% to 6.4%(143).

Table (3-20) Many researchers have looked at the link between mean blood glucose levels and HbA1c levels, and various equations have been developed, Triglycerides were found to be a significant predictor of body fat in a linear regression study. BMI and body fat had a substantial negative connection with triglycerides. HDL cholesterol was shown to be favorably connected with body fat and negatively correlated with waist circumference. The total cholesterol/HDL ratio was shown to have a positive relationship with waist circumference and a negative relationship with body fat. There was also a substantial positive association between FBG and waist circumference. 34.2 percent of healthy people had pre-diabetes, and 13.6 percent had diabetes(144).

Obesity's proatherogenic effects are attributed to the dyslipidemia that comes with it. Low levels of high-density lipoprotein (HDL-C) cholesterol (HDL-C) and apolipoprotein A-I cholesterol (Apolipoprotein A-I) cholesterol (HDL-C). Obesity has a significant adverse relationship with HDL-C, apoA-I, and obesity, according to epidemiological research.

Higher total, dietary, and supplementary calcium intakes were substantially and inversely linked with the prevalence of metabolic syndrome in age- and calorie-adjusted analyses. After controlling for smoking, exercise, alcohol consumption, multivitamin use, and parental history of myocardial infarction before the age of 60 years, the odds of having

metabolic syndrome for increasing quintiles of total calcium intake were 1000-1200mg/daily(145).

To calculate daily intake, the average daily intakes of individual dairy items were added together: low-fat dairy products, such as skim or low-fat milk, sherbet, yogurt, and cottage/ricotta cheese; high-fat dairy foods, such as whole milk, cream, sour cream, ice cream, cream cheese, and other cheese; and total dairy products, which included everything. Skim, low-fat, and whole milk were included in the total milk.

Table (3-22) Pearson Correlation Gp1&Gp2 for CHOL,TG,LDL,HbA1c.

Correlation Gp1&Gp2		T.G	LDL	VLDL	HbA1c
CHOL (mmol/l)	Pearson Correlation	.274*	.933**	.284*	.273*
	Sig. (2-tailed)	0.041	0.0001	0.034	0.042
	N	60	60	60	60

***. Correlation is significant at the 0.05 level (2-tailed).**

****. Correlation is significant at the 0.01 level (2-tailed).**

When compared to other common lipid markers, our study reveals that lipid characteristics have a discordant relationship with blood glucose levels and that TG/HDL-C is a better predictor for evaluating insulin resistance and diabetes in the IRAG population(146). LDL cholesterol (LDL-C) is the major goal in the therapy of diabetic dyslipidemia, according to the latest lipid management recommendations ,Table (3-22).

However, blood lipid levels and the prevalence of dyslipidemia in diabetic patients differ significantly depending on the area, nationality, economic status, and healthcare level. Other aberrant lipid ingredient compositions, in addition to LDL-C, can increase the risk of cardiovascular disease and alter diabetes prognosis.

Other lipid metabolism markers, such as the combined lipid ratio, may provide a more accurate picture of the entire interaction between lipid and lipoprotein fractions. But, for the

time being, it's uncertain whether lipoprotein characteristics other than LDL-C can provide additional clinical information about diabetes-related insulin resistance or point to better glycemic control therapy targets. When compared to other common lipid markers,

our study reveals that lipid characteristics have a discordant relationship with blood glucose levels and that TG/HDL-C is a better predictor for evaluating insulin resistance and diabetes in the IRAG population. One of the features of insulin resistance and T2DM is dyslipidemia, notably high triglyceride (TG) and low HDL-C. Furthermore, specific lipid measurements obtained from a normal blood test have been linked to an increased risk of developing T2DM. This link is independent of recognized T2DM risk factors, implying that unique lipid profiles linked to a higher risk of T2DM could be markers of lipotoxicity or more severe cell dysfunction. The question is whether a lipid profile may be used to forecast the onset of T2DM.

Dyslipidemia is a hallmark of T2DM, and as such, analyses of lipid metabolic profiles in affected patients have the potential to permit the development of an integrated lipid metabolite-based biomarker model that can facilitate early patient diagnosis and treatment (147)and if so, how Despite the lack of physical contact between CHOL and the lipoprotein particles, serum CHOL levels are linked to large VLDL and small LDL particles.

A proatherogenic plasma lipoprotein profile may include higher CHOL. However, it appears unlikely that changes in circulating CHOL play a significant role in the diabetes predominance of large VLDL and small LDL, In diabetes, circulating cholesterol is important. Reduced HDL cholesterol, a prevalence of tiny dense LDL particles, and increased triglycerides are among the aberrant plasma lipid and lipoprotein patterns linked to type 2 diabetes(148).

In the pathogenesis of this dyslipidemia, increased hepatic production of big triglyceride-rich VLDL and poor clearance of VLDL appear to be of fundamental relevance.

Specific bigger VLDL precursors undergo intravascular processing to produce small dense LDL particles. Due to their higher vulnerability to oxidative alteration and increased absorption by the artery wall, small dense LDL particles are extremely atherogenic. Small LDL particles become formed with triglyceride levels more than 132 mg/dl, small LDL particles become common

Table (3-23) Pearson Correlation Gp1&Gp2 for TG, VLDL, GSH, HbA1C.

CorrelationGp1&Gp2		VLDL	GSH	HbA1C
T.G (mmol/l)	Pearson Correlation	.990**	.268*	.406**
	Sig. (2-tailed)	0.001	0.045	0.001
	N	60	60	60

***. Correlation is significant at the 0.05 level (2-tailed).**

****. Correlation is significant at the 0.01 level (2-tailed).**

Tables (3-6) (3-7) (3-8) (3-16) Large VLDL, total LDL, and small LDL were increased in T2DM subjects, Several methodological concerns in the current study must be considered. To avoid confounding due to the effects of insulin and lipid-lowering medicines on glucose and lipid metabolismIt has been shown that people with type 2 diabetes mellitus (T2DM) have higher levels of big VLDL, total LDL, and small LDL. When analyzing the findings of research examining the association between T2DM and lipid levels, it is crucial to take into account the potential confounding effects of insulin and cholesterol-lowering drugs on glucose and lipid metabolism. VLDL, LDL, and other lipoprotein levels can be affected by insulin and lipid-lowering medicines' effects on glucose and lipid metabolism. Therefore, while doing research in this field, it is crucial to thoroughly control for these aspects(149).

diabetic patients taking insulin and lipid-lowering drugs were not allowed to participate. As a result, T2DM is on the rise. Subjects with modest hyperglycemia and dyslipidemia were preferred, which could explain why.

Table (3-23) T.G -dysglycemia relationships are masked to some extent, which may lead to underestimation of T.G -dysglycemia associations. T.G. interacts with (apo)lipoproteins and subfractions of lipoproteins. the relationship between triglycerides (TG) and dysglycemia. TG is a type of fat found in the blood, and dysglycemia refers to abnormal blood sugar levels. Research has shown that there is an association between TG levels and the risk of prediabetes and diabetes1,We also didn't include people who were obese or had recently given birth. (apo)lipoproteins rate is compromised(150).

In women with type 2 diabetes, there is evidence to support a link between triglyceride (TG) levels and glycemic management. The risk of developing diabetes and prediabetes is known to rise with high blood triglyceride levels, according to a study published in The Journal of Clinical Endocrinology & Metabolism1. The study looked at the relationship between high triglyceride levels and insufficient glycemic control in people with type 2 diabetes who were using insulin. The findings demonstrated a substantial correlation between high triglyceride levels and insufficient glycemic control(151), indicating that lowering triglyceride levels may facilitate achieving more ideal glycemic control. This was done to reduce confounding when it came to circulating data. Because T.G. has an adverse connection with VLDL rate, it is associated with dyslipidemia disease. (apo)lipoproteins rate Obviously, the cross-sectional form of our study limits determining cause-and-effect relationships. LEAN of the right part of the trunk and TC/HDL ($R = -0.020$, $p < 0.001$) and LDL/HDL ($R = -0.72$, $p < 0.001$), and LEAN and RMR ($R = 0.44$, $p = 0.022$) of NWO women.

fore groups were evaluated 120 samples, 60 type 2 diabetes mellitus (T2DM) patients, and 60 healthy individuals as the control (NC). Fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), TG, TC, and fasting plasma insulin concentrations were measured and homeostasis was calculated. GSH & VIT-C were measured. HbA1c was positively associated with both measured and self-reported BMI.

Table (3-24) Pearson Correlation Gp1&Gc1 for Age, VIT-C, GSH.HbA1c.

CorrelationGp1&Gc1		VIT-C	GSH	HbA1c
Age(years)	Pearson Correlation	-.276*	-.382**	-.378**
	Sig. (2-tailed)	0.03	.003	0.002
	N	60	60	60

***. Correlation is significant at the 0.05 level (2-tailed).**

****. Correlation is significant at the 0.01 level (2-tailed).**

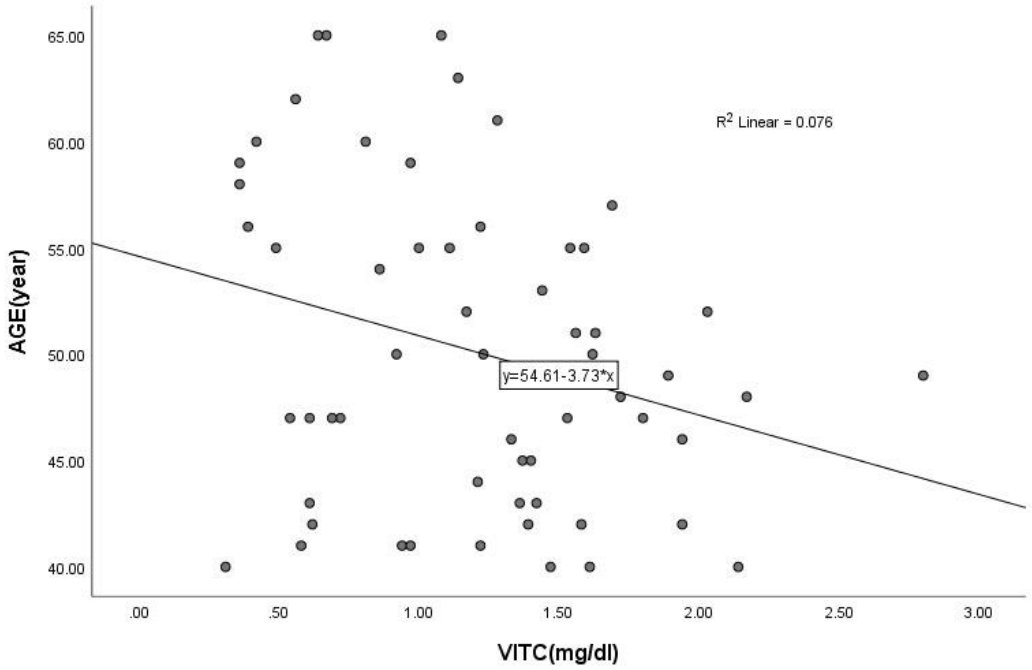
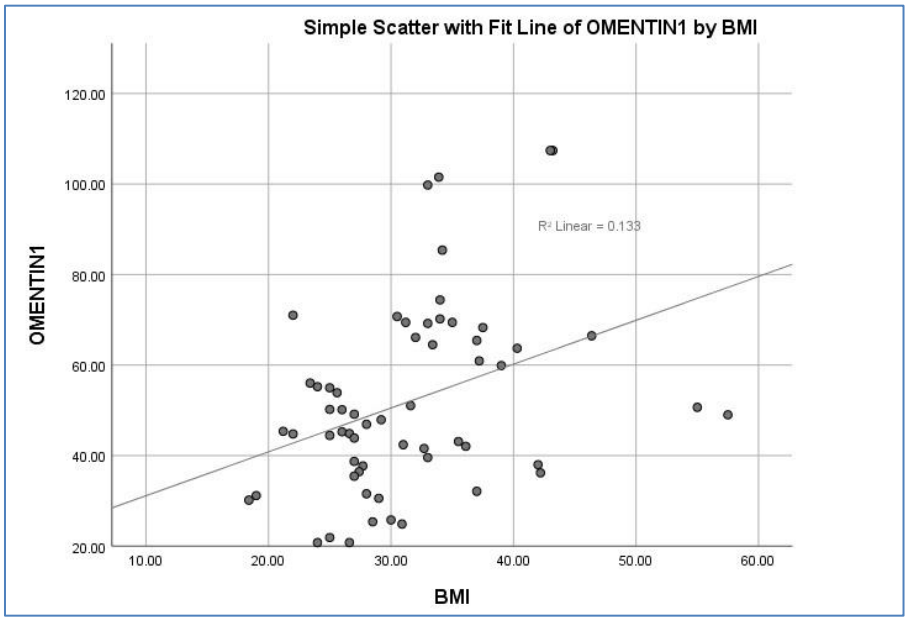


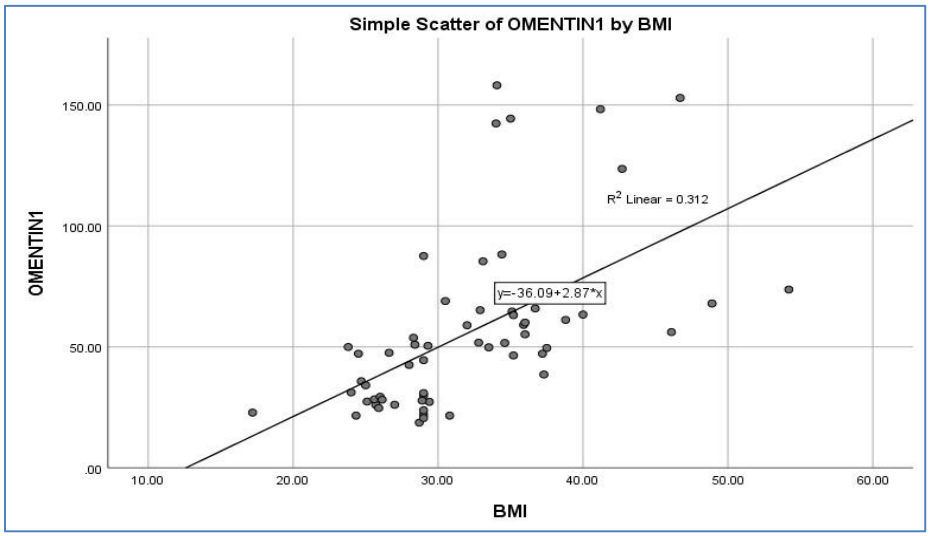
Figure (3-7) The Correlation between Vit.C levels for Groups (Gp1,Gc1)and Age(year).

In individuals with chronic diabetes, the antioxidant system is related to their age.(Table 3-25), Figure (3-8) vitamin C ($p<0.03$) R=-.276** It does, indeed. In contrast to circulating vitamin C concentrations, which were significantly lower in the middle and older age groups (p 0.001), vitamin C intake was similar in the younger (18-36), middle (37-58), and older (59-80+) age groups, according to a study by (Anitra C. Carr and Jens Lykkesfeldt)(152). Men should consume 90 mg per day of vitamin C and women should consume 75 mg per day of vitamin C, with a daily maximum of 2,000 mg, But for both men and women,

circulation vitamin C levels were lower in the middle-aged and older age group compared to the younger age group chronic diseases in the older age group (Tabel 3-13) (Tabel 3-16) (153).



Figure(3-8) The significant connection between BMI and serum Omentin-1 among may be seen in this scatter plot graph for Gc1, and Gc2.



Figure(3-9) The significant connection between BMI and serum Omentin-1 among type 2 diabetic patients may be seen in this scatter plot graph for Gp1, and Gp2.

The univariate correlations did not dier in diabetic and non-diabetic subjects.

The most notable outcome of this research is that serum omentin-1 levels increased considerably after the intervention BMI for Gc2=97.8± 22.59 & Gp2=94.2± 12.29(22)(23).

Table (3-18)Obesity and adult-onset diabetes or type 2 diabetes have been linked or leading effect factors to Hypertension, Hypertension has been connected to type 2 diabetes and obesity. A person with diabetes has a twofold increased risk of developing high blood pressure compared to someone without the disease(154). Obesity can result in intricate bodily adjustments that work together to either produce or exacerbate hypertension. According to an analysis from 2020, obesity causes 65 to 78 percent of main hypertension patients. High blood pressure can cause heart disease and stroke if it is not addressed. Compared to people without either of the illnesses, those with diabetes and high blood pressure are four times more likely to develop heart disease.

We still don't know the precise mechanisms by which obese type 2 diabetes patients and healthy obese women have higher omentin levels. Omentin-1 is a new adipokine that was very recently identified, thus there isn't much information regarding how it affects vascular health in type 2 diabetes(155).

Table (3-18)Obesity and type 2 diabetes have been related to hypertension. One of the main reasons of hypertension in these people was assumed to be the anti-natriuretic effects of insulin. According to clinical research, at least 80% of people with type 2 diabetes also have concomitant hypertension, whereas around 50% of hypertensive subjects also have comorbid hyperinsulinemia or glucose intolerance. Diabetes patients who also have hypertension have a much higher risk of getting cardiovascular disease(156).

In our investigation, we discovered a statistically significant difference in mean fasting glucose and HbA1C between diabetic obese womenGp2 and the control obese group (P-value 0.001). In both patients and controls, serum omentin-1 was found to be inversely

linked with both FBS, (P-value= 0.001) SBP(mmHg)DBP(mmHg)FBG (mmol/l)HbA1C(mmol/l)Total chol(mmol/l)HDL-C (mmol/l)LDL-C(mmol/l)T.G (mmol/l)vLDL-C (mmol/l)S.Omentin (ng/ml) .

Table (3-18) We found no significant connections between fasting glucose, HbA1C, and serum omentin-1 in cases but in controls, We found significant connections between fasting glucose when looking at the relationship between omentin-1 and glycemic management, It is interesting that we found no significant connections between fasting glucose, HbA1C, and serum omentin-1 in cases but found significant connections between fasting glucose and serum omentin-1 in controls. A systematic review and meta-analysis published in PLOS ONE found that lower concentration levels of omentin-1 were observed in patients with gestational diabetes mellitus or type 2 diabetes mellitus than in the controls1. Another study published in SpringerLink found that circulating maternal omentin-1 concentrations are inversely associated with serum glucose concentrations2. These findings suggest that there may be a relationship between omentin-1 and glycemic control, but more research is needed to fully understand this relationship(157).

We found no significant associations between serum omentin-1 and lipid profile as indicators of lipid metabolism when looking at the relationship between omentin-1 and fasting lipids(158).

According to several research, metformin therapy raises the amount of omentin-1 in the blood serum. According to one study, women with polycystic ovary syndrome showed a substantial rise in serum omentin-1 levels after receiving metformin therapy for 6 months. According to different research, metformin raises blood omentin-1 levels, which are indicative of improved insulin sensitivity and BMI(157)(159), Another confounding aspect is that we did not include therapy as one of the important variables, and statins and hypoglycemic medications may have influenced the results. This adipokine's homeostasis

can be influenced. More large-scale research is needed to determine the precise effect of omentin-1 on glucose homeostasis and related genes and receptors, which could be exploited as a targeted therapy for the prevention of obesity-related metabolic vascular problems in the future.

Signaling Mechanisms Involved in Omentin's Metabolic Activities Scientific data supports the significance of omentin in obesity and glucose metabolism regulation(119), as evidenced by the studies mentioned above. However, information on the systems involved is limited at this time. Omentin may play a role in appetite regulation, according to Brunetti et al (120).

Angiopoietin-like protein 4 (ANGPTL-4) influences energy balance and controls lipid metabolism.

In contrast, further studies on the metabolic effects of the administration of adipokines as a therapeutic drug are necessary. Administration of adipokines could trigger unexpected effects.

Conclusion

The conclusions of this study indicate that;

In type 2 diabetic obese insulin-resistant females, serum omentin-1 levels were shown to be significantly upper in obese T2DM. serum omentin-1 concentration is significantly and positively associated with Obesity, insulin resistance, and systolic blood pressure are all inversely associated with serum omentin-1 levels. Fasting glucose, HbA1C, fasting lipids, and serum omentin-1 levels have been reported to have no significant relationships.

According to our findings, circulating omentin-1 anomalies could be employed as a biomarker for obesity and related metabolic and vascular problems To summarize, we have demonstrated that there is a link between omentin-1 levels and the prevalence of obesity in a diabetic population and that omentin-1 levels are lower in diabetics non-obese T2DM. BMI has an impact on T2DM. According to our findings, patients with good to moderate blood glucose control are not completely effective in regulating their blood glucose, as seen by their Angptl-4 & omentin-1 levels, and the relationship between the FBS and omentin-1. Angptl-4 levels vary depending on blood glucose control.

Our findings support the idea that omentin-1 is a connection between obesity and insulin resistance since it is reversibly reduced in non-obese people with T2DM and increases in obese T2DM.

Adipose tissue associated with increment Angplt4 & omentin-1 in healthy females and decrease in non-obese patient females with T2DM

Recommendation

1. It is necessary to conduct many studies on the possible effects of the genetic factor on the level of omentin in obese women (is unclear and complex) due to conflicting results regarding the decrease and increase of omentin in obese subjects.
2. It is important to know the extent to which genetic factors control the ratio of each of these two biomolecular parameters (angiopoietin-like protein 4 and omentin-1).

3. We need Study analyze the correlation between the change in serum omentin-1 levels before and after metformin therapy analyzed the correlation between the change in serum omentin-1 levels before and after metformin therapy more research is needed to fully understand the relationship between metformin treatment and omentin-1 levels.
4. More research is needed to fully understand the complex interactions between calcium, insulin action, and metabolic health.

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APPENDIX

Table (3-1): Descriptive statistics, Correlations Gc1.

Tabel 3-1. Descriptive statistics, Correlations Gc1

			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	18	20	21	22
1	AGE	PCC																						
		p-value																						
2	WEIGHT	PCC	-0.28																					
		p-value	0.13																					
3	HEIGHT	PCC	-.43*	0.35																				
		p-value	0.02	0.06																				
4	BMI	PCC	0.09	0.32	-0.34																			
		p-value	0.64	0.08	0.06																			
5	WaistCirc	PCC	-0.07	0.35	-.39*	.83**																		
		p-value	0.69	0.05	0.03	0.00																		
6	HipCirc	PCC	-0.01	.37*	-.54**	.74**	.90**																	
		p-value	0.98	0.05	0.00	0.00	0.00																	
7	SBP	PCC	.57**	-0.08	-0.18	0.21	-0.10	-0.04																
		p-value	0.00	0.66	0.33	0.27	0.59	0.84																
8	DBP	PCC	0.29	-0.12	0.21	0.14	-0.28	-.38*	.60**															
		p-value	0.12	0.54	0.25	0.46	0.13	0.04	0.00															
9	DMED	PCC	0.02	-0.21	0.28	-0.34	-.46*	-.48**	0.09	0.34														
		p-value	0.92	0.27	0.13	0.07	0.01	0.01	0.64	0.06														
10	DDIS	PCC	0.02	-0.21	0.28	-0.34	-.46*	-.48**	0.09	0.34	1.00**													
		p-value	0.92	0.27	0.13	0.07	0.01	0.01	0.64	0.06	0.00													
11	FBS	PCC	0.34	0.21	0.05	0.26	0.01	-0.11	.57**	.63**	0.28	0.28												
		p-value	0.07	0.26	0.78	0.16	0.95	0.57	0.00	0.00	0.13	0.13												
12	HbA1c	PCC	-0.12	-0.16	0.12	0.21	0.10	-0.05	0.17	.46*	0.21	0.21	.49**											
		p-value	0.53	0.39	0.52	0.26	0.62	0.78	0.38	0.01	0.26	0.26	0.01											
13	Ca	PCC	-0.18	0.08	0.29	0.00	-0.22	-0.33	-0.14	0.08	0.13	0.13	0.15	-0.04										
		p-value	0.34	0.69	0.12	0.99	0.24	0.08	0.45	0.67	0.51	0.51	0.44	0.82										
14	CHOL	PCC	.42*	0.29	-0.34	.38*	0.23	0.26	.53**	.39*	0.01	0.01	.66**	0.06	-0.22									
		p-value	0.02	0.12	0.07	0.04	0.23	0.17	0.00	0.03	0.94	0.94	0.00	0.77	0.24									
15	T.G	PCC	.43*	0.18	-.43*	.64**	.46*	.42*	.39*	0.18	-0.11	-0.11	0.31	-0.05	-0.13	.69**								
		p-value	0.02	0.35	0.02	0.00	0.01	0.02	0.03	0.34	0.56	0.56	0.09	0.80	0.50	0.00								
16	HDL	PCC	-0.20	.48**	0.04	0.11	0.23	0.16	-0.03	-0.11	-0.07	-0.07	0.26	0.06	-0.26	.44*	0.34							
		p-value	0.28	0.01	0.84	0.58	0.22	0.41	0.86	0.57	0.72	0.72	0.17	0.77	0.16	0.02	0.07							
17	LDL	PCC	.50**	0.01	-0.33	0.34	0.09	0.14	.54**	.56**	0.12	0.12	.57**	0.19	-0.03	.63**	0.34	-0.29						
		p-value	0.00	0.96	0.08	0.07	0.63	0.47	0.00	0.00	0.54	0.54	0.00	0.31	0.89	0.00	0.07	0.13						
18	VLDL	PCC	.43*	0.18	-.43*	.64**	.46*	.42*	.39*	0.18	-0.11	-0.11	0.31	-0.05	-0.13	.69**	1.00**	0.34	0.34					
		p-value	0.02	0.35	0.02	0.00	0.01	0.02	0.03	0.34	0.56	0.56	0.09	0.80	0.50	0.00	0.00	0.07	0.07					
19	OMINT1	PCC	0.19	-.50**	0.00	-0.24	-0.31	-0.36	0.02	-0.12	0.04	0.04	-0.23	-0.15	0.34	-0.26	0.01	-0.22	-0.20	0.01				
		p-value	0.31	0.01	1.00	0.20	0.10	0.05	0.91	0.53	0.85	0.85	0.23	0.43	0.06	0.17	0.95	0.25	0.30	0.95				
20	ANGPTL4	PCC	0.33	0.16	0.14	0.26	0.03	-0.11	.58**	.56**	0.29	0.29	.75**	0.22	0.24	0.31	0.17	-0.02	.45*	0.17	-0.12			
		p-value	0.08	0.41	0.45	0.17	0.88	0.55	0.00	0.00	0.12	0.12	0.00	0.25	0.19	0.10	0.38	0.91	0.01	0.38	0.52			
21	VITC	PCC	0.16	-0.31	-0.34	-0.12	0.19	0.26	-.38*	-.67**	-0.33	-0.33	-.53**	-0.20	-0.25	-.40*	-0.11	-0.12	-.43*	-0.11	.36*	-.44*		
		p-value	0.41	0.10	0.06	0.54	0.31	0.16	0.04	0.00	0.08	0.08	0.00	0.28	0.19	0.03	0.55	0.54	0.02	0.55	0.05	0.02		
22	GSH	PCC	-0.08	-0.24	-0.34	0.28	.50**	.41*	-.49**	-.46*	-0.28	-0.28	-.42*	0.12	-0.07	-0.32	0.07	-0.08	-0.24	0.07	0.22	-.40*	.69**	
		p-value	0.66	0.19	0.07	0.14	0.01	0.02	0.01	0.01	0.13	0.13	0.02	0.53	0.72	0.08	0.72	0.67	0.21	0.72	0.25	0.03	0.00	

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

PCC, PearsonCorrelationCofficient; WaistCirc, WaistCircumference; Hipcirc, HipCircumference; DMED, DurationOfMEDication; DDIS; DurationOfDisease

Table (3-2): Descriptive statistics, Correlations Gc2.

Tabel 3-2. Descriptive statistics, Correlations Gc2																							
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1	AGE	PCC																						
		p-value																						
2	WEIGHT	PCC	-0.20																					
		p-value	0.29																					
3	HEIGHT	PCC	-0.19	.69**																				
		p-value	0.33	0.00																				
4	BMI	PCC	-0.19	.95**	.46*																			
		p-value	0.32	0.00	0.01																			
5	WaistCirc	PCC	-0.09	.78**	0.22	.89**																		
		p-value	0.63	0.00	0.24	0.00																		
6	HipCirc	PCC	-0.12	.81**	0.24	.91**	.99**																	
		p-value	0.52	0.00	0.20	0.00	0.00																	
7	SBP	PCC	0.28	.67**	0.18	.75**	.78**	.78**																
		p-value	0.14	0.00	0.33	0.00	0.00	0.00																
8	DBP	PCC	0.24	.44*	-0.03	.54**	.54**	.54**	.72**															
		p-value	0.21	0.01	0.86	0.00	0.00	0.00	0.00															
9	DMED	PCC	.48**	0.15	-0.18	0.25	0.26	0.24	0.29	0.25														
		p-value	0.01	0.44	0.35	0.18	0.16	0.19	0.12	0.18														
10	DDIS	PCC	.45*	0.27	-0.10	0.36	0.35	0.33	.36*	0.32	.98**													
		p-value	0.01	0.15	0.58	0.05	0.06	0.07	0.05	0.09	0.00													
11	FBS	PCC	-0.04	0.07	0.16	0.04	0.13	0.11	-0.05	-0.25	-0.08	-0.09												
		p-value	0.84	0.73	0.41	0.83	0.51	0.57	0.77	0.18	0.67	0.63												
12	HbA1c	PCC	0.00	.40*	-0.07	.51**	.58**	.59**	0.33	0.31	0.23	0.27	0.09											
		p-value	0.98	0.03	0.72	0.00	0.00	0.00	0.07	0.10	0.22	0.15	0.63											
13	Ca	PCC	0.08	-0.15	-0.11	-0.19	-0.26	-0.23	-0.18	0.25	-0.23	-0.21	0.26	0.01										
		p-value	0.67	0.43	0.56	0.32	0.17	0.21	0.33	0.18	0.22	0.27	0.16	0.94										
14	CHOL	PCC	-0.19	0.12	0.07	0.11	0.15	0.17	0.13	-.40*	-0.04	0.00	0.22	0.07	-0.28									
		p-value	0.32	0.54	0.72	0.57	0.42	0.38	0.51	0.03	0.84	1.00	0.25	0.73	0.14									
15	T.G	PCC	0.31	-0.09	-.39*	0.04	0.15	0.12	0.27	0.25	0.15	0.14	0.10	0.29	0.27	0.08								
		p-value	0.09	0.63	0.03	0.84	0.44	0.53	0.15	0.18	0.43	0.46	0.61	0.12	0.15	0.68								
16	HDL	PCC	-0.06	-0.07	0.13	-0.13	-0.25	-0.26	-0.24	-0.10	0.08	0.06	-0.06	-.53**	-0.19	-0.20	-.48**							
		p-value	0.73	0.70	0.49	0.50	0.17	0.16	0.20	0.60	0.68	0.77	0.76	0.00	0.32	0.29	0.01							
17	LDL	PCC	-0.22	0.13	0.11	0.11	0.17	0.19	0.13	-.39*	-0.12	-0.08	0.15	0.13	-0.29	.96**	0.04	-.38*						
		p-value	0.24	0.50	0.58	0.57	0.38	0.32	0.48	0.03	0.54	0.66	0.44	0.49	0.12	0.00	0.84	0.04						
18	VLDL	PCC	0.31	-0.09	-.39*	0.04	0.15	0.12	0.27	0.25	0.15	0.14	0.10	0.29	0.27	0.08	1.00**	-.48**	0.04					
		p-value	0.09	0.63	0.03	0.84	0.44	0.53	0.15	0.18	0.43	0.46	0.61	0.12	0.15	0.68	0.00	0.01	0.84					
19	OMINT1	PCC	-0.24	-0.08	-0.01	-0.08	0.02	-0.02	-0.20	-0.33	-0.07	-0.09	.43*	-0.10	-0.15	0.01	-0.28	0.32	-0.06	-0.28				
		p-value	0.21	0.69	0.94	0.68	0.91	0.93	0.28	0.07	0.73	0.63	0.02	0.60	0.42	0.96	0.13	0.08	0.75	0.13				
20	ANGPTL4	PCC	-0.05	-0.01	0.22	-0.07	-0.01	-0.02	-0.21	-.47**	-0.07	-0.10	.87**	-0.06	0.09	0.28	-0.20	0.23	0.19	-0.20	.54**			
		p-value	0.78	0.98	0.25	0.71	0.97	0.93	0.27	0.01	0.70	0.60	0.00	0.74	0.62	0.13	0.29	0.23	0.31	0.29	0.00			
21	VITC	PCC	-0.11	-0.21	-0.11	-0.24	-0.27	-0.28	-0.07	0.08	-0.09	-0.07	-0.20	-.42*	0.24	0.05	-0.25	0.12	0.08	-0.25	0.06	-0.15		
		p-value	0.55	0.27	0.56	0.20	0.15	0.13	0.71	0.67	0.65	0.72	0.30	0.02	0.21	0.79	0.19	0.53	0.66	0.19	0.74	0.42		
22	GSH	PCC	-0.01	-.42*	-0.11	-.46*	-.43*	-.45*	-.46*	-0.21	-0.15	-0.19	0.08	-0.32	0.19	-0.18	-0.25	.51**	-0.24	-0.25	0.31	0.28	.45*	
		p-value	0.96	0.02	0.58	0.01	0.02	0.01	0.01	0.26	0.44	0.31	0.66	0.08	0.32	0.35	0.18	0.00	0.21	0.18	0.10	0.14	0.01	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table (3-3): Descriptive statistics, Correlations Gp1.

Tabel 3-3. Descriptive statistics, Correlations Gp1

			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1	AGE	PCC																						
		p-value																						
2	WEIGHT	PCC	0.03																					
		p-value	0.86																					
3	HEIGHT	PCC	0.09	.73**																				
		p-value	0.63	0.00																				
4	BMI	PCC	-0.04	.82**	0.23																			
		p-value	0.82	0.00	0.23																			
5	WaistCirc	PCC	0.11	.62**	0.10	.82**																		
		p-value	0.56	0.00	0.61	0.00																		
6	HipCirc	PCC	0.10	.38*	0.23	.39*	.50**																	
		p-value	0.61	0.04	0.23	0.03	0.00																	
7	SBP	PCC	0.00	.63**	0.24	.74**	.70**	.47**																
		p-value	0.99	0.00	0.21	0.00	0.00	0.01																
8	DBP	PCC	-0.03	.58**	0.28	.64**	.65**	.58**	.86**															
		p-value	0.89	0.00	0.14	0.00	0.00	0.00	0.00															
9	DMED	PCC	0.05	0.09	-0.11	0.25	0.13	-0.11	0.07	0.08														
		p-value	0.81	0.65	0.57	0.19	0.48	0.55	0.70	0.68														
10	DDIS	PCC	0.05	0.09	-0.11	0.25	0.13	-0.11	0.07	0.08	1.00**													
		p-value	0.81	0.65	0.57	0.19	0.48	0.55	0.70	0.68	0.00													
11	FBS	PCC	0.03	-0.17	-0.11	-0.14	0.13	0.02	-0.24	-0.16	-0.30	-0.30												
		p-value	0.86	0.36	0.56	0.45	0.48	0.92	0.20	0.41	0.10	0.10												
12	HbA1c	PCC	0.14	-0.33	-0.25	-0.20	0.03	0.07	-0.29	-0.16	-0.08	-0.08	.79**											
		p-value	0.47	0.07	0.19	0.30	0.89	0.70	0.12	0.40	0.66	0.66	0.00											
13	Ca	PCC	0.26	-0.07	0.09	-0.21	-.47**	-0.25	-0.25	-0.30	-0.08	-0.08	-.45*	-0.36										
		p-value	0.17	0.72	0.62	0.27	0.01	0.19	0.18	0.11	0.68	0.68	0.01	0.05										
14	CHOL	PCC	0.17	0.05	0.06	-0.05	-0.14	-0.24	-0.07	-0.17	-0.31	-0.31	0.29	0.20	0.13									
		p-value	0.38	0.79	0.74	0.81	0.46	0.20	0.71	0.36	0.09	0.09	0.12	0.28	0.49									
15	T.G	PCC	0.23	0.21	-0.02	0.31	.49**	0.24	0.32	0.35	-0.07	-0.07	.37*	0.21	-0.24	0.34								
		p-value	0.23	0.26	0.92	0.09	0.01	0.19	0.08	0.06	0.70	0.70	0.04	0.27	0.21	0.07								
16	HDL	PCC	-0.12	0.07	0.07	0.01	0.05	-0.15	-0.01	0.07	0.02	0.02	0.01	-0.02	0.04	0.16	0.16							
		p-value	0.53	0.73	0.69	0.95	0.78	0.42	0.98	0.70	0.90	0.90	0.96	0.91	0.82	0.39	0.39							
17	LDL	PCC	0.14	-0.04	0.03	-0.13	-0.29	-0.27	-0.16	-0.29	-0.32	-0.32	0.22	0.20	0.17	.91**	0.05	-0.18						
		p-value	0.45	0.84	0.85	0.48	0.12	0.16	0.41	0.11	0.09	0.09	0.23	0.28	0.36	0.00	0.79	0.35						
18	VLDL	PCC	0.23	0.21	-0.02	0.31	.49**	0.24	0.32	0.35	-0.07	-0.07	.37*	0.21	-0.24	0.34	1.00**	0.16	0.05					
		p-value	0.23	0.26	0.92	0.09	0.01	0.19	0.08	0.06	0.70	0.70	0.04	0.27	0.21	0.07	0.00	0.39	0.79					
19	OMINT1	PCC	0.30	-0.04	-0.21	0.13	0.01	-0.08	-0.09	0.02	.36*	.36*	-0.12	0.08	0.00	-0.11	-0.16	0.01	-0.08	-0.16				
		p-value	0.10	0.85	0.26	0.50	0.98	0.69	0.64	0.93	0.05	0.05	0.52	0.66	0.99	0.55	0.40	0.97	0.68	0.40				
20	ANGPTL4	PCC	-0.04	-0.12	-0.18	-0.04	-0.04	-0.08	-0.23	-.42*	-0.33	-0.33	-0.08	-0.11	0.08	-0.07	-0.26	-0.04	0.01	-0.26	-0.11			
		p-value	0.85	0.53	0.35	0.83	0.85	0.67	0.22	0.02	0.07	0.07	0.66	0.58	0.66	0.72	0.17	0.85	0.97	0.17	0.55			
21	VITC	PCC	-0.28	-0.27	-.38*	0.02	0.11	0.05	0.07	0.15	0.30	0.30	0.00	0.05	-.38*	-.64**	-0.05	-0.01	-.64**	-0.05	0.16	0.07		
		p-value	0.13	0.14	0.04	0.92	0.58	0.78	0.72	0.42	0.11	0.11	0.99	0.80	0.04	0.00	0.80	0.95	0.00	0.80	0.39	0.70		
22	GSH	PCC	-0.18	0.08	0.19	-0.07	-0.18	-0.15	0.03	-0.02	0.10	0.10	-.49**	-.61**	0.11	-0.27	-0.32	0.00	-0.21	-0.32	0.10	0.24	0.14	
		p-value	0.35	0.67	0.31	0.72	0.34	0.43	0.87	0.92	0.61	0.61	0.01	0.00	0.56	0.16	0.08	1.00	0.27	0.08	0.59	0.20	0.47	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table (3-4): Descriptive statistics, Correlations Gp2.

Tabel 3-4. Descriptive statistics, Correlations Gp2

			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1	AGE	PCC																						
		p-value																						
2	WEIGHT	PCC	-0.08																					
		p-value	0.66																					
3	HEIGHT	PCC	-0.16	0.11																				
		p-value	0.41	0.56																				
4	BMI	PCC	0.01	.86**	-.41*																			
		p-value	0.95	0.00	0.02																			
5	WaistCirc	PCC	-0.05	.60**	-.65**	.88**																		
		p-value	0.80	0.00	0.00	0.00																		
6	HipCirc	PCC	-0.02	.60**	-.63**	.88**	.98**																	
		p-value	0.91	0.00	0.00	0.00	0.00																	
7	SBP	PCC	-0.13	0.32	0.10	0.24	0.32	.37*																
		p-value	0.51	0.08	0.62	0.20	0.09	0.04																
8	DBP	PCC	0.20	0.12	0.13	0.04	0.06	0.11	.64**															
		p-value	0.28	0.51	0.50	0.84	0.74	0.57	0.00															
9	DMED	PCC	0.02	0.13	-0.10	0.16	0.18	0.20	.37*	.41*														
		p-value	0.91	0.51	0.60	0.39	0.33	0.29	0.05	0.03														
10	DDIS	PCC	0.02	0.13	-0.10	0.16	0.18	0.20	.37*	.41*	1.00**													
		p-value	0.91	0.51	0.60	0.39	0.33	0.29	0.05	0.03	0.00													
11	FBS	PCC	-0.27	0.11	0.35	-0.08	-0.20	-0.23	0.22	-0.03	0.16	0.16												
		p-value	0.14	0.56	0.06	0.69	0.29	0.22	0.24	0.87	0.39	0.39												
12	HbA1c	PCC	-0.28	0.15	0.07	0.10	0.03	0.01	0.22	0.16	0.08	0.08	.67**											
		p-value	0.13	0.44	0.71	0.61	0.86	0.97	0.23	0.41	0.67	0.67	0.00											
13	Ca	PCC	.45*	0.22	0.21	0.09	-0.02	0.05	0.27	0.29	0.05	0.05	-0.14	-0.04										
		p-value	0.01	0.23	0.27	0.63	0.92	0.79	0.15	0.11	0.77	0.77	0.46	0.85										
14	CHOL	PCC	0.06	-0.23	0.17	-0.31	-0.34	-0.32	-0.10	0.00	0.30	0.30	0.24	0.17	0.13									
		p-value	0.74	0.22	0.37	0.10	0.06	0.08	0.60	0.99	0.11	0.11	0.20	0.37	0.48									
15	T.G	PCC	0.10	0.01	0.17	-0.08	-0.09	-0.07	-0.12	-0.13	0.13	0.13	0.08	-0.07	0.12	0.23								
		p-value	0.62	0.95	0.37	0.68	0.65	0.72	0.53	0.48	0.48	0.48	0.68	0.72	0.52	0.22								
16	HDL	PCC	-0.06	-0.19	-0.04	-0.16	-0.08	-0.09	0.10	0.08	-0.13	-0.13	-0.17	-0.12	-0.13	0.08	-0.15							
		p-value	0.74	0.33	0.85	0.39	0.67	0.62	0.60	0.66	0.50	0.50	0.37	0.53	0.51	0.66	0.42							
17	LDL	PCC	0.06	-0.21	0.13	-0.27	-0.31	-0.29	-0.08	0.03	0.30	0.30	0.25	0.22	0.14	.95**	-0.03	-0.08						
		p-value	0.77	0.27	0.48	0.15	0.09	0.11	0.67	0.85	0.11	0.11	0.18	0.24	0.47	0.00	0.88	0.69						
18	VLDL	PCC	0.08	0.01	0.17	-0.08	-0.08	-0.07	-0.12	-0.13	0.15	0.15	0.08	-0.07	0.12	0.24	1.00**	-0.16	-0.02					
		p-value	0.68	0.95	0.37	0.67	0.66	0.72	0.54	0.49	0.44	0.44	0.68	0.72	0.52	0.21	0.00	0.39	0.93					
19	OMINT1	PCC	0.34	0.09	-0.07	0.15	0.05	0.06	-0.07	0.11	-0.19	-0.19	-0.12	0.14	0.12	-0.20	0.00	-0.07	-0.18	-0.01				
		p-value	0.07	0.63	0.70	0.44	0.79	0.74	0.73	0.58	0.32	0.32	0.53	0.45	0.54	0.30	0.98	0.72	0.34	0.95				
20	ANGPTL4	PCC	-.41*	0.23	.45*	-0.02	-0.20	-0.19	0.31	-0.03	0.12	0.12	.78**	.63**	-0.02	.43*	0.16	-0.04	.40*	0.16	-0.15			
		p-value	0.03	0.22	0.01	0.92	0.30	0.32	0.10	0.89	0.52	0.52	0.00	0.00	0.91	0.02	0.40	0.84	0.03	0.41	0.43			
21	VTC	PCC	0.04	-.48**	-0.28	-0.32	-0.15	-0.22	-0.33	0.03	0.16	0.16	-0.16	0.04	0.05	0.15	0.09	-0.15	0.16	0.10	-0.20	-0.26		
		p-value	0.85	0.01	0.13	0.08	0.41	0.25	0.07	0.89	0.39	0.39	0.40	0.85	0.79	0.44	0.65	0.44	0.40	0.58	0.29	0.16		
22	GSH	PCC	-0.25	-0.06	0.18	-0.14	-0.11	-0.16	0.06	-0.26	0.04	0.04	.61**	0.11	-.41*	-0.06	0.31	-0.06	-0.15	0.31	-0.15	0.33	-0.14	
		p-value	0.18	0.75	0.35	0.46	0.56	0.38	0.76	0.17	0.82	0.82	0.00	0.58	0.02	0.77	0.10	0.73	0.44	0.09	0.44	0.07	0.46	

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

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Acceptance of article for publication in Medical Journal of Babylon

Dear Dr.

Date: 11-06-2023

Amjed H. Ali* and Lamia AM. Almashhedy

I am pleased to inform you that your manuscript (**MJBL_439_23**) titled as:

Associated Between Serum Omentin-1 and Risk Factors of Obesity in Diabetes Mellitus (T2DM) Females

has been accepted for publication in Medical Journal of Babylon.

We have received the payment for publication. So, you will receive the galley proof within 4-5 weeks. You must have to solve the query if we point out any in the galley proof.

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Best Regards

Prof. Mufeed J. Ewadh
Editor-in-Chief-MJBL

Corresponding author: Amjed Ali, Chemistry, College of Science, University of Babylon, Hilla, Iraq. Email: amjed.hayder@student.uobabylon.edu.iq

الخلاصة

تمهيد: ان معدلات انتشار السمنة المفرطة وكذلك مرض السكري النوع الثاني ازدادت كثيرا واصبح ذلك كوباء يوثر على المجتمعات واقتصادها ومنها المجتمع العراقي وتعتبر السمنة أحد عوامل الخطر الشائعة التي يمكن أن تؤدي إلى الإصابة بمقدمات مرض السكري وبالخصوص مرض السكري من النوع الثاني. الآليات التي تربط السمنة ومرض السكري من النوع الثاني معقدة ولا تزال غير مفهومة، ولكن من المحتمل أن تنطوي على مزيج من إطلاق الأنسجة الدهنية للأحماض الدهنية الزائدة المنتشرة والجلسرين والهرمونات والسيتوكينات المسببة للالتهابات. تعمل هذه العوامل على إضعاف إشارات الأنسولين الخلوي وزيادة مقاومة الأنسولين. يمكن أن تؤدي مستويات الدهون المرتفعة بشكل مزمن أيضًا إلى ضعف وظيفة خلايا بيتا في البنكرياس وانخفاض مستويات إنتاج الأنسولين.هناك العديد من البروتينات التي تشارك في عملية تكوين الأوعية الدموية ومنها الانجيوبيوتين -4وهو بروتين ينظم تقسيم الدهون عن طريق تثبيط الدورة الدموية والأنسجة.يتم تصنيع البروتين أومينتين-١ بواسطة الأنسجة الدهنية. وقد تم اكتشاف أنه يرتبط بشكل كبير بكل من مرض السكري من النوع ٢ والسمنة. يُظهر جين omentin-1 تعبيرًا متناقصًا لدى الأشخاص الذين يعانون من السمنة المفرطةوبعض الدراسات تشير الى زيادة النسبة عند تعاطي العقارات المضادة لداء السكري النوع الثاني وبالاخص عقار الميتفورمين. يتأثر تطور مرض السكري من النوع ٢ بشكل كبير بمقاومة الأنسولين، والتي ترتبط أيضًا بهذا البروتين.

الأهداف:تهدف هذه الدراسة الى تقييم تأثير السمنة على انجيوبوتين-شبيه بروتين-٤ ومستويات الاومنتين-١ كدليل على داء السكري (النوع الثاني)في الاناث وكان من المثير للاهتمام التساؤل عما إذا كانت مستوياتهما قد تلعب أيضا دورا في تنظيم الجلوكوز وحساسية الانسولين,امراض القلب والاوعية الدموية واثار السمنة عليها . وهل تلعب أيضًا دورًا في تنظيم توازن الكوليستيرول والدهون عالية ومنخفضة الكثافة والدهون الثلاثيةوكذلك تأثيرها على نسبة مضادات الاكسدة في الجسم.

طرق العمل: تتكون الدراسة من ١٢٠ متطوعًا (٦٠ مريضًا و ٦٠ مجوعة سيطرة) وكل ستين شخص يتم توزيعهم لمجموعتين من ثلاثين شخص لذلك تم تقسيمهم إلى أربع مجموعات ، Gp1 هم مجموعة المصابين بالسكري(النوع ٢) ولكن غير مصابين بالسمنة اما المجموعة الثانية Gp2 فهم من المصابين بالسكري والسمنة ايضا وتم توزيع مجموعة السيطرة الاصحاء الغير مصابين بالسكري الى مجموعتين مجموعة Gc1 وهم الاصحاء الغير مصابين بالسمنة اما المجموعةGc2 فهم مجموعة السيطرة الاصحاء المصابين بالسمنةوكل مجموعة ايضا متكونة من ٣٠ متطوعة للدراسة

قمت بقياس المؤشرات الحيوية السريرية في الدم والمقاييس الجسمية الانثروبومترية. بما في ذلك العمر والجنس ومحيط الورك ومحيط الخصر والقياسات الأساسية للطول والوزن ومؤشر كتلة الجسمBMI، الخصائص الديموغرافية،البيئة الحضرية أو الريفية، والعلامات الحيوية لضغط الدم(ضغط الدم الانقباضي SBPوالانبساطي DBP) وكذلك المقاييس الكيميائية الحيوية في الدم (الاومنتين-١ ، الانجيبوبويتين-٤، ونسبة السكر في الدم أثناء الصيام FBS، والتراكمي HbA1c، الكالسيوم في المصل، ومستويات مضادات الأكسدة مثل الجلوتاثيون المختزل GSH وفيتامين سي Vit-C، فحوصات الدهون (HDL، LDL، VLDL، T.G، T.Cholesterol).

النتيجة: هناك اختلافات كبيرة بين كل من omentin-1 و Angplt-4والأفراد الذين تمت دراستهم (P = 0.011و0.0001 = P، على التوالي). كلا المستويين من omentin-1 ويرتبطان بشكل كبير بمؤشر HbA1cأعلى (P = 0.030 وP = 0.046، على التوالي). ومع ذلك، كان الأومينتين-١ مرتبطًا فقط بالأفراد الذين يعانون من زيادة الوزن/السمنة. بالإضافة إلى ذلك، ارتبط كل من omentin-1 و ANGPLT-4بشكل إيجابي كبير بالتاريخ العائلي لمرض السكري (P = 0.046 وP = 0.024، على التوالي). الاستنتاجات :Omentin-1 و.ANGPLT-4

أشارت تقديرات البيانات البيوكيميائية إلى وجود فروق معنوية في الأومينتين-١ (٠،٠٠٠١) بين (Gp1, (0.09) (Gp2بين (Gp1,Gc1) و (٠،٠٠٠١) بين HbA1c (Gp2, Gc1) بين) (Gp1, Gc2) (0.083)بينGp2) ، (Gc2، (0.0001) ANGPTL4بينGc2) ، (Gp2، (0.001)بينGp1) ، (Gc2، (0.0001)بينGp2) ، (Gc1، (0.002) HDLبينGc1) ، (0.000) (Gp2بينGc1) ،(Gc2، LDL (0.217)بينGc2) ، (Gp2، الكالسيوم في مصل الدم (0.01) بين (Gp1 Gc1) ، و (0.003) بين (Gp2 Gc2)، و (0.05) بين(Gp1 Gc2) ، أما الGSH الجلوتاثيون المختزل في مصل الدم GSH (0.0001) بين Gp1Gc1 و (0.0001 بينGp2 Gc2) ، (Gc2وGp2) (0،0001) ، وفي مستوى سكر الدم الصائم FBS(0.0001) بين(Gp1Gc1) ، (0.0001)بينGp1) ، (0.001) (Gc2بينGp2) ، (0.001) (Gc1بينGp2) ، (Gc2، (0.001) GSHبين (Gc1) ، (0.000) (Gp2بينGc2) ، T.cholsterol نسبة الكوليسترول الكلي (0.022) بين(Gc1 Gp1) ، LDLالدهون منخفض الكثافة بين(Gp2 Gc2) (0.217)، (0.0004) (Gc1وGp1) ، (0.004)بين (Gp2- Gp1)

(0.0001) VIT-Cبين (0.003) (Gp1,Gc1) بين (0.001) (Gp2,Gc2) بين (Gp2,Gc1) (0.0001)بين (Gp1,Gc2) ، (0.006) VLDLبين ((Gp1,Gc1) ، (0.004)بين (Gp1,Gc2) (0.0001)بين (0.002) (Gp2,Gc1) بين (Gp2,Gc2) في المرضى الذين يعانون من السكري النوع ٢ مع وبدون السمنة بالمقارنة مع مجموعة السيطرة. التوزيع الاحصائي بين (Gc1> Gp1) ANGPTL-4 و (Gp2> Gc2) omentin-1في جميع مجاميع المرضى وكذلك Gc1> Gp1 بين مجموعة السيطرة Gc1 ومجموعة المرضى Gp1

أظهرت النتائج وجود فروق معنوية في تركيز فيتامين C حيث كان هناك انخفاض معنوي ($p<0.05$) في المجموعة[Gp1 (0.9+0.4) Gp2 (0.7+0.6)]

لم يلاحظ أي فروق ذات دلالة إحصائية بالنسبة لـ Angptl-4 معDBP ، Ca^{2+}

الاستنتاج: ان مريض السكري من النوع الثاني المرتبط بنمط زيادة النشاط و قلة الحركة والنظام الغذائي عالي السكرات الحرارية قد يغير استقلاب الأنسولين ويلعب دورا هاما في تطور مرض السكري من النوع الثاني الناتج عن نشاط مقاومة الأنسولين. ارتبط اعتلال الكلية السكري عند المجموعتينGp1,Gp2 بزيادة مستويات أنواع الأكسجين التفاعلية وانخفاض إجمالي مستويات مضادات الأكسدة Vit-c وكذلك GSH، والتي ارتبطت أحصائيا بزيادة تركيزات الأومينتين-١، وقد يكون هذا تشخيصًا جيدًا لمرض السكري ومرض السكري من النوع ٢. هناك حاجة إلى مزيد من البحث لتأكيد هذه النظرية وتحديد مدى أهمية تركيزات الأومينتين-١ في مرض السكري من النوع الثاني. وارتباطها بأنخفاض VIT-C والجلوتاثيون.

جمهوريـــة العـــــــراق
وزارة التعليم العالي والبحث العلمي
جامعة بابل
كلية العلوم/ قسم الكيمياء

تأثير السمنة على انجيوبويتين-شبيه بروتين-٤ ومستويات الاومنتين-١ كدليل على داء السكري (النوع الثاني) في الاناث

رسالة مقدمة
إلى مجلس كلية العلوم/ جامعة بابل
كجزء من متطلبات نيل شهادة الماجستير في العلوم/ الكيمياء

من قبل
امجد حسين علي حيدر الكمالي
بكالوريوس علوم كيمياء / الجامعة المستنصرية
٢٠٠٧

بإشراف
الأستاذ الدكتور لمياء عبدالمجيد المشهدي
كلية العلوم / جامعة بابل

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