University of Kerbala

College of Education for pure sciences

Department of Chemistry

The role of inflammatory markers in hypertensive patients in holy Karbala city

A Thesis

submitted to the Council of the College of Education for Pure Sciences / University of Kerbala as part of the requirements for obtaining a

Master's Degree in Chemistry Sciences

written by

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2024 A.D **1446 A.H**

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Dedication

To… the All-Powerful Allah, who would grant me everything I ask for and enhance my benefits if I thank him.

To...Muhammad (PBUH), the prophet of kindness, the light of the worlds, the owner of Israa and Miraj, the commander of the messengers.

To… my father, the generous person who built kingdoms of trust in my heart, who painted the features of happiness on my face free of charge

For my mother, the great human being, the true treasure is a paradise that God created for me.

To …my lovely sisters and brothers for their assistance when I need it

To… my husband for his love, support, and encouragement; to everyone who has helped me, even with a smile.

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Finally, I would like to express my thanks, gratitude and love to my friends for their support and assistance.

Thanks for all…

Rasha abass

Abstract

Hypertensive is a common disease that can be dangerous if it is left untreated. Also, many factors can cause high blood pressure, including high fat content, high fats can contribute to hardening of the arteries or thickening of the artery walls; which increases the risk of atherosclerosis, stroke, heart attack, and heart disease. There is a strong relationship between high blood pressure and kidney weakness, this is because uncontrolled hypertensive is a major cause of chronic kidney disease. Chronic kidney disease (CKD) is a major cause of hypertensive, and high urea and creatinine are the most important factors that increase the rate of high blood pressure. Hypertensive significantly increases the risk of cardiovascular disease, kidney failure, and stroke. Hypertensive can be caused by several factors such as excessive salt or alcohol consumption, stress, age, and genetics, family history, obesity, and physical condition.

This study was designed to evaluate the levels of some inflammatory markers which are heat shock protein- 70 (HSP-70), human tumor necrosis factor alpha (TNF-α), high sensitivity C reactive protein (HS CRP), in addition lipid profile, urea and creatinine in hypertension patients. The study included 50 patients suffering from hypertensive and 40 individuals from the healthy control group. Those patients consist of 28 males and 22 females, with ages ranging from 40 to 70 years, they were compared with the healthy group. The parameters were measured in these groups are cholesterol, triglycerides, LDL, HDL, VLDL, urea, creatinine, HSP-70, TNF-α and HS CRP. The result analyzed in significant difference p value ≤ 0.0001 when a comparison was done between the data of patients of high blood pressure and the group of healthy people. It is noticed that the results were higher than the normal limit of cholesterol, triglycerides, LDL, HDL, VLDL, urea and creatinine, Hsp-70, CR-protein in patients with high blood pressure, while the results showed a no significant difference of TNF- α in hypertension patients. In addition, it showed the effect of gender on the levels of parameters by the difference between groups of males and females. That was a significant difference p value = 0.02 in triglycerides, p value = 0.03 with VLDL, p value = 0.01 of LDL and cholesterol No Significant difference with HDL compared to patients of hypertension and patients of hypertension with other diseases, In addition, it was shown that there was no significant difference in TNF-alpha and HS CRP and HSP-70 between patients with high blood pressure only and

patients with other diseases, also it was a significant difference p value = 0.05 in the percentage of urea and p value = 0.04 in creatinine in patients hypertension with other diseases when compared with group of patients of hypertension only. The results of effect of age showed that there was no significant difference in the percentage of cholesterol, triglycerides, HDL, LDL, VLDL in the group of age between 40-55 years but in age 56-70 years , Additionally, it showed there was no significant difference P- value $\leq$ 0.0001 in HSP-70, C-reactive protein, TNF-alpha, creatinine, urea in patients according age. It showed a sensitivity of HSP-70 in hypertension when compared with the control group. Further one, it showed that is a correlation between the groups of BMI were obese, the morbidly obese, and the normal in patients of hypertension with the levels of parameters. The role of duration of disease can be shown by the effect of duration on the levels of parameters.

Immunological cells and inflammation are major contributors to hypertension, which is a risk factor for cardiovascular disease. The results showed a significant difference (P value = $\leq$ 0.0001) in HSP-70 and HS CRP but there was no significant difference in TNF-alpha in patients of hypertension and results showed a significant difference (P value = $\leq$ 0.0001) in lipid profile and urea and creatinine.

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Abbreviations

The Term	Definition
µl	Microliter
A	Absorbance
Ac	corrected absorption
ACE	Angiotensin converting enzyme
ACE2	Angiotensin - converting enzyme 2

acetyl- CoA	acetyl coenzyme A
Af	final average absorbance
AH	Atrial hypertension
Ai	initial average absorbance
Ang II	Angiotensin II
AngI	Angiotensin I
ATR1	Angiotensin type 1 receptor
ATR2	Angiotensin type 2 receptor
BP	Blood pressure
BMI	Body mass Index
CKD	Chronic kidney disease
CRP	C- reactive protein
CVD	Cardio Vascular Disease
ECFV	Extra cellular fluid volume
eGFR	estimated glomerular filtration rate
ELISA	enzyme- Linked Immeuno sorbent Assay
EP	Endo peptidases
ESRD	End-stage renal disease
GM-CSF	Granulocyte-monocyte colony stimulating factor
HDL	High-density lipoproteins
HLA-B	Human Leukocyte Antigen –B
HLA-DR	Human Leukocyte Antigen –DR
HMGCR	3-hydroxy-3-methylglutaryl coenzyme A reductase
HS CRP	High-sensitivity c reactive protein
HSF	Heat shoct factor
HSP	Henoch-schonlein purpura
HSP-70	Heat Shock Protein 70
HSPs	Heat Shock Proteins
IL-1	Interleukin-one
IL-6	Interleukin-six
IL-8	Interleukin-eight
IMCL	Intra myocellular lipids
IMID	immune-mediated inflammatory diseases
JNC	Joint National Committee
K	Kilo
KDa	Kilo Dalton
Kg	Kilogram
KU	Kilo unit
L	Liter

LDL	Low density Lipoprotein
LDLR	Low density Lipoprotein receptors
LMICs	low- and middle-income countries
LPL	lipoprotein lipase
LSD	least significant difference
LVH	Left venticular hypertrophy
LVM	left ventricular mass
m^2	Square meter
mg	Milligram
mL	Milliliter
MHC	major histocompatibility complex
N	Number
NAFLD	Non alcoholic fatty liver disease
OD	optical density
ºC	Degrees Celsius
Pg	Pictogram
P-value	Probability level of statistical
R	Correlation coefficient
RA	Rheumatoid arthritis
RAAS	renin-angiotensin aldosterone system
SREBP-2	Sterol regulatory element-binding protein 2
SLE	Systemic lupus erythematosus
SNS	sympathetic nervous system
TG	Triacylglycerides
TNF-α	Tumor Necrosis Factor-alpha
VLDL	Very low density lipoprotein
WHO	World health organization

Chapter One

Introduction

1. Introduction

1.1. Hypertension

An unusually high systemic arterial blood pressure level that lasts for a prolonged period of time is called hypertension. As for people's age, hypertension becomes increasingly prevalent [1].

Persistently high arterial blood pressure causes major pathological changes in the heart and arteries. A blood pressure (BP) reading of ≥140/90 mmHg indicates the presence of cardiovascular disease (CVD) linked to hypertension, necessitating prompt medical intervention [2].

One of the most researched topics of the last century was hypertension, which was also a major comorbidity that contributed to heart failure, stroke, myocardial infarction, and renal failure [3]. It has been said that hypertension is the "silent killer" since the majority of those who have it either show no symptoms at all or very hazy ones. Because of this, hypertension is underdiagnosed, and even when it is, there are issues with management strategy adherence and compliance [4].

The risk of CVD in hypertensive patients has decreased as a consequence of the recent discovery of a new class of antihypertensive drugs that not only allow for appropriate blood pressure control but also allow for the customized selection of preferred treatments based on the unique circumstances of each patient [5].

Clinical research indicates that ARBs, including candesartan-based treatment, effectively reduce the amount of left ventricular hypertrophy (LVH) in hypertension patients as determined by echocardiography [6].

1.2. Types of hypertension

1.2.1. Primary Hypertension

Essential hypertension is a multifactorial disorder in which a large number of individuals have elevated blood pressure as a result of several underlying causes. Ninety-five percent of people with hypertension have essential hypertension. It might be brought on by unknown causes of hypertension, hereditary, environmental, or a mix of factors[7].

1.2.2 Secondary Hypertension:

Just 5–10% of people with hypertension may be attributed to it. Renal parenchymal disorders, pheochromocytoma, Cushing's syndrome, primary hyperaldosteronism, myxoedema, and renal vascular illnesses are among the conditions that might result in secondary hypertension [8].

1.3. Epidemiology of hypertension

In the world, hypertension is the biggest avoidable cause of Cardio Vascular Disease and death Due to the extensive use of antihypertensive medications, the global mean blood pressure has either stayed steady or significantly decreased during the past forty years; nonetheless, the prevalence of hypertension has increased, especially in low- and middle-income countries (LMICs) [9].

Adults with hypertension were more likely to have the condition in low- and middle-income countries (LMICs) (31.5%) than in high-income nations (349 million people) (28.5%). This is likely due to inadequate access to healthcare and low illness knowledge [10].

Differences in the prevalence of the condition's risk factors, such as low potassium and excessive salt intake, obesity, alcohol use, physical inactivity, and poor nutrition, may account for some of the geographical variance in the incidence of hypertension [11].

Significantly more people in Middle Eastern nations suffer from hypertension. In a 2006 Iraqi survey on risk factors for chronic noncommunicable diseases, the prevalence of hypertension was 40.4% in both sexes in the 25–65 age range [12].

According to WHO (World Health Organization) Eastern Mediterranean Region health data from 2008, 29.4% of Iraqi adults and children aged 15 and older have hypertension [13].

Between 1990 and 2019, the proportion of individuals aged 30 to 79 who had hypertension quadrupled. This increase occurred despite a steady worldwide age-standardized prevalence [14].By that is anticipated that up to 60% of the population would suffer from hypertension by the end of 2025 [15].

1.4. Regulation of blood pressure.

The force of blood pressing against the peripheral artery walls is known as blood pressure. The unit of measurement for mercury is millimeters (mm Hg) [16].

While stress, hypertension, and other medical problems can cause variations in this range, the usual range for blood pressure (Bp) is 120/80, with 120 representing systolic pressure and 80 representing diastolic pressure [17].

The complicated physiologic function of regulating blood pressure is dependent on several functions of the endocrine, brain, kidney, and cardiovascular systems. Blood pressure regulation is the process of modifying blood flow to a specific tissue in response to its metabolic requirements. Local blood flow regulation processes known as vasoconstriction and vasodilation are triggered by both acute and chronic variations in the quantity and width of blood arteries feeding a certain tissue. Endothelium autocrine secretions regulate both dilatation and constriction of blood vessels. Apart from the regulation of blood flow locally, the autonomic nervous system plays a major role in the regulation of systemic blood flow. While the parasympathetic

nervous system predominantly regulates heart function, the sympathetic nervous system (SNS) is principally in charge of altering cardiac output and arterial blood pressure [18].

1.4.1 Regulation by nervous system

The autonomic nervous system uses a specific type of mechanoreceptor known as a baroreceptor to convey data obtained from blood pressure readings. Stretching of the vascular wall activates two different types of baroreceptors: high-pressure artery baroreceptors and low-pressure volume receptors. The aortic arch and carotid sinuses contain arterial baroreceptors. The ventricles, atria, and pulmonary vasculature include low-pressure volume receptors, also known as cardiopulmonary receptors [19].

The autonomic nervous system is notified by arterial baroreceptors of variations in arterial blood pressure that take place on a heartbeat basis. Action potential frequency and artery wall stretching were both decreased by abrupt blood pressure drops, such as orthostatic hypotension. Blood pressure rose as a result of these variables' subsequent increases in cardiac output and vasoconstriction. It is established that elevated blood pressure has the opposite impact. Low volume settings cause alterations in the circulation and kidneys that lead to greater salt and water resorption in the kidneys, slower, longer-term mean pressure fluctuations, and increased oral salt and water consumption [20].

1.4.2 Regulation by renal mechanism

Long-term processes controlling extracellular fluid volume (ECFV) and sodium balance are related to each other. Since blood volume and ECFV excesses or deficits are closely related, a range of cardiovascular receptor

systems can identify them. The kidneys then receive signals that alter renal salt and water excretion, correcting the ECFV imbalance [21].

There is a clear correlation between sodium excretion and renal perfusion pressure. An abrupt rise in renal perfusion pressure results in natriuretic. A number of significant neurohumoral systems impact the way the pressure-natriuretic mechanism is built up, which leads to a long-term link between arterial pressure and salt excretion that is far more complicated and sensitive. By resetting the pressure-natriuretic Relationship, neurohumoral systems enable fast changes in sodium excretion with slight variations in arterial pressure. In healthy individuals, a rise in blood volume sets off a sequence of synchronized physiological responses that improve the connection between pressure and natriuretic. In contrast, following sodium depletion or a decrease in blood volume, the pressure-natriuretic relationship's slope is significantly lessened [22].

1.4.3 Regulation by endocrine system

The most significant endocrine system for controlling hemodynamic stability, the renin-angiotensin-aldosterone system (RAAS) regulates blood pressure, fluid volume, and sodium-potassium balance. Atrial hypertension (AH) is brought on by alterations in these molecules [23].

The breakdown of the glycoprotein angiotensinogen, which is aided by active renin, results in the production of angiotensin I (Ang I). The angiotensin-converting enzyme (ACE) hydrolyzes bradykinin, a vasodilator molecule, by cleaving angiotensin I into angiotensin II. On the other hand, angiotensin I is broken down by neutral endopeptidases (EP) to create an additional active peptide in this system called angiotensin-(1–7), which often mitigates the effects of Ang II [24].

Angiotensin-converting enzyme 2 (ACE2) may also cleave angiotensin II, resulting in the production of angiotensin-(1–7)[25]. Another RAAS effector is aldosterone, which is produced and released by Ang II in the adrenal cortex through the ATR1. Through specific effects on the kidney's distal nephron, aldosterone promotes the reabsorption of sodium, water retention, and the loss of potassium and magnesium. As a result, blood pressure and extracellular fluid volume are changed [26].

1.5. Pathophysiological mechanisms of essential hypertension

High Bp has been associated with a number of risk factors, including heredity, sympathetic hyperactivity, salt sensitivity, increased renin production, obesity, obstructive sleep apnea, insulin resistance, and others. The etiology of hypertension is still unknown, despite the knowledge of several risk factors [27].

1.5.1 Genetics

The likelihood of hypertension in children is higher when both parents have the ailment, especially if there is a family history of the illness. Primary hypertension results from a genetic and environmental cocktail; high blood pressure is 30% to 50% heritable [28].

Renal, neural, endocrine, vascular, and other pathways are among the many interconnected networks that govern the primary determinants of cardiac output and total peripheral resistance. In each of these systems, specific functions that control blood pressure are mediated by many genes [29]. Genome-wide association has revealed over 100 single nucleotide polymorphisms associated with BP symptoms, along with possible new pathways of BP control and treatment targets. Allelic differences in a gene

may cause an increase or decrease in Bp. The traditional model states that these numerous alleles have cumulative effects, with each genetic variety contributing a little change in Bp [30].

1.5.2 Renal mechanisms: hypertension and salt sensitivity

The pathophysiology of hypertension and salt sensitivity are closely linked to the kidneys. Elevated salt intake raises extracellular fluid volume and cardiac output, which in turn raises pulse volume. The kidney's function as the primary regulator of fluid volume via the traditional sodium-pressure mechanism is compromised, leading to an increase in both the pulse volume and blood pressure [31].

People who are sensitive to salt experience an aberrant renal response to salt intake; the kidneys retain most of the salt because of an overly sensitive (SNS) and a weakened inhibition of the renin-angiotensin axis. Furthermore, due to a reduction in nitric oxide production in the endothelium, salt-sensitive individuals have greater vascular resistance rather than lower peripheral vascular resistance. Thirty to fifty percent of the hypertension sufferers are reportedly affected by salt sensitivity [32].

1.5.3 Hormonal mechanisms: The renin-angiotensin aldosterone system (RAAS)

Renin levels are higher in hypertensive individuals, and this is assumed to be the cause of hypertension. Angiotensin I is generated following renin's breakdown of angiotensinogen. Ang I is converted by the angiotensin converting enzyme into Ang II, the most vasoactive peptide and strong constrictor of blood vessels. It elevates Bp, increases peripheral resistance,

and affects the artery muscle. The proximal tubule's Na+/H+ exchanger and Na+/K+ ATPase, the loop of Henley's Na+/K+/2Cl transport, and the distal nephron's and collecting tubules' different ion transporters are all activated when angiotensin II is administered, which results in direct sodium retention effects [33]. Additionally, angiotensin II stimulates the adrenal glands to generate aldosterone, which increases the kidney's epithelial cells' ability to reabsorb salt and water, raising blood volume and blood pressure [34]. Cardiomyocytes become hypertrophic due to angiotensin II directly, and the primary mechanism responsible for the creation of LVH is believed to be overstimulation of RAAS in hypertension [35].

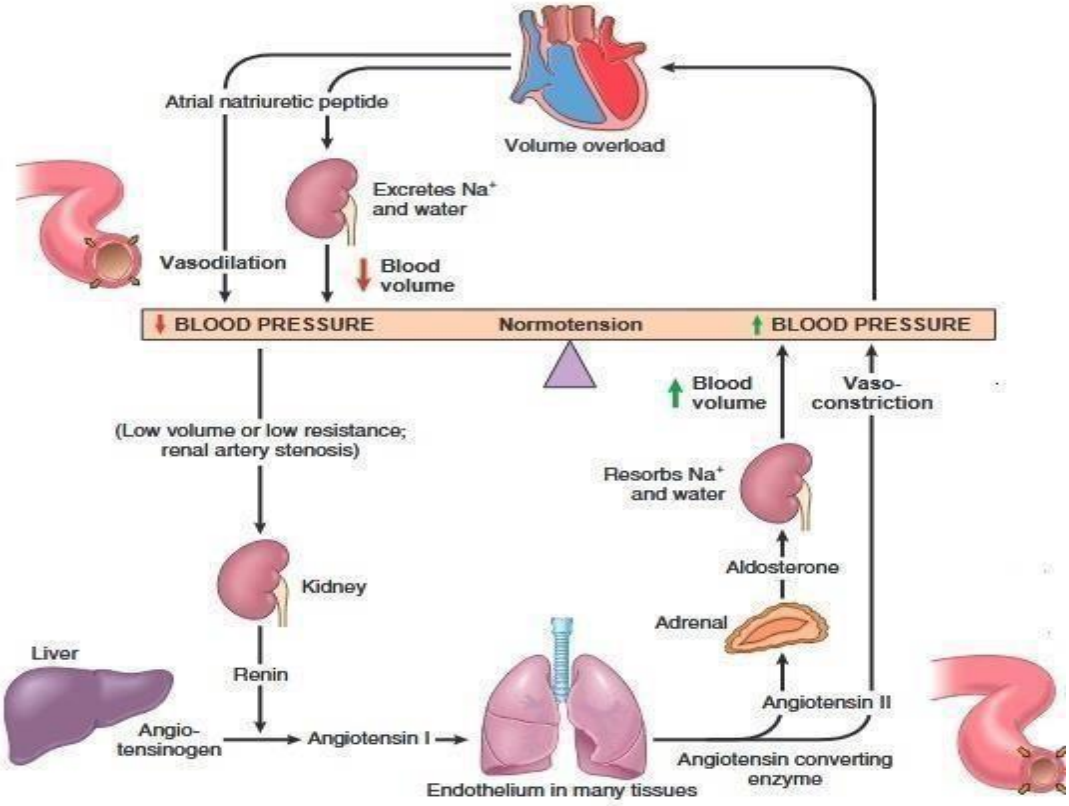


Fig. (1.1): Interplay of renin-angiotensin-aldosterone and atrial natriuretic peptide in maintaining blood pressure homeostasis [36].

1.6. Complication of hypertension

1.6.1Vasculopathy

The clinical manifestation of angina is a decrease in the dilation of the high resistance vasculature due to endothelial dysfunction and remodeling of the small and major arteries, plaque accumulation, stenosis and aneurysms, especially in the aorta, and a reduction in the coronary reserve [37].

1.6.2. Heart disease

With left ventricular hypertrophy being of special significance, this phrase encompasses a wide range of anatomical and functional alterations in the heart [38].

An excessive volume and/or pressure causes the heart to structurally remodel itself, leading to left ventricular hypertrophy. It has been shown that increases in left ventricular mass (LVM) found by echocardiography are a strong independent predictor of adverse cardiovascular events in hypertensive individuals, such as heart failure, coronary artery disease, stroke, and sudden cardiac death. It has been demonstrated that a variety of other factors, such as age, gender, ethnicity, and heredity, have an influence on LVM in addition to the intensity and duration of hypertension. It has also been discovered that comorbid conditions including diabetes, obesity, and chronic renal sickness affect LVM [39]. LVH in hypertensive individuals has been linked to a number of hereditary factors [40].

There are three stages of left ventricular hypertrophy: pathogenic, compensatory, and adaptive. Contractile dysfunction can be reversed in the first two phases but cannot be reversed in the third. 50% of individuals with severe hypertension and 15-20% of people with moderate arterial hypertension develop LVH. Heart myocyte hypertrophy, interstitial and

perivascular fibrosis, coronary macroangiopathy, and coronary microangiopathy are among the pathogenesis of left ventricular hypertrophy. Patients with LVH have a 2-4 times increased chance of experiencing a CV event compared to those without the condition [41].

Initially asymptomatic, hypertensive heart disease can eventually cause angina pectoris, dyspnea, and arrhythmia. These symptoms can be caused by reduced coronary reserve, ventricular arrhythmia, atrial fibrillation, and poor systolic and diastolic left ventricular function [42].

1.6.3 Cerebrovascular damage

The most common cause of stroke is arterial hypertension, which develops as an underlying ischemic infarction in 80% of cases. Micro hemorrhages, localized or widespread white matter lesions, and lacunar infarctions are examples of early hypertensive micro angiopathic consequences. Another major contributing factor to the onset of vascular dementia is untreated or insufficiently managed hypertension [43].

1.6.4 Nephropathy

One of the leading causes of end-stage renal disease (ESRD) is hypertension, followed by diabetes mellitus [44]. Most hypertension individuals experience mild-to-moderate hypertensive nephropathy, which seldom advances to end-stage renal disease (ESRD). However, if a patient has previous kidney disease or if blood pressure is left uncontrolled for a lengthy period of time, the likelihood of them acquiring end-stage renal disease (ESRD) increases significantly [45].

1.6.5 Retinopathy

Hypertensive retinopathy is a consideration in assessing cardiovascular risk in hypertensive patients because it results from damage to the retinal microcirculation caused by poorly treated systemic hypertension [46]. It has long been recognized as standard practice to use an ophthalmoscope to check for hypertensive retinopathy in patients with hypertension [47].

Retinopathy is one of numerous markers of target-organ damage in hypertension listed by the Joint National Committee (JNC) on prevention, detection, evaluation, and treatment of high blood pressure. According to the JNC, the appearance of retinopathy may be a clue that antihypertensive medication should be started even in patients with stage 1 hypertension (blood pressure 140-159/90-99 mm Hg) who do not exhibit any other symptoms of damage to target organs [48].

1.7 Clinical Manifestations of hypertension.

Numerous symptoms, including headache, tinnitus, dizziness, nausea, and fainting, that are frequently linked to simple hypertension are probably psychogenic in nature [49]. These may be the result of hyperventilation triggered by the fear of being told a terminal illness that puts one's life in danger. Surprisingly, though, new research shows that a person's general sense of well-being often improves when hypertension medication is started. According to these recent discoveries, hypertension may not be as asymptomatic as previously believed. Even while hypertension is rarely totally silent, it can go undiagnosed for years since overt symptoms and indicators typically appear at the same time as target organ damage begins. Therefore, using an accurate Bp measuring technique is essential for detecting hypertension [50].

The underlying causes of secondary hypertension, such as primary hyperaldosteronism, which can lead to tiredness, hypokalemia, metabolic alkalosis, and hypernatremia, are frequently implicated in the symptoms of secondary hypertension. Periodic bouts of hypertension accompanied by flushing, diaphoresis, and headaches are caused by phenochromocytomas. Obesity, irregular menstrual cycles, abdominal striae, hyperglycemia, and muscular weakness are all symptoms of Cushing syndrome [51].

1.8. Diagnosis of hypertension

Early detection and appropriate treatment of hypertension can reduces the risk of many diseases . Unlike the diagnosis of other no communicable illnesses like diabetes, detecting high Bp is relatively easy, inexpensive, and doable in low-resource settings. It is also something that all individuals can accomplish on their own, particularly in situations where measuring instruments are readily available and reasonably priced [52].

Three main types of devices—mercury, aneroid, and electronic—can be used to measure blood pressure. WHO advises utilizing affordable, trustworthy electronic gadgets that have a manual reading selection feature. Digital blood pressure monitors make it possible to collect readings outside of a clinic, which is frequently a more practical and precise method[53].

1.9. Lipids and Lipoproteins

1.9.1 Lipids

Because so many different chemicals can be classified as lipids, there is not a single, widely-accepted definition for this term. Hydrophobicity is the key qualification for membership in this group, rather than chemical properties. Generally speaking, molecules with more than three carbon atoms and organic materials containing attached fatty acids are referred to as lipids [54]. Plasma lipids consist of 16% triacylglycerol (triglycerides), 30% phospholipids, 14% cholesterol, 36% cholesterol esters, and a comparatively smaller fraction of free fatty acids (4%), which are long-chain fatty acids without esterification [55].

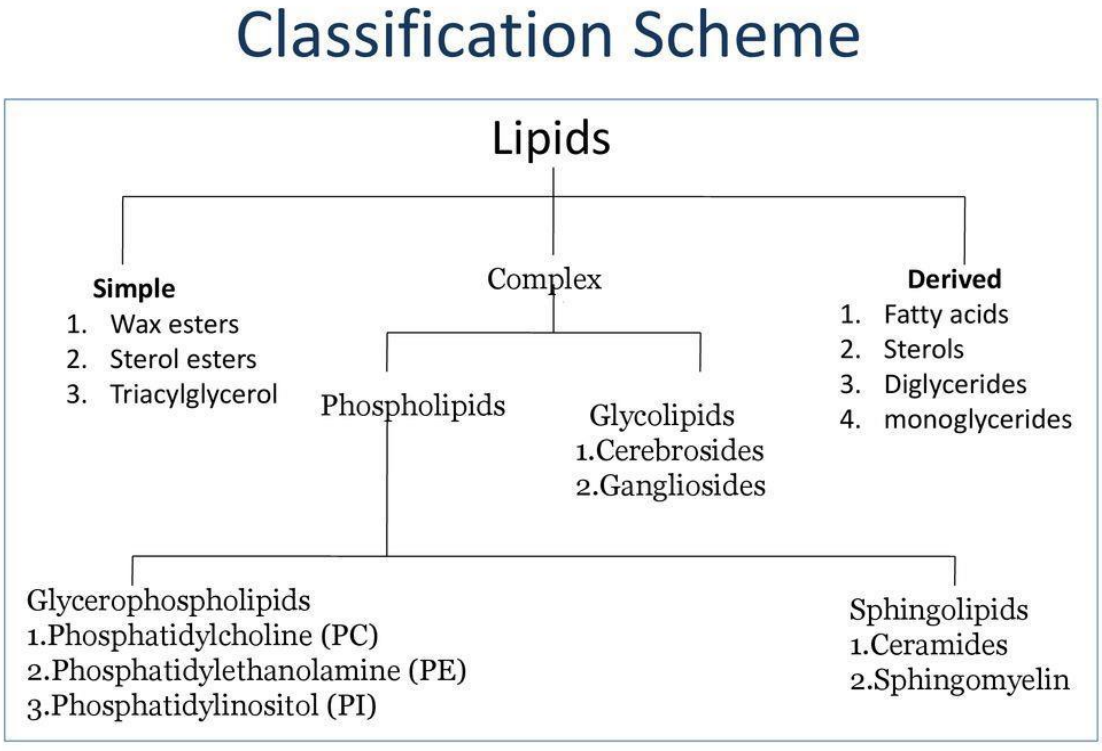


Fig. (1.2): Clinically significant lipid categorization [56]

1.9.2 Cholesterol

In the human body, the biomolecule cholesterol is present in nearly all cells. Cholesterol plays both beneficial and detrimental functions in the body [57, 58], and it has the chemical formula $C_{27}H_{46}O$ [59]. The amphipathic sterol molecule, or cholesterol, is composed of four hydrocarbon rings, a hydrocarbon tail, and a hydroxyl group [60], as seen in Figure (1.2). As a component of all cell membranes, the precursor to bile acids, the building block of steroid hormones, and a signaling molecule in the central nervous system, cholesterol performs a multitude of vital physiological functions[61].

The bulk of the cholesterol in our bodies is created internally by the liver, with only a little amount coming from external dietary sources[62].

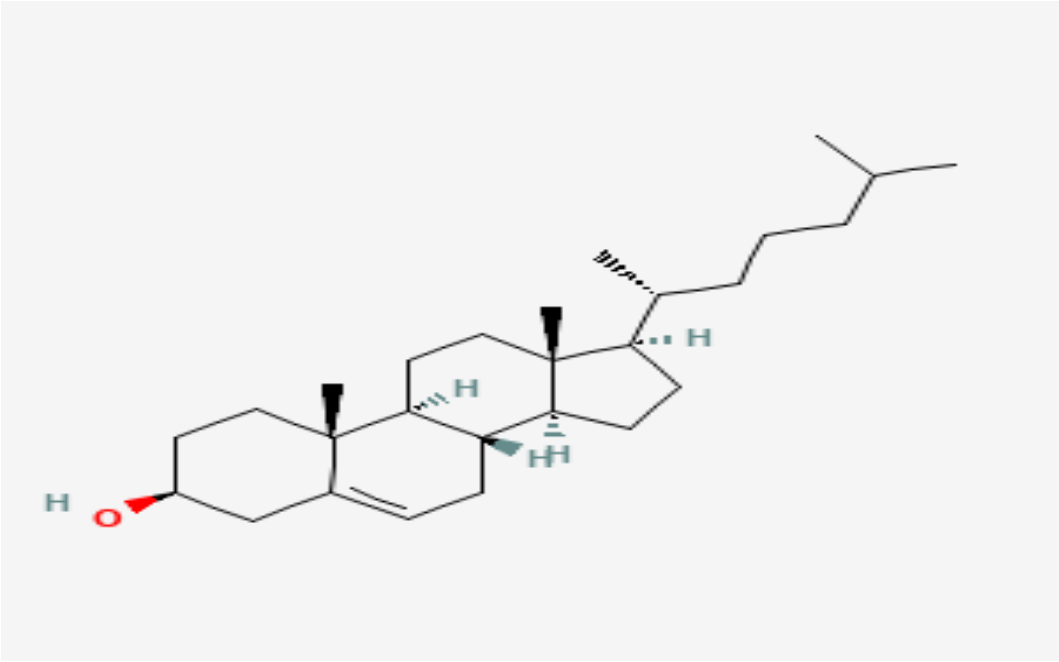


Figure (1.3): Chemical Structure of Cholesterol [59]

The pace at which cholesterol is produced in the liver is largely dependent on the amount of cholesterol present in cells and the rate at which it is absorbed in the small intestine. SREBP-2, a protein that binds to sterol regulatory elements, regulates this the second rate-limiting step in the synthesis of cholesterol is the catalysis of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) to produce mevalonate. Triglycerides and cholesterol from food are absorbed in the small intestine, where they are converted into chylomicrons. The liver absorbs the chylomicron residues and fatty acids that are produced when lipoprotein lipase (LPL) breaks down chylomicrons in the plasma. like VLDL, generates the precursor HDL.The cholesterol manufacturing enzyme, HMGCR, is "sensed" by SREBP-2 and activated when the quantity of free cholesterol in the hepatocytes rises owing to conversion to bile acids or falls due to the import of lipoproteins. According to figure (1.3), SREBP-2 also stimulates the development of LDL receptors (LDLR), which increases the rate at which cholesterol is absorbed from LDL and promotes cholesterol accumulation in the liver [63].

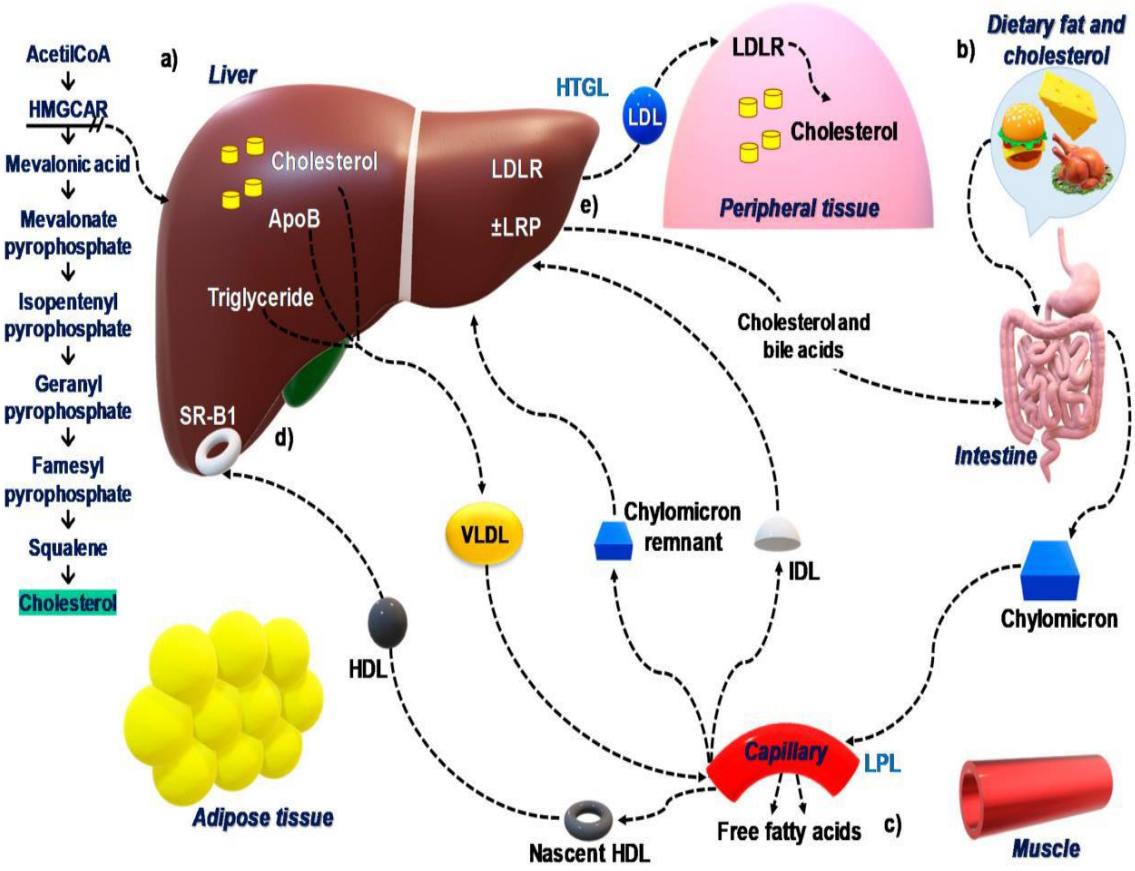


Figure (1.4): The body's equilibrium of cholesterol [63]

1.9.3 Triglycerides

A triglyceride is a non-polar lipid molecule that is based from a glycerol esterified to three fatty acid chains,, as seen in the Figuer (1.4). To further characterize these lipid molecules, consider their fatty acid composition. The number of double-bonded carbon (C=C) molecules in triglycerides determines whether they are unsaturated (one or more C=C) or saturated (no C=C). Moreover, triglycerides can be further classified according to the position of the C=C molecules in the fatty acid chain. Triglycerides are a major energy source in adipose tissue. During metabolism, their fatty acid chains are liberated through hydrolysis and oxidized to produce acetyl

coenzyme A (acetyl-CoA), which is used in the Krebs cycle and mevalonate pathway. Triglycerides are mostly derived from external food sources [62].

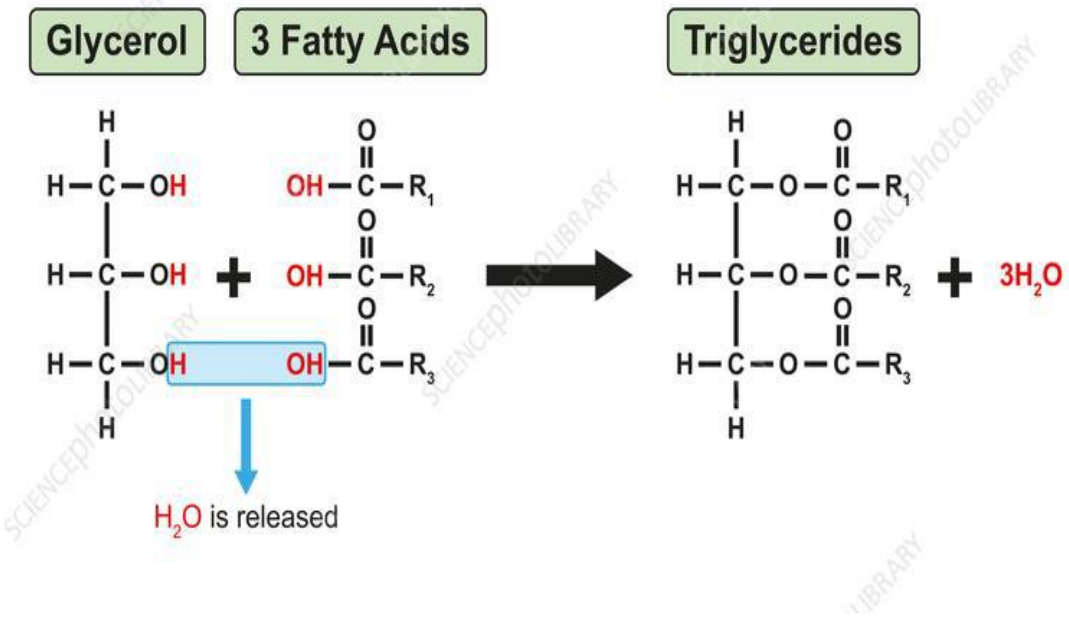


Fig. (1.5): Formation of triglyceride [64]

It is possible for the liver and skeletal muscle to have triacylglycerides (TG), a kind of fat that is normally formed in adipose tissue. Overaccumulation of TG in the liver, sometimes referred to as nonalcoholic fatty liver disease (NAFLD) and characterised by TG concentrations above 5% of liver weight, is linked to the metabolic syndrome. Likewise, increased TG in skeletal muscle, often referred to as intramyocellular lipids (IMCL), has been associated with insulin resistance in individuals suffering from obesity and type 2 diabetes [65].

1.9.4 Lipoproteins

Lipoproteins are the most important complex lipids because they contain both proteins and lipids. Polar lipids (free cholesterol, phospholipids) encircle the non-polar lipids (cholesterol esters and triacylglycerols) in the core of lipoprotein particles and aid in the binding of lipids to proteins. The most often evaluated lipoproteins are serum lipoproteins [61].

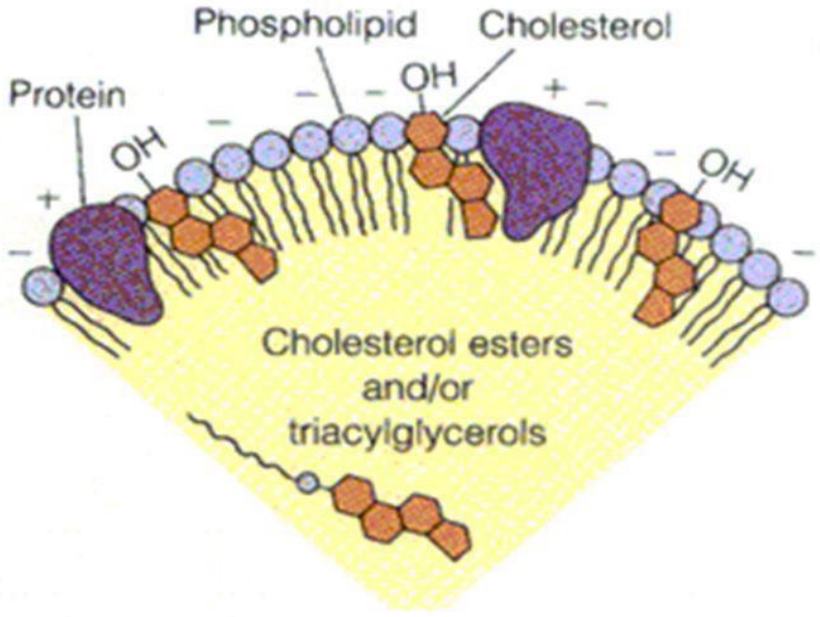


Fig. (1.6): The generalized structure of plasma lipoprotein [62]

1.9.5 High Density Lipoprotein (HDL)

High-density lipoproteins (HDL) assist in transporting excess cholesterol from the body's external tissues to the liver [66]. HDL-C, or high-density lipoprotein cholesterol, has long been regarded as "good cholesterol," partially because of its apparent inverse relationship with the risk of CVD. It is advised that women take no less than 55 mg/dL and males take no less than 45 mg/dL.

HDL cholesterol aids the liver in eliminating excess cholesterol that has accumulated in blood vessel walls via the digestive tract. The function of HDL cholesterol in preserving dilated blood arteries promotes improved blood flow. Its anti-inflammatory and antioxidant qualities, among other things, reduce blood vessel damage. HDL cholesterol carries "old" cholesterol back to the liver for excretion or recycling after it is removed by cells [67]. More recent research, however, has called into doubt whether HDL-C is a causal factor in this connection, as no evidence of a cardiovascular protective benefit associated with increasing HDL-C levels has been found in genetic studies or several large-scale randomised controlled trials. Rather, the functional properties of the HDL particle are currently being studied. Evidence suggests that in an inflammatory environment, HDL's composition and function change significantly from that of a vasoprotective anti-atherogenic particle to a toxic pro-atherogenic counterpart [68].

1.9.6 Low density Lipoprotein (LDL)

Low-density lipoprotein is sometimes referred to as "bad cholesterol". The acceptable range for LDL is 130 mg/dL; however, the most current recommendations stress lower levels (less than 100 mg/dL). linked to CVD and plays a key effect. Agencies and more current standards have different thresholds [69, 70].When excessively elevated, one of the key laboratory markers, LDL-C, confers a significant risk of cardiovascular disease; prescription therapy has been centered around these molecules [71]."

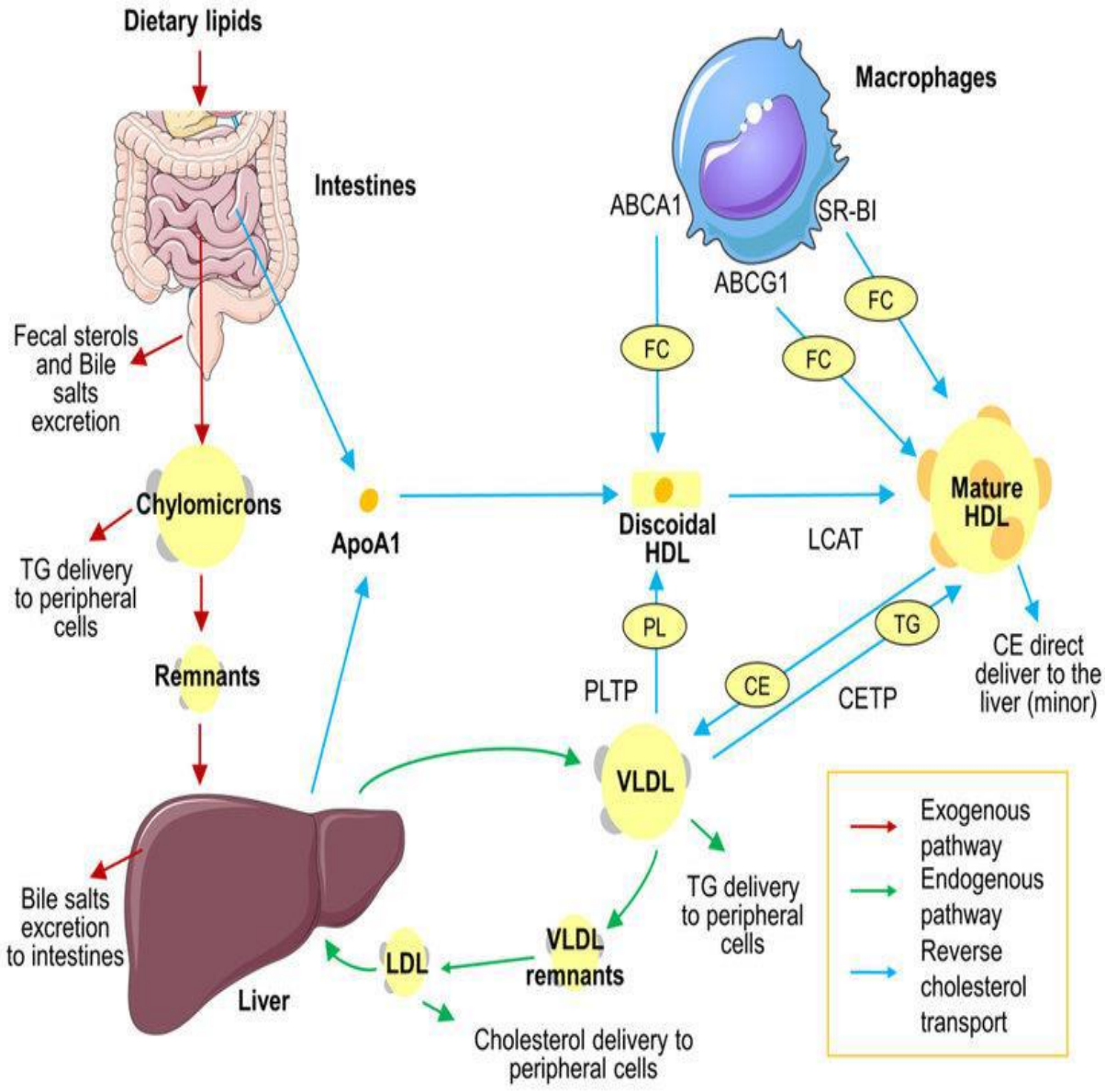


Fig. (1.7): Lipoprotein metabolism overview [72]

According to figure (1.7), 70% of patients have dyslipidemia, the most common metabolic disease associated with PCOS. Atherogenic dyslipidemia, which is typical of insulin-resistant states, is characterized by hypertriglyceridemia, low HDL-C levels, and small dense LDL-C particles [73].

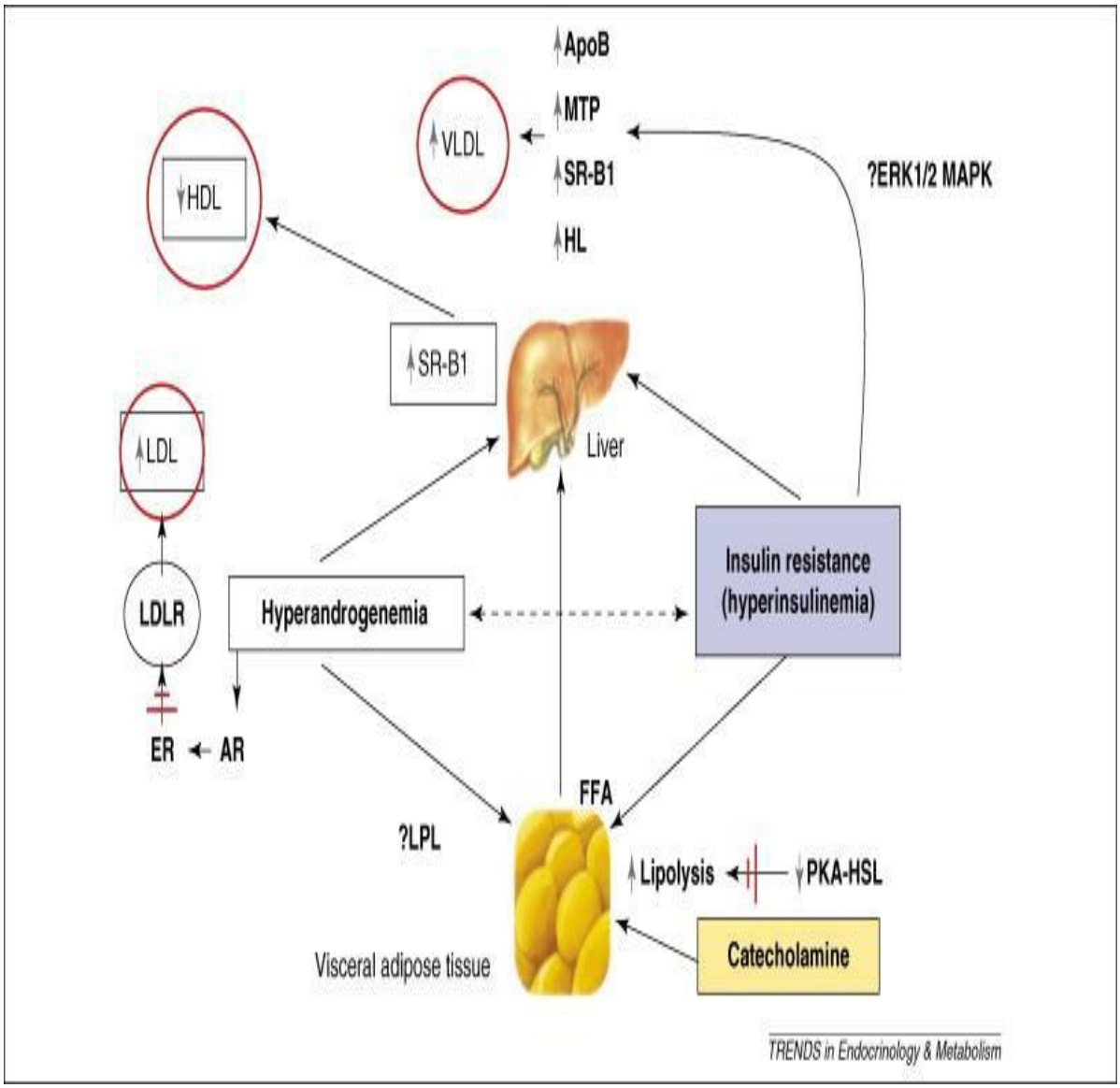


Fig. (1.8): Dyslipidemia in PCOS [74]

1.10 Inflammation and inflammatory markers

A complicated process, inflammation is brought on by chemical, physical, or biological triggers. It is a defense mechanism in reaction to viruses, external objects, or damage to the host tissue. Vasodilation, increased capillary permeability, increased blood flow, and leukocyte recruitment are

the characteristics of this process. The process and the ensuing reaction should stop when the molecular mediators produced by inflammation are lost. The decrease in inflammation and the return of equilibrium are both passive and active processes, which are highly regulated and closely related to levels of inflammatory mediators. Biomarkers have attracted increasing attention as indicators of disease status in patients with inflammatory diseases. As clinical research advances, flow cytometry analysis of cell populations and serum solubility media detection have revealed novel markers of disease activity in peripheral blood and damaged organs. [75] These newly discovered biomarkers have the potential to uncover novel therapeutic targets, shed light on the illness process, and offer immediate measures of therapy efficacy. As a result, inflammatory biomarkers are effective predictors of the course and severity of illness as well as how effectively a treatment is working [76].

1.10.1 Inflammation and hypertension

Despite the fact that the precise pathophysiology of essential hypertension is yet unknown, endothelial dysfunction is thought to be a major factor in the development of the condition. Although it was often believed that the vascular endothelium served as an inert barrier separating the blood from the blood vessels, it is now recognized as a key hub for vascular regulation. The endothelium is crucial for controlling the tension in vascular walls, the distribution of nutrients, elimination of trash, inflammation, coagulation, and thrombosis. As a result, it is claimed that hypertension is partially an inflammatory illness [77]. Oxygen metabolism produces reactive oxygen species. Reactive oxygen species are produced as a result of oxidative stress, which happens when pro-oxidative factors outweigh anti-oxidative factors [78]. shown the critical role that oxidative stress plays in the pathogenesis of

hypertension. The inflammatory response is heightened by oxidative stress, which raises the synthesis of pro-inflammatory molecules [79].

Reduced levels of regulatory immune cells and cytokines and higher levels of pro-inflammatory immune cells and cytokines lead to a persistent and uncontrollably inflammatory state [80]. Increased vascular endothelial injury and tumor necrosis factor (TNF)-α and IL-6 levels can cause widespread inflammation and cell damage by causing endothelial dysfunction [81].

Pro T-cell subsets of many kinds induce hypertension [82]. Renal salt and water retention are encouraged by activated T cells that invade the kidney and circulatory system and release cytokines [83]. Blood pressure increases noticeably as a result of vasoconstriction and remodeling brought on by hypertension in the vascular system [84]. The recruitment and buildup of immune cells, particularly lymphocytes and macrophages, in blood pressure-regulating organs including the kidney and vascular system is linked to hypertension and is caused by the immune system being activated. This immune infiltration leads to localized fibrosis and inflammation, which damages organs and impairs blood pressure regulation. Low-grade inflammation may have a role in the development and maintenance of hypertension due to the control of innate and adaptive immune responses.

1.11. Inflammation Factors

TNF-α,C-reactive protein (CRP) ,and other inflammatory markers are factors linked to inflammation.These variables have been found to increase the risk of CVD [85]. TNF-alpha levels in the blood are linked to an elevated risk of cardiovascular disease [86],One reliable independent predictor of CVD is the high-sensitivity C-reactive protein (HS-CRP) [87].

1.11.1 C-Reactive Protein with High Sensitivity (HS-CRP)

The polypeptide molecule known as C-reactive protein (CRP) belongs to the pentraxin family. It has a molecular mass of 120,000 Daltons and is composed of five identical subunits, each of which has 206 amino acids. When certain pro-inflammatory cytokines are present, the liver is the main organ where CRP is synthesized. It has important roles in complement activation, opsonization because of its properties, innate immunity, and immunoglobulin receptor binding [88]. CRP is frequently measured as an indicator of systemic inflammation in people with rheumatoid arthritis (RA). It also has the function of being an immunological regulator, which is crucial in the inflammatory pathways linked to RA that encourage atherogenic consequences. Systemic inflammatory comorbidities are widespread in RA patients, and elevated CRP has been associated with an increased risk of depression, diabetes, metabolic syndrome, cardiovascular disease, and lung disorders [89].

″ CRP is an important inflammatory marker since it is protein associated with acute systemic inflammation [90]. More sensitive and capable of detecting very low CRP concentrations are the high sensitivity CRP (HS-CRP) tests [88].It is an inflammatory biomarker that, like blood pressure and cholesterol, predicts cardiovascular risk [91]. Furthermore, in healthy individuals without a history of cardiovascular illness, it predicts recurrent

events, mortality, incident myocardial infarction, stroke, peripheral artery disease, and sudden cardiac death [92]. Values ranging from 1 to 3 and greater than 3 mg/L suggest lower, medium, or higher relative cardiovascular risk [91]. To test CRP, one can utilize immunoturbidimetry or immunoonephelometry. There is no set protocol. Based on "immunolatex" immunonephelemetry sensitized techniques, the measurement of HS-CRP is performed [88].

1.11.2 Tumor Necrosis Factor

Among the several cytokines generated as part of the host's fight against infection is TNF. A cytotoxin produced from monocytes, TNF has been implicated in tumor regression, sepsis, shock, and cachexia (fever) [93]. One cytokine with a variety of uses is TNF. Certain tumor cells are cytolyzed by it, and it also contributes to the development of cachexia. It is a strong pyrogen that may either directly produce fever or stimulate the release of IL-1; in certain situations, TNF can promote cell division and proliferation [94].

TNF is implicated in several inflammatory processes that are occurring as well as the pathophysiology of numerous viral and autoimmune disorders as well as immune responses [95]. As seen in figures 1–5, the TNF gene is located on chromosomal number 6p21.3, which covers around three kilobases and has four exons. The last exons code for around 85% of proteins that are secreted [96]. TNF is flanked by the lymphotoxin into (a) and (b) genes in the (class III) region of the major histocompatibility complex (MHC), as shown in figure (1-6) previous studies have been reported a close linkage among HLA class I (HLA-B), class II (HLA-DR) and TNF genes [97]. Furthermore, the TNF gene tightly controls the transcription process [98].

1.11.3 Tumor necrosis factor- alpha (TNF-α)

Numerous cell types can create TNF-α, however the cell types most linked to the manufacture of this TNF-α protein include macrophages and monocytes [99]. Other cells including B-cells, T-cells, and fibroblast cells also release TNF-α. TNF-α that has just been generated is inserted into the cell membrane and released when a unique enzyme known as a serine metalloproteinase cleaves its membrane-anchoring domain [100]. Suppressive TNF-α release may result from this enzyme's inhibitors [101]. TNF-α functions as an autocrine inducer, prompting cells to release, and a powerful paracrine inducer, triggering the secretion of other inflammatory interleukins such as IL-1, IL-6, IL-8, and granulocyte-monocyte colony stimulating factor (GM-CSF) from one cell to another [102].

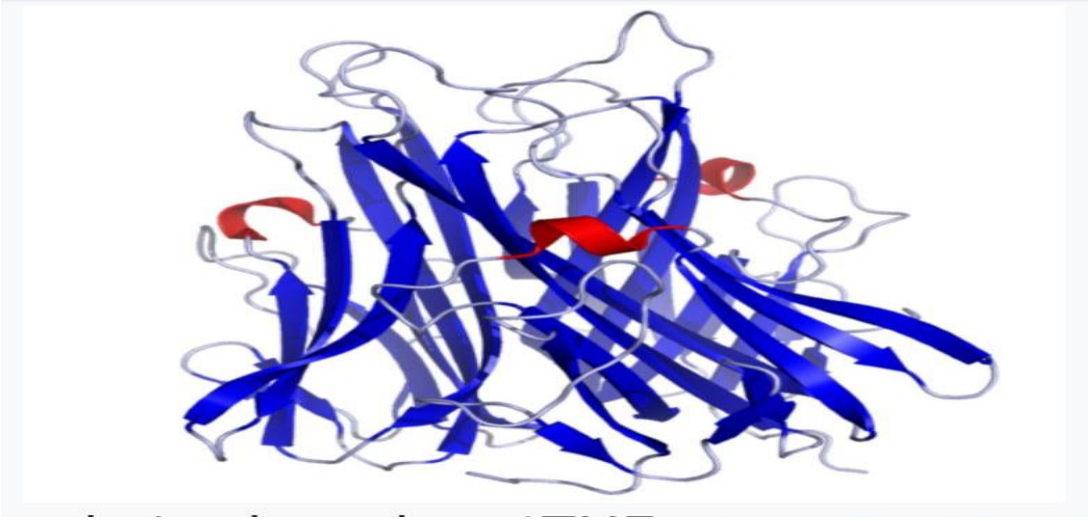


Fig. (1.9): Tumor necrosis factor (TNF-α)[103]

1.11.4 Heat shok protein-70

A class of proteins known as heat shock proteins (HSP) is created by cells in reaction to stressful environments [104].These proteins were originally identified in connection with heat shock, but it is now understood that they

are also produced in response to various stimuli, including as exposure to cold[105] and UV radiation, malnourishment, oxidative stress, wound healing, and tissue remodeling [106].

Numerous individuals within this group carry out chaperone duties, which involve stabilizing newly formed proteins to guarantee proper folding or aiding in the reconstruction of proteins broken due to cellular stress[107]. transcription is the mechanism that controls this rise in expression. Heat shock factor (HSF) is the primary cause of the overexpression of heat shock proteins, which is a crucial component of the heat shock response [108].

Heat shock proteins are found in almost all living organisms, from bacteria to humans. Heat shock proteins are named according to their molecular weight. For example, Hsp60, Hsp70, and Hsp90 (these most extensively studied proteins) refer to families of heat shock proteins on the order of 60, 70, and 90 kDa in size, respectively [110]. The small 8-kDa ubiquitin protein also contains On the properties of heat shock protein[109]. Heat shock proteins perform critical functions in ensuring correct folding of proteins, their transport as well as the assembly and disassembly of protein complexes. Because heat shock proteins aid in these functions, they have been described as molecular chaperones [110].

It is believed that these proteins may play a role in cancer[111] and some potential treatments such as anti-cancer vaccines [112]. There are some studies examining the agricultural importance of these proteins as they may help plants adapt to difficult environmental conditions such as drought and poor soil. A family of conserved heat shock proteins that are widely expressed is known as the 70 kilodalton heat shock proteins, or Hsp70s or DNAK. Nearly every living thing has proteins with a similar structure. The cell's

machinery relies on intracellularly localized Hsp70s to fold proteins, carry out chaperoning tasks, and shield cells from the damaging effects of physiological stressors [113].

Furthermore, extracellularly localized Hsp70s have been found to have both membrane-bound and membrane-free forms [114], and membrane-bound Hsp70s have been identified as a possible target for cancer therapy [115]. Ferruccio Ritossa made the initial discovery of shock in the 1960s when a lab technician unintentionally raised the temperature at which fruit flies, or Drosophila, were cultured. Ritossa discovered a "puffing pattern" on the chromosomes that suggested an unidentified protein's gene transcription was enhanced [116]. This was later described as the "Heat Shock Response" and the proteins were termed the "Heat Shock Proteins" (Hsps).

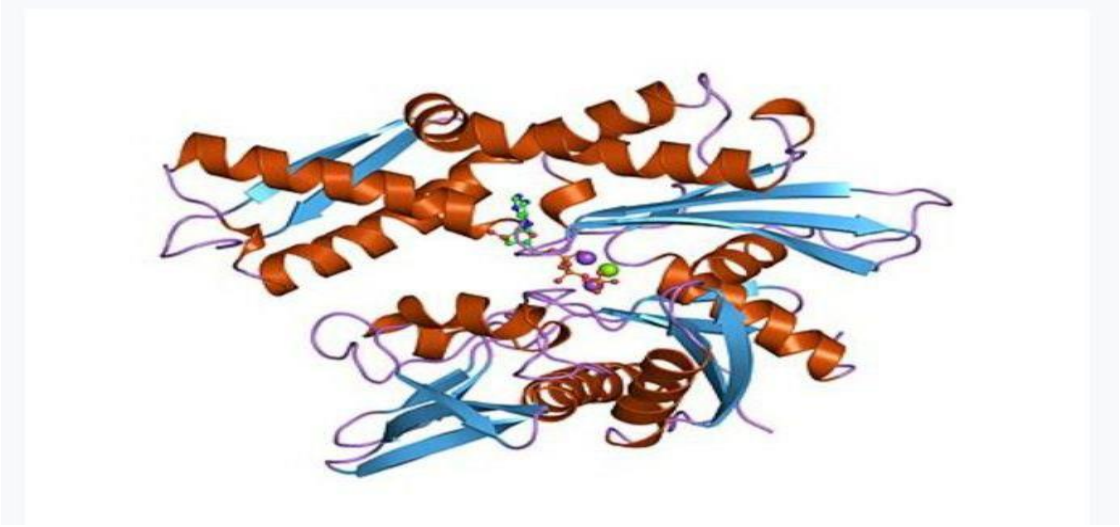


Fig. (1.10): Heat shok protein-70 [117]

1.12 Biochemical phenotype parameters

Kidney function analysis a person may have chronic kidney disease and not know anything about it, as the symptoms of kidney disorders and problems do not appear clearly in the first, early stages of the disease. This is considered a dangerous matter, as the condition worsens and develops without the patient's knowledge and without taking steps toward treatment. Hence the importance of performing a Kidney Function Test, which is a group of tests, each of which measures a specific characteristic of the kidneys[118].

1.12.1 Urea

The little molecule urea dissolves in water. There are two nitrogen atoms in it. It is the product of the metabolism of proteins and nitrogen. In individuals with uremia, it is the component with the highest blood level [118]. Upon digesting proteins in the liver, the primary nitrogenous by-product is urea, a white, crystalline substance weighing 60,056 daltons molecularly. Since the renal system generally filters it outside the body, it is vital to evaluate its blood level since abnormal levels might be a sign of a number of ailments, including liver or kidney disease. It is a highly reliable sign of adequate dialysis [119].

When renal function declines, carbamylation often increases, which is followed by urea accumulation. Dietary restriction helps lower the generation of urea since urea synthesis is strongly correlated with protein consumption. In addition to causing an overall accelerated aging phenotype, urea per se is probably linked to intestinal illness, anemia, CKD development, and CVD.

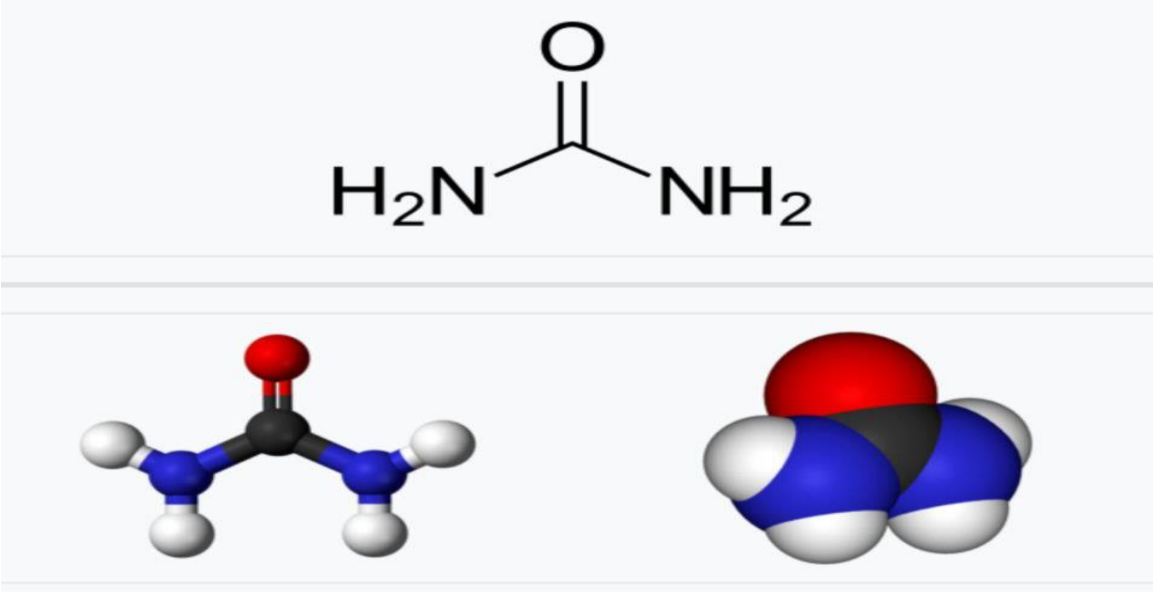


Fig. (1.11): The structural formula of urea [120].

1.12.2 Creatinine

Phosphocreatine is broken down non-enzymatically in the muscle to create creatinine. Most of it is filtered and eliminated in the urine by the kidneys after being transported there by the circulatory system [121], Creatine is released by skeletal muscle continuously. Skeletal muscle is closely associated with its serum level. It is filtered by the glomerular, and a little amount is secreted into the glomerular filtrate by the proximal tubule. Gaining muscle mass and eating a diet high in protein may be the cause of elevated creatinine levels in healthy individuals. Males were found to have higher serum levels than females, which might be explained by the manly muscular mass of men (20–25 mg/kg/day against 15–20 mg/kg/day in females) [122].

The amount of creatinine in the blood is influenced by a number of parameters, including its formation, glomerular filtration, tubular secretion, age, gender, race, body habits, food, and physical condition [123]. Elevations in creatinine levels may cause irritation and injury to the nerve endings.

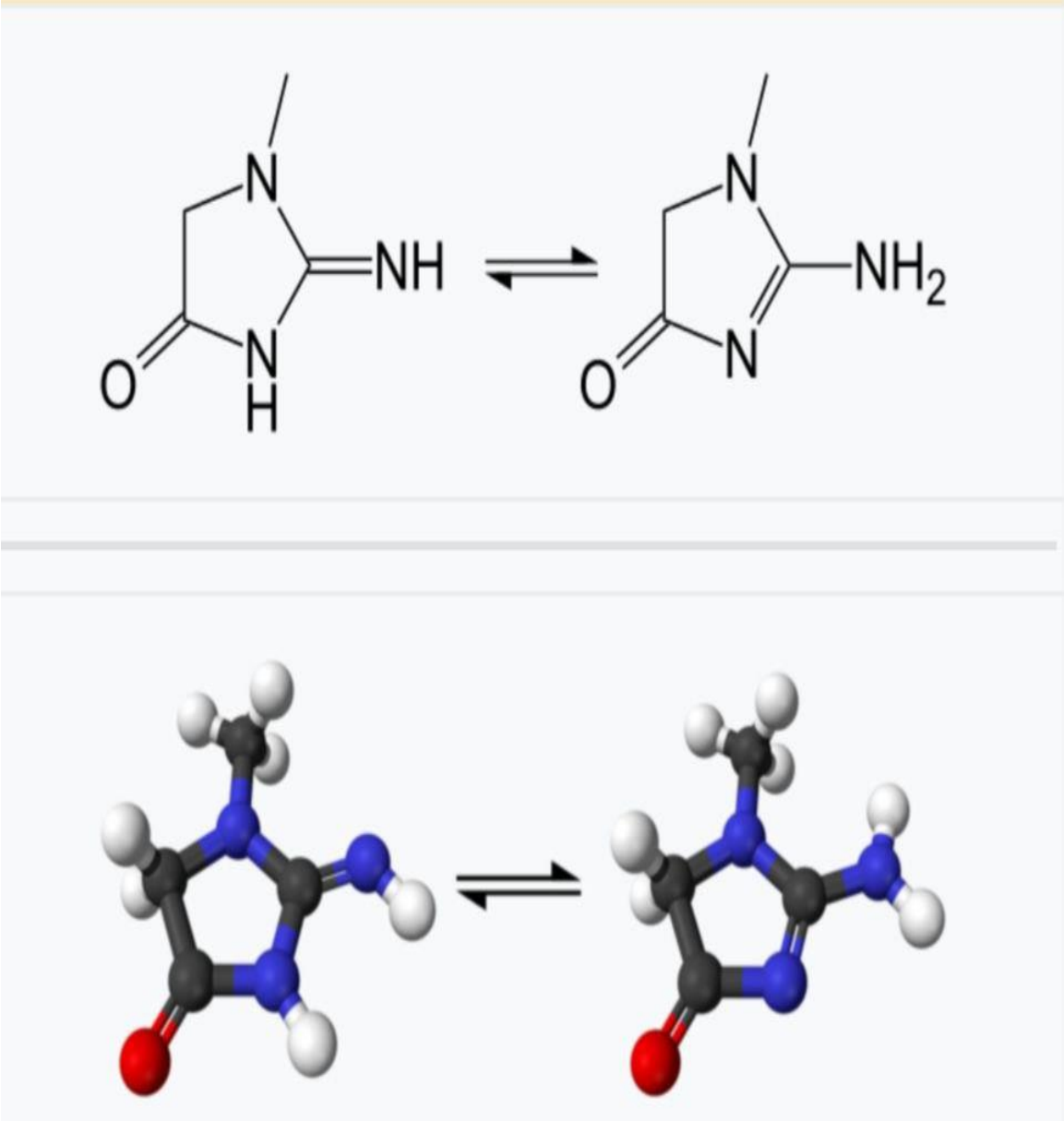


Fig. (1.12): The structural formula of creatinine [124].

1.13 Aims of the Study and objectives

The objectives of this investigation are as follows:

1- Show the effect of the duration of hypertension and the level of (Lipid profile and HS-CRP, TNF- α, HSP-70 urea, creatinine).

2-Evaluate of the level of inflammatory factors (HS-CRP, TNF- **α**) and (HSP-70) in patients of hypertension, and compared with a healthy group.

3- Demonstrate of the level of lipid profile in patients of hypertension, and compared with a healthy group.

4- Demonstrate of the level of urea and creatinine in patients of hypertension, and compared with a healthy group.

5-Examine the correlation between biomarkers (Lipid profile and HS-CRP, TNF- α, HSP-70) (HS-CRP and TNF- α, HSP-70) (HS-CRP, TNF- α, HSP-70, urea and creatinine).

Chapter Two Materials and Method

2. Materials and Methods

2.1 Subjects and Study Design

This study was conducted in outpatient Clinic, Internal Medicine Department, Imam Hussein Medical Teaching Hospital in the Holy Governorate of Karbala, patients were diagnosed by Dr. Lamya Abd Karim Darwish. Between October 2023 and February 2024, samples were gathered. The study was conducted on 50 Patient of hypertension and 40 healthy people, aged 40-70 years. All of them underwent medical examination, Giving them a short questionnaire asking about age, weight, height, gender, the duration of the illness, the diseases they suffer from, and the medications they take then they all underwent medical examination and had blood tests done (lipid profile, urea, creatinine, HS CRP, TNF-α, HSP-70) . Table (2.1) is a compilation of all the information gathered from both patients and healthy individuals.

Table 2.1 Questionnaire of this Study

Patient and Control profile
Questionnaire Number: Name:
Gender: Male female Mobile:
Date of the sample:
Age: Weight : Height: BMI:
Place of birth
marital state :single married Divorce Widow
Education: Bachelor postgraduate Secondary Primary illiterate
Number of Children: ( ) Males ( ) Females ( )
Occupation: employee ( ) self-employed unemployed
Place of residence: Rural Urban
Duration of hypertension:
Type of treatment for hypertension:
Other diseases: Diabetes mellitus (yes no) CVS (yes no), hyperlipidemia (yes no) chronic kidney disease (yes no),
Smoking status :(current former never)
prescription medication use of anti-hypertensive yes No
hypoglycemic: yes No lipid-lowering medications: yes no
Other treatment

2.2 Groups of this Study

The following was verified in the two research groups:

1.Control group (healthy people): The healthy group includes 40 people Ages range between 40-70 years.

2. Patients group: The group consists of 50 people suffering from high blood pressure and aged between (40-70) years.

The research techniques were authorized by the University of Karbala, and all individuals provided verbal informed permission.

2.3. Exclusion Criteria

1) Individuals with coronary arterial or cerebrovascular disease,
2) Fever
3) malignancy
4) Haematological disease.
5) Patients with acute or chronic respiratory diseases including obesity hypoventilation syndrome and sleep apnea syndrome
6) Patients suffering from any cause of acute or chronic inflammatory diseases like RA, SLE….ect
7) Infectious disease

2.4. Collection Blood Samples

Venous blood samples were taken for analysis (lipid profile, HS CRP, Hsp-70, TNF-alpha, urea, creatinine) from patients in the Consultation Clinic, Internal Medicine Department, and Imam Hussein Medical Teaching Hospital. A 5 ml blood sample was taken. Using a 5 ml medical syringe, blood was drawn They are inserted into anticoagulant-free gelatin tubes, often known as gel tubes, and that these tubes include a gelatinous substance

that aids in the procedure used to separate serum following centrifugation. After 15 minutes of standing Before being used, the serum was separated from the samples and kept at -20°C by centrifuging them for 10 minutes at room temperature at a speed of 3000 rounds per minute.

2.5 The Chemicals

Table (2.2) provides a description of the compounds employed in this investigation.

Table 2.2 The chemicals Kits

Chemicals	Company
LDL-Cholesterol Kit	Mindray, China
HDL-Cholesterol Kit	Mindray, China
Total Cholesterol Kit	Mindray, China
Triglycerides Kit	Mindray, China
High sensitivity C-reactive protein Kit	Mindray, China
Human heat shock protein-70 Kit	Pars biochem China
Human Tumor necrosis factor- α Kit	Pars biochem China
Serum urea Kit	Architect, Abbott laboratories US
serum creatinine Kit	Bio system

2.6 Instrument Analysis and Equipments

Equipments and instruments that are used in this study are shown in table (2.3).

Table 2.3 Instrument analysis and Equipments

Instruments	Supplied Company
Disposable syringe 5 ml	DMK KOLOING- P.R.C
Gelatin tubes (Jell tube) 5 ml	China
Disposable Eppendorf tube 1ml	Afco/Jorden
Centrifuge	Heraeus-Germany
Refrigerator	Samsung (Korea)
MAGLUMI 800	Snibe-China
Elisa Human	Germany
BS-430	Mindray-China
BS-200	Mindray-China

2.7 Methods

2.7.1 BMI (body mass index) measurement

Following the recommendations provided by the World Health Organization (WHO), the body mass index (BMI) was computed. It is computed as the square of a person's height in meters divided by their weight in kilograms (kg/m2) [125].The following formula may be used to express the body mass index:

BMI = Weight (Kg) / Height (m2)

BMI were classified into three group:

1. The normal weight range's BMI is 18.5-24.9 kg/m.

2. The BMI range for overweight individuals is (25-29.9) kg/m2.

3. The obese have a BMI of > 30 kg/m.

2.7.2 Total Serum Cholesterol Determinations

TC concentration in serum and plasma was quantitatively determined using an in vitro test using photometric equipment.

Method

Cholesterol oxidase- peroxidase (CHOD-POD) method

Reaction Principle

$$\text{Cholesterol esters} \xleftrightarrow{\text{cholesterol esterase}} \text{Cholesterol} + \text{Fatty acids}$$

$$\text{Cholesterol} + O2 \xleftrightarrow{\text{cholesterol oxidase}} \text{4-Cholestenone} + H2O2$$

$$2H2O2 + Phenol + 4 - aminoantipyrine \xleftrightarrow{peroxidase} Quinoneimine\ (Pink) + 4H2O$$

The production of H2O2, which oxidizes 4-aminoantipyrine with phenol to create a colorful quinoneimine dye, was accelerated by CHE and CHO on cholesterol ester. There was a clear correlation between the rise in absorbency and the cholesterol level.

Reagents

particpants and focal points

R: Phosphate buffer (100mmol/L)

Phenol (5mmol/L)

4-Aminoantipyrine (0.3mmol/L)

Cholesterol esterase (>150KU/L)

Cholesterol oxidase (>100 KU/L) Peroxidase(5KU/L)

Setting Up Reagents

One reagent was prepared for udage.

Table .4: Assay Method for Cholesterollesterol

Materials	Blank	Sample
R:	1000 µL	1000 µL
Distilled water	10 µL	----------
Sample	----------	10 µL

After properly mixing the mixture at 37°C, the absorbance was measured ten minutes later.

Calculation

Following calibration, the analyzer automatically determined each sample's TC content.

Conversion factor: mmol/L = mg/dL x 0.026

The cholesterol measurement standard curve was depicted in Figure (2.4), and the amount of Cholesterol in every sample was computed.

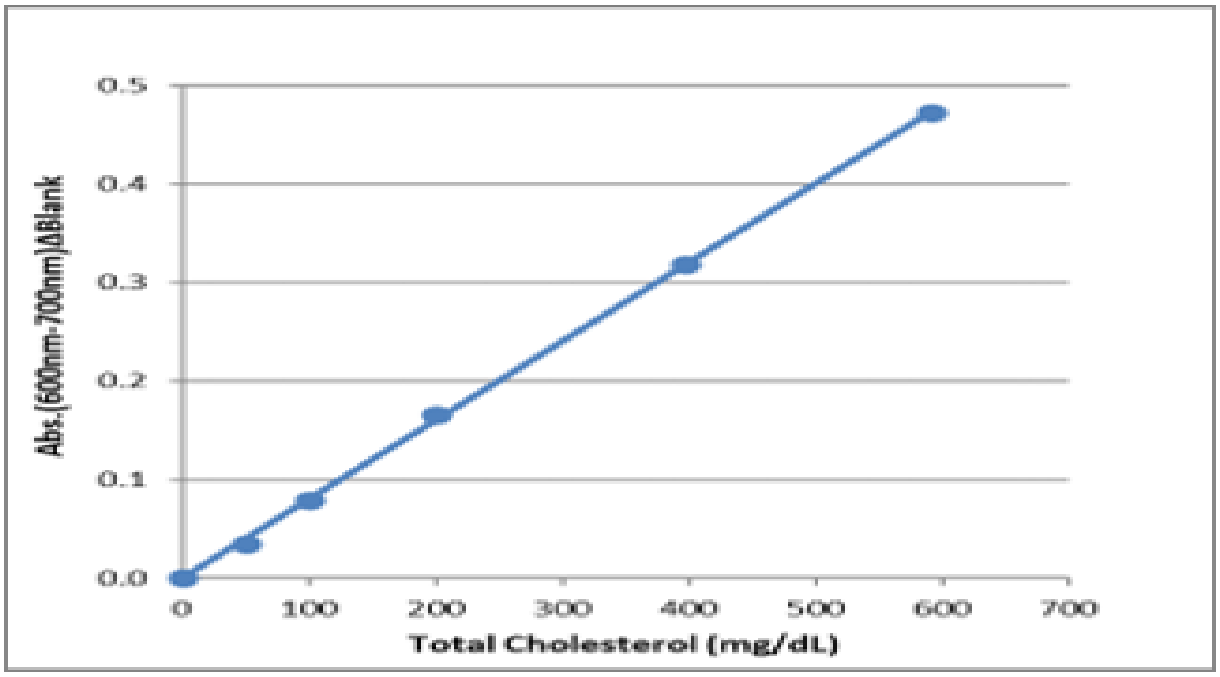


Fig (2.1): Standard Curve for calculating Cholesterol Concentration.

2.7.3 Determinations Total Serum Triglyceride

Photometric devices were utilized in an in vitro test to quantitatively determine TG concentrations in serum and plasma.

Method

The Peroxidase method using glycerokinase Peroxidase.

Principle of Reaction.

$$\text{Triglycerides} + 3H_2O \xrightarrow{\text{Lipase}} \text{Glycerol + fatty acid}$$

$$\text{Glycerol} + \text{ATP} \xleftrightarrow{\text{Glycerol Kinase}} \text{Glycerol-3-phosphate} + \text{ADP}$$

$$\text{Glycerol} - 3 - \text{phosphate} + O^2 \xleftrightarrow{\text{Glycerol}-3-\text{phosphate oxidase}}$$

Dihydroxyacetone Phosphate + H_2O_2

$$H_2O_2 + 4 - \text{Aminoantipyrine} + 4 - \text{Chlorophenol} \xleftrightarrow{\text{Peroxidase}}$$

Quinoneimine + HCl + $2H_2O$

Triglycerides are oxidized to H2O2 by the action of lipase, GK, and GPD. This forms a colored quinoneimine dye when 4-Aminoantipyrinel is oxidized. Reduced cholesterol levels were adversely linked with increased absorption.

Reagents

Components and concentrations are given below:

Phosphate buffer	50 mmol/L
4-Chlorophenol	5 mmol/L
ATP	2 mmol/L
Mg2+	4.5 mmol/L
Glycerokinase	≥0.4 U/mL
Peroxidase	≥0.5 U/mL
Lipoprotein lipase	≥1.3 U/mL
4-Aminoantipyrine	0.25 mmol/L
Glycerol-3-phosphate-oxidase	≥1.5 U/Ml

Table 2.5 Triglyceride Assay Procedure

Materials	Blank	Sample
R: **Distilled water** **Sample**	1000 µL 10 µL ----------	1000 Ml ---------- 10 Ml

The mixture was completely mixed at 37°C, and the absorbance was measured 10 minutes later.

Calculation

After calibration, the analyzer automatically determined the TG concenteation of each sample.

Conversion factor: ″mg/dL x 0.0113=mmol/L

Figure (2.5) depicts the triglyceride level in each sample as estimated using the triglyceride determination standard curve.

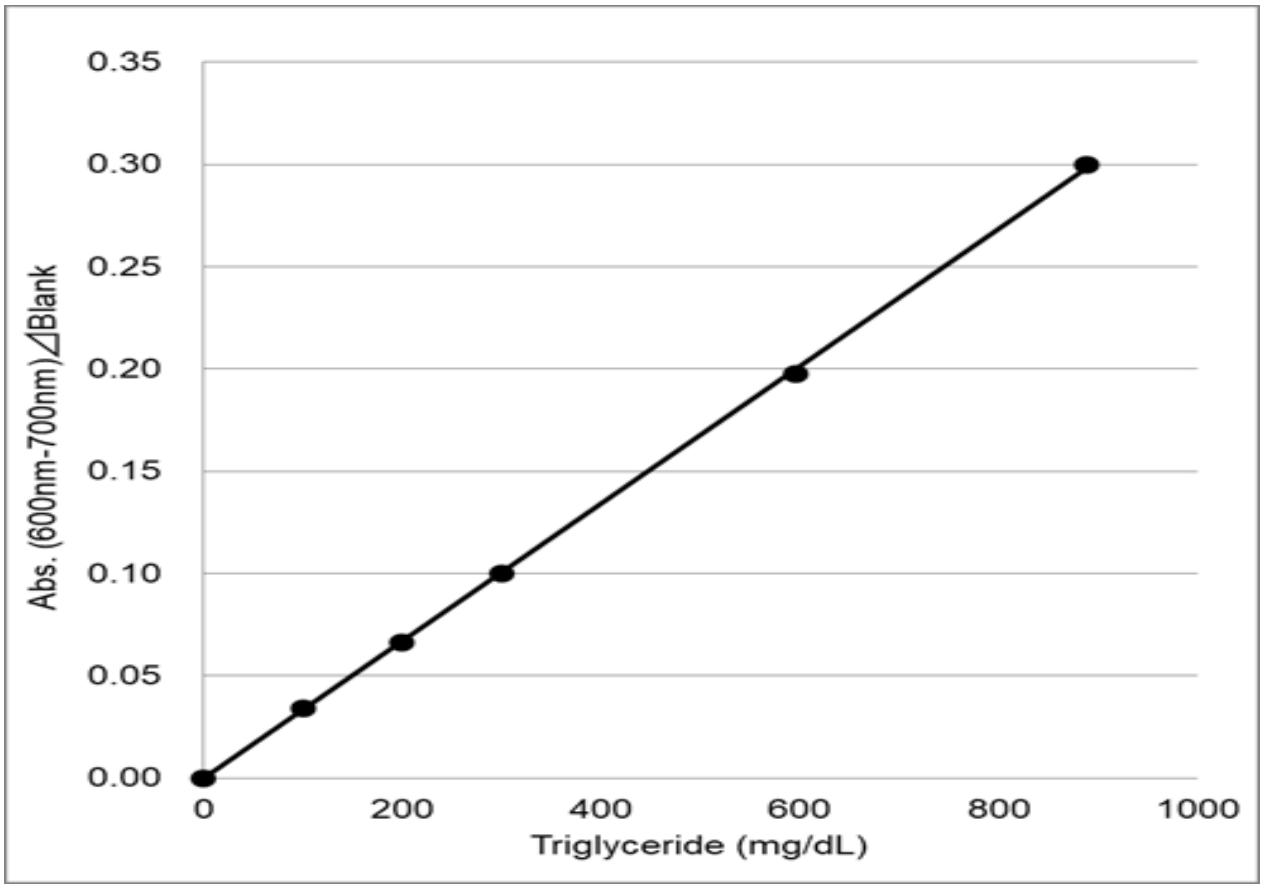


Fig (2.2): Shows the Standard Curve for calculating the Concentration of Triglyceride.

2.7.4 Serum HDL-Cholesterol Determinations

photometric systems were employed in a vitro test for the quantitative assessment of In an experiment conducted in vitro,photometric devices were utilized to HDL-Cholesterol (HDL-C) present in serum˝.

Method

Direct method was used.

Reaction Principle

$$(1)\ \text{LDL, VLDL, Chylomicron} \xleftrightarrow{Cholestrol\ esterase\ Cholestrol\ oxidase} \text{Cholestenone} + H_2O2$$

$$2H2O \xleftrightarrow{\text{catalase}} 2H2O+O2$$

$$(2)\ \text{HDL} \xleftrightarrow{cholestrol\ esterase\ Cholestrol\ oxidase} \text{Cholestenone} + H_2O_2$$

$$H2O2 + \text{HDAOS} + 4 - \text{aminoantipyrin} \xleftrightarrow{Peroxidase} \text{Quinonimine}$$

At 600 nm, the System tracks changes in absorbance. The system employed this shift in absorbance to express and quantify the HDL-cholesterol concentration, which was directly proportional to the amount of cholesterol in the sample.

Reagents

Components and Concentrations were given below:

R1: Good's buffer (100 mmol/L)

Cholesterolesteras (600U/L)

Cholesteroloxidase (380U/L)

Catalase(600 KU/L)

HDAOS (0.42 mmol/L)

R2: Good's buffer (100mmol/L)

4-aminoantipyrine (1.0mmol/L)

Peroxidase (>2.8U/mL)

Surfactant (<2%)

Table 2.6 Shows the of HDL-Cholesterol Assay protocol.

Materials	Blank	Sample
Reagent 1 **Distilled water** **Sample**	900 µL 12 µL ----------	900 Ml ---------- 12 Ml

The mixture was mixed thoroughly for 5 min. at 37°C, then add

Reagent 2	**300 µL**	**300 Ml**

The mixture was mixed thoroughly at 37°C for 5 min., and then read the absorbance change value.

Calculation

Each sample's HDL-Cholesterol level was ascertained charting the HDL-Cholesterol determination standard curve in Figure (2.6) .

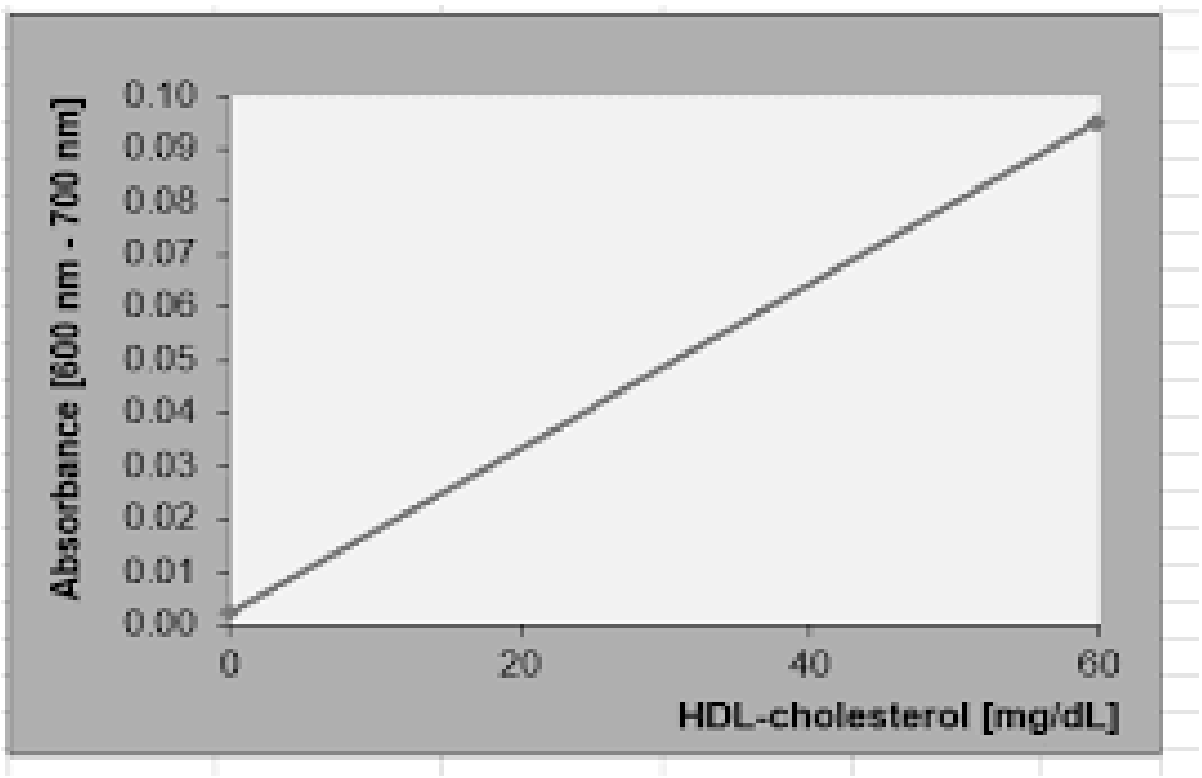


Fig (2. 3):Standard Curve of determining the Concentration of HDL-Cholesterol.

2.7.5 Serum LDL-Cholesterol Determinations

The LDL-Cholesterol (LDL-C) content in serum was quantitatively determined using an in vitro test using photometric equipment.

Method

The direct approach was employed.

Reaction Principle

$$(1)\ \text{HDL, VLDL, Chylomicrons} \xrightarrow{\text{cholesterol esterase + cholesterol oxidase}} \text{Cholestenone} + H_2O_2$$

$$2H_2\acute{O} \xrightarrow{\text{catalase}} 2H_2O + O_2$$

$$(2)\ \text{LDL} \xleftrightarrow{\text{cholesterol esterase + cholesterol oxidase}} \text{Cholestenone} + H_2O_2$$

$$H2O2 + TOOS + 4-\text{aminoantipyrin} \xleftrightarrow{\text{peroxidase}} \text{Quinonimine}$$

Any changes in absorbance at 600 nm are monitored by the system. The LDL-cholesterol concentration is expressed by the method based on this shift in absorbance, which was negatively correlated with the amount of cholesterol in the sample.

Reagents

R1: Good's buffer (50 mmol/L)

Cholesterol esterase (600 U/L)

Cholesterol oxidase (500 U/L)

Catalase (600 KU/L

TOOS (2 mmol/L)

R 2: Good's buffer (50 mmol/L)

4-aminoantipyrine (4 mmol/L)

Peroxidase (4 U/mL)

Table 2.7 Assay procedure of LDL-Cholesterol

Materials	Blank	Sample
Reagent 1 **Distilled water** **Sample**	900 Ml 12 µL ----------	900 µL ---------- 12 µL

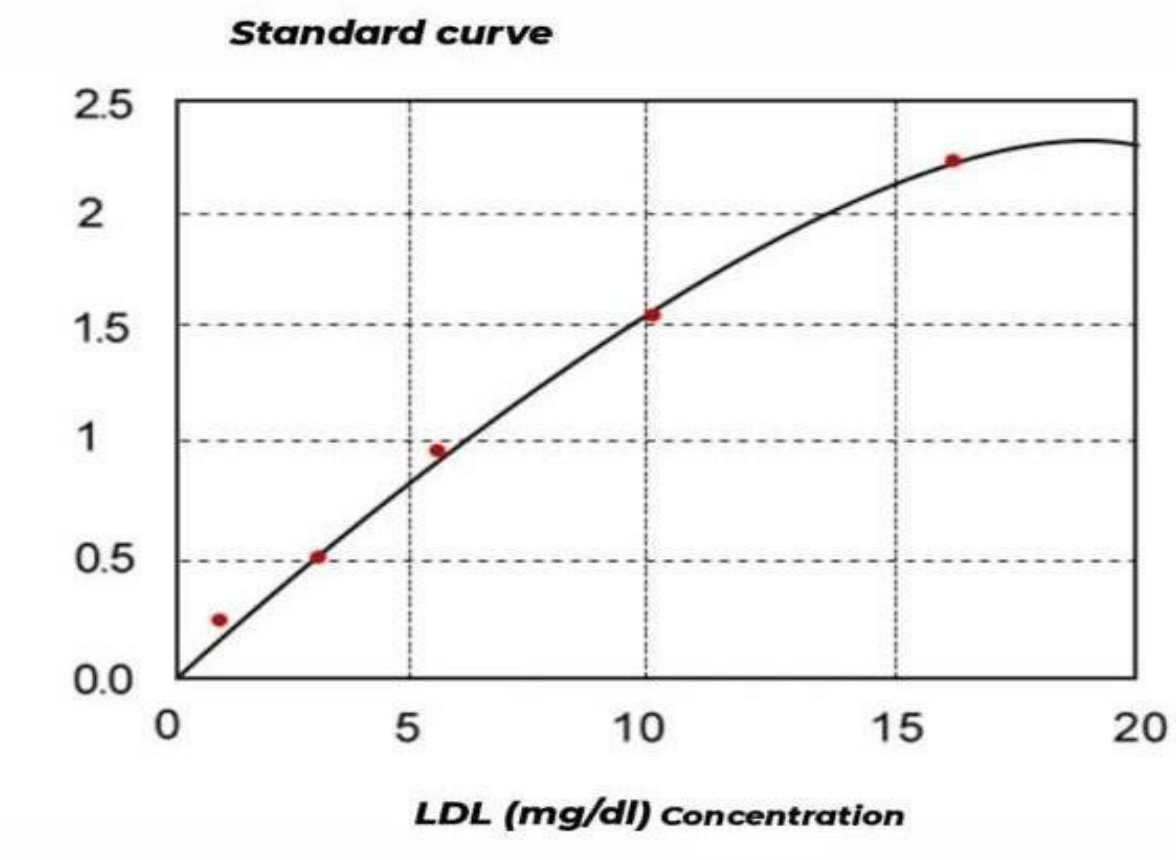
Combine well, let stand at 37°C for five minutes, and then check the absorbance change value.

Reagent 2	300 Ml	300 µL

Mix thoroughly, incubate at 37°C for 5 min, and then read the absorbance change value.

Calculation

The standard curve for calculating LDL-Cholesterol, shown in Figure (2.7), was used to determine the LDL-Cholesterol level in each sample.



Fig(2.4): Standard Curve of determining the Concentration of LDL-Cholesterol.

2.7.6 Inflammation Parameters

2.7.6.1 "High Sensitivity C-Reactive Protein Measurement"

The latex particle enhanced immunoturbidimetric test quantifies the concentration of high-sensitivity C-reactive protein in blood or plasma using the Mindray BS-200 Analyzer. only while doing in vitro experiments.

Principle of the Test

Antibody-specific to that protein-coated latex particles cluster together to form immunological complexes when human CRP from the sample is present. The immune complexes increase light scattering in proportion to the blood amount of CRP. The quantity of light scattering is measured by reading the turbidity (absorbance) at 570 nm. The CRP concentration was determined by creating a calibration curve with CRP standards at predetermined values.

Reagents

R-1: Glycine buffer as a buffer reagent: 170 mm

R-2: Textile Gel

The latex particles is 0.20% (w/v) in size.

Reagent Preparation

Reagents do not require reconstitution as they are ready for use. Before using, carefully combine.

Calculations

Figure (2.8) displays the standard curve for the determination of high sensitivity C-reactive protein, which was used to determine the amount of this protein in each sample.

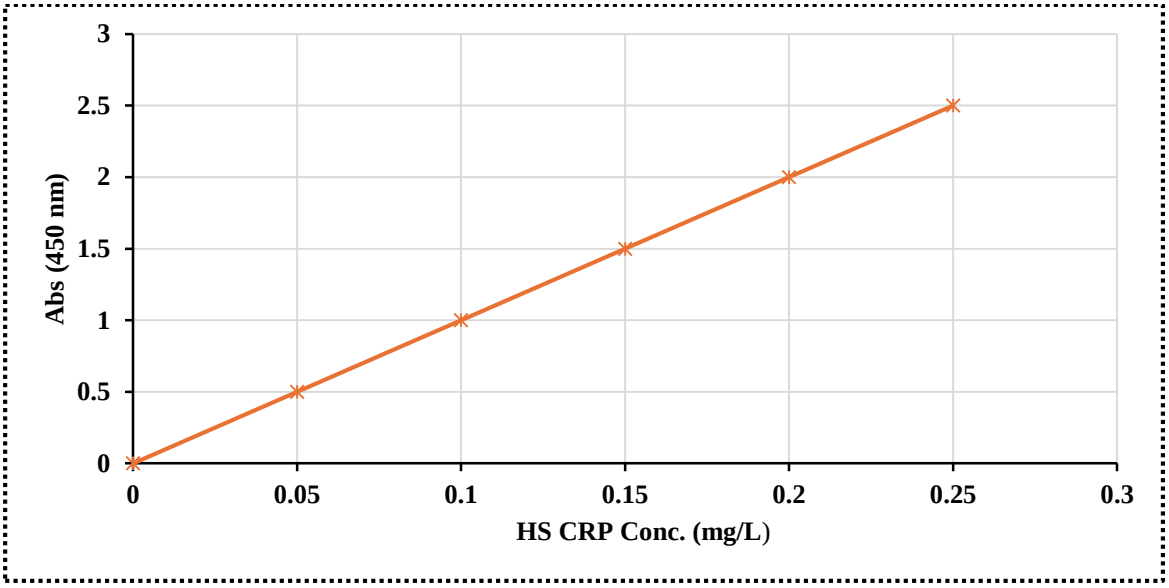


Fig. (2.5) shows the standard curve for calculating the concentration of C-reactive protein with high sensitivity.

Expected Values

In healthy individuals, a CRP level of less than 3.0 mg/L is normal. It is advised that every laboratory define its own acceptable range.

2.7.6.2 Estimation of Tumor necrosis factor, TNF- α in serum concentration

Using an enzyme-linked immunosorbent assay (ELISA) approach and a ready test kit of Chinese origin, the TNF-α content in the serum was calculated.

Principle

To coat microtiter plate wells, generate a solid-phase antibody, and subsequently introduce TNF-α into the wells, the reagent quantifies the amount of pure human TNF-α antibody in the sample; the combined TNF-α antibody binds to both TNF-α and solid-phase antibody. An extensive rinsing process results in the formation of antibody-antigen-enzyme-antibody complexes containing HRP-labeled HRP. The substrate becomes blue upon the addition of the TMB substrate solution. Reactions that are HRP-catalyzed can be stopped by adding a solution of sulfuric acid. Spectrophotometric measurement of the hue shift is done at a wavelength of 450 nm. Next, the optical density (OD) of the samples is compared to the standard curve to ascertain the TNF-α content in the samples.

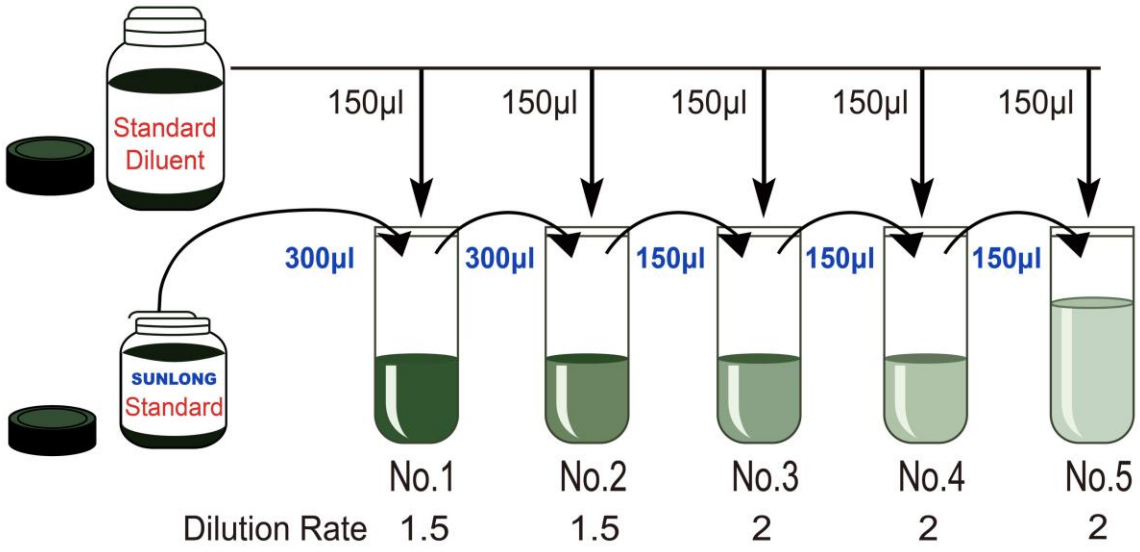
Table 2.8: Materials provided with the kit

Materials provided	with the kit 96	determinations Storage
User manual	1	R.T.
Closure plate membrane	2	R.T.
Sealed bags	2	R.T.
Microelisa stripplate	1	2-8℃
Standard：360 pg/ml	0.5ml×1 bottle	2-8℃
Standard diluent	1.5ml×1 bottle	2-8℃
HRP-Conjugate reagent	6ml×1 bottle	2-8℃
Sample diluent	6ml×1 bottle	2-8℃
Chromogen Solution A	6ml×1 bottle	2-8℃
Chromogen Solution B	6ml×1 bottle	2-8℃
Stop Solution	6ml×1 bottle	2-8℃
wash solution	20ml (30X)×1bottle	2-8℃

Procedure

1.The sample was diluted and added to standard: ten standard wells were produced on coated ELISA plates; wells 1 and 2 were then filled with 100 L of the standard, followed by 50 L of the diluted standard, and mixed; The first and second wells' 100 liters should be taken out and added individually to the third and fourth wells. After that, the traditional 50 L dilution was added to the third and fourth wells and mixed; The third and fourth wells were then empty and 50 liters were added to the fifth and sixth wells; the fifth and sixth wells were then mixed with a 50 L standard dilution; the fifth and sixth wells were then cleared of 50 liters and added to the seventh and eighth wells; finally, the seventh and eighth wells received the standard dilution of 50 liters.

After being taken out of the refrigerator, the kit equilibrated at ambient temperature for fifteen to thirty minutes. After opening, the coated ELISA plates should be stored in a sealed bag if they are not going to be utilized. In order to separate crystallization, wash buffer can be heated to dissolve fully and mixed; 50 L were taken out of the 7th and 8th wells and added to the 9th and 10th wells; the standard dilution then added 50 L to the 9th and 10th wells, mixed them, and then took 50 L out of the 9th and 10th wells. discarded a 50 L sample was added to each well after dilution.



360pg/ml	240pg/ml	120pg/ml	80pg/ml	60pg/ml	20pg/ml

2. Sample added: The empty comparison wells apart (the other procedure is the same, However, the HRP-Conjugate reagent and sample are added to the empty comparison wells. Examine the sample thoroughly. The test sample well received a 40 µL sample dilution, a 10 µL test sample (the final 5-fold dilution sample), and the sample was put to the wells, gently mixed, and as much of the well wall as possible was contacted.

3. Incubate: The plate was incubated at 37 °C for 30 minutes following the plate sealing film's application.

4. Composition fluid: reserve after diluting the solution 30-fold (or 20-fold) with distilled water.

5. Washing and discarding the liquid from the closing plate membrane, followed by swing drying, adding the wash solution to each well, waiting 30 seconds, blotting, repeating five times, and patting dry.

6. All wells received a volume of 50 μL of HRP-Conjugate reagent, with the exception of the empty control well.

7. Step 3 describes the incubation process.

8. Washing followed the instructions in step 3.

9. Coloring: Pour 50 μl of each Chromogen Solution A and B into each well, stir gently, and let stand at 37°C for 15 minutes.

10. Termination: To end the reaction, 50 μL of stop solution was applied to each well. The well need to turn yellow instead of blue.

11-Elsevier used a microtiter plate reader to read the O.D. absorbance at 450 meters. The blank control well was configured to have an OD value of 0. The experiment was completed in fifteen minutes following the stop solution's administration.

Calculation

With reference to the TNF-α concentration estimate standard curve in pg/ml is displayed in the (fig 2-9)

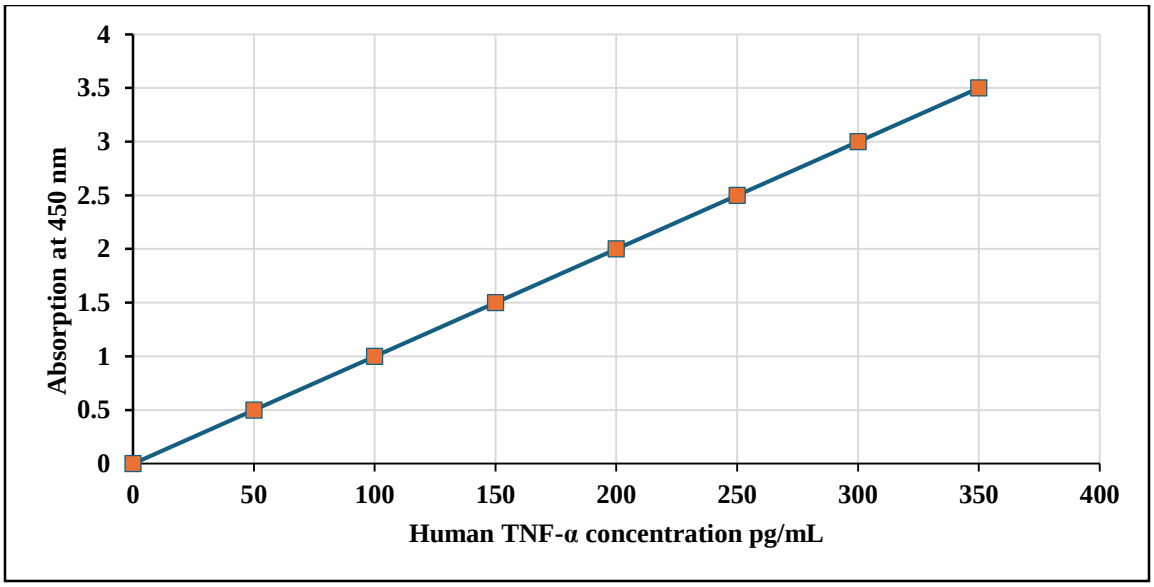


Fig. (2.6): Standard curve for estimating TNF-α levels in serum

2.7.6.3 Calculating the serum concentration of human heat shock protein-70 (HSP_70)

The enzyme-linked immunosorbent assay (ELISA) method and a ready test kit of a Chinese origin were used to determine the HSP-70 content in the serum.

Principle

Purified human HSP-70 antibody was used in the reagent experiment HSP-70 is added to microtiter plate wells after coating them with solid-phase antibody and solid-phase antibody have been mixed such that the combined HSP-70antibody binds to both. An extensive rinsing process results in the formation of antibody-antigen-enzyme-antibody complexes containing HRP-labeled HRP. Addition of the TMB substrate solution causes the substrate to become blue. A process catalyzed by HRP is stopped by the addition of a sulphuric acid solution. Spectrophotometric measurement of the hue shift is done at a wavelength of 450 nm. The optical density (OD) of the samples is

then compared to the standard curve to ascertain the HSP-70 content in the samples.

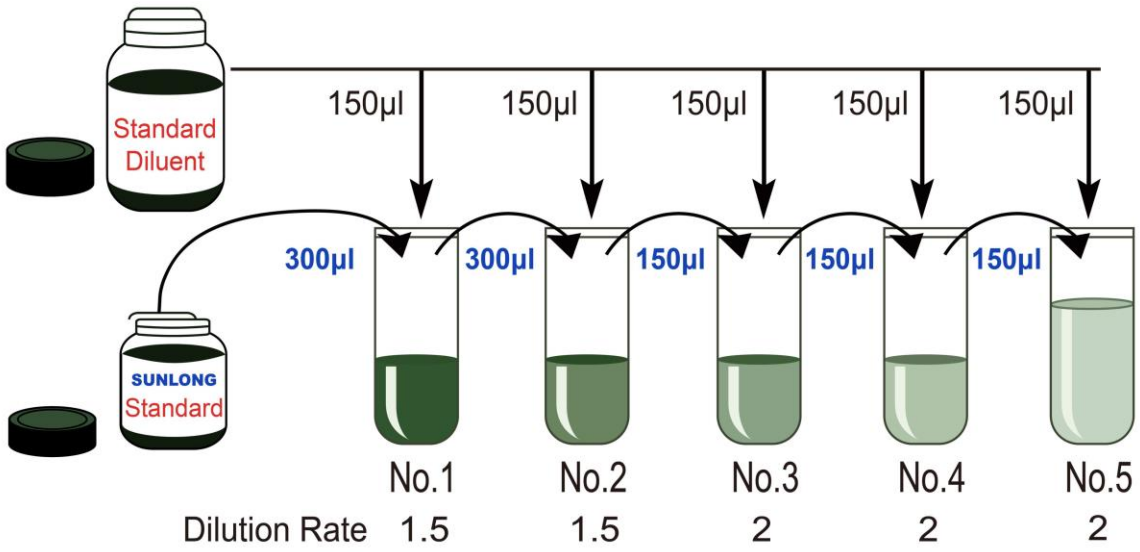
Table 2.9: Materials provided with the kit

Materials provided with the kit	**96 determinations**	Storage
User manual	1	R.T.
Closure plate membrane	2	R.T.
Sealed bags	1	R.T.
Microelisa stripplate	1	2-8℃
Standard：54ng/ml	0.5ml×1 bottle	2-8℃
Standard diluent	1.5ml×1 bottle	2-8℃
HRP-Conjugate reagent	6ml×1 bottle	2-8℃
Sample diluent	6ml×1 bottle	2-8℃
Chromogen Solution A	6ml×1 bottle	2-8℃
Chromogen Solution B	6ml×1 bottle	2-8℃
Stop Solution	6ml×1 bottle	2-8℃
wash solution	20ml (30X)×1bottle	2-8℃

Procedure

1. The sample was diluted and added to standard: ten standard wells were produced on coated ELISA plates; wells 1 and 2 were then filled with 100 L of the standard, followed by 50 L of the diluted standard, and mixed; The first and second wells' 100 liters should be taken out and added individually to the third and fourth wells. The third and fourth wells were then filled with the conventional 50 L dilution and stirred; The third and fourth wells were then

empty and 50 liters were added to the fifth and sixth wells; the fifth and sixth wells were then mixed with a 50 L standard dilution; the fifth and sixth wells were then cleared of 50 liters and added to the seventh and eighth wells; finally, the seventh and eighth wells received the standard dilution of 50 liters. After being taken out of the refrigerator, the kit equilibrated at ambient temperature for fifteen to thirty minutes. After opening, the coated ELISA plates should be stored in a sealed bag if they are not going to be utilized. Wash buffer will separate crystallization, can be heated to dissolve well, and mix; 50 L were removed from the 7th and 8th wells and added to the 9th and 10th wells, the standard dilution added 50 L to the 9th and 10th wells, mixed, and then 50 L were removed from the 9th and 10th wells discarded (a 50 L sample was added to each well after dilution, (density: 48 ng/ml, 32 ng/ml



54ng/ml	36ng/ml	24ng/ml	12ng/ml	6ng/ml	3ng/ml

2. Sample added: Place the empty comparison wells apart (the other procedure is the same, but the empty comparison wells add sample and HRP-Conjugate

reagent). Examine the sample thoroughly. The test sample well received a 40 µL sample dilution, a 10 µL test sample (the final 5-fold dilution sample), and the sample was put to the wells, gently mixed, and as much of the well wall as possible was contacted.

3. Incubate: The plate was incubated at 37 °C for 30 minutes following the plate sealing film's application.

4. Composition fluid: reserve after diluting the solution 30-fold (or 20-fold) with distilled water.

5. Washing and discarding the liquid from the closing plate membrane, followed by swing drying, adding the wash solution to each well, waiting 30 seconds, blotting, repeating five times, and patting dry.

6. All wells received a volume of 50 µL of HRP-Conjugate reagent, with the exception of the empty control well.

7. Step 3 describes the incubation process.

8. Washing followed the instructions in step 3.

9. Coloring: Pour 50 µl of each Chromogen Solution A and B into each well, stir gently, and let stand at 37°C for 15 minutes.

10. Termination: To end the reaction, 50 µL of stop solution was applied to each well. The color of the well should change from blue to yellow.

11. A microtiter plate reader was used to read the O.D. absorbance at 450 nm. The OD value of the blank control well was set as zero. The experiment was completed in fifteen minutes following the stop solution's administration.

Calculation

Referring to the standard curve of HSP-70 concentration estimation serum in unit (ng/ml) as shown in the (fig 2-10)

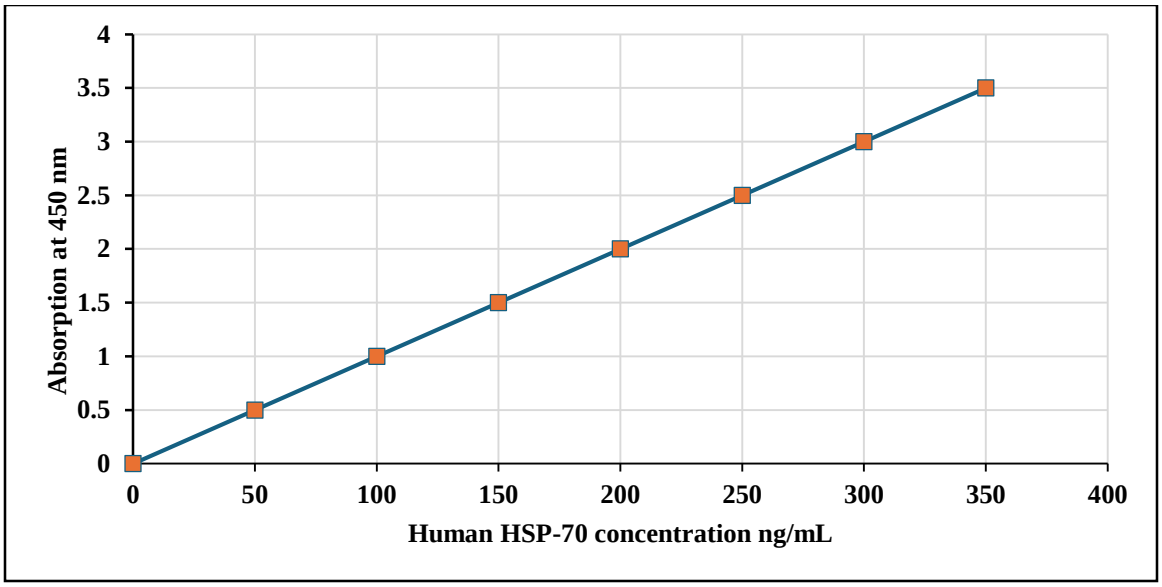


Fig (2.7): standard curve of HSP-70 concentration estimation in serum

2.7.7. Assessment of Urea Concentration.

Abbott Laboratories US Kit, the architect, was used to calculate the urea content.

Principle

The urea test kit is designed to identify the presence of urea in biological fluids such as urine, serum, plasma, cell lysates, and tissue homogenates. To get a blue-green result, samples are compared to a known concentration of urea standard in a 96-well microliter plate design. The samples and standards are then incubated with the urea-hydrolyzing enzyme urease, a chromogenic in alkali standard solution, for 10 minutes. After 30 minutes, a standard 96-well spectrophotometric microplate reader is used to read the plate at an optical density of 580 nm to 360 nm. Increases of the urea concentration are correlated with increased OD values. The sample's urea concentration is

assessed by contrasting it with accepted urea standards. Up to 50 mg/dl urea, the standard curve is linear.

Preparation of Reagents

Assay buffer 1-1X, Mix thoroughly after dilution of the assay buffer 1:10 with deionized water. You can keep the 1X assay buffer for up to six months at 4°C.

Ammonia/urease reagent Place 40 mg of urease 10 ammonia reagent into a 10 MI solution or 100 tests to reconstitute the urease enzyme at a concentration of 4 mg/ml and well mix until dissolved. Only prepare what you will need at that moment, discarding the solution of urease ammonia reagent.

Calculation of Results

1. For every sample, control, and standard, the average absorbance and value were calculated.
2. The average zero standard value, along with all other standard and sample values, were removed. There has been a backdrop change.
3. For samples with two paired wells, one with urease and the other without, the absorbance difference was calculated by deducting the urease-treated sample well absorbance values (A+U) from the sample well absorbance values (A-U) without urease. The sample's ammonia background concentration is represented by the (A-U) sample value, while the sample's total urea and ammonia background concentration is represented by the (A+U) sample value. The absorbance disparity (A) is caused by the urea concentration.

4-To measure and approximate the quantity of urea in each sample, the absorbance value was compared to the standard curve. Utilize values only within the range of the standard curve.

(A)=(A+U)-(A-U)

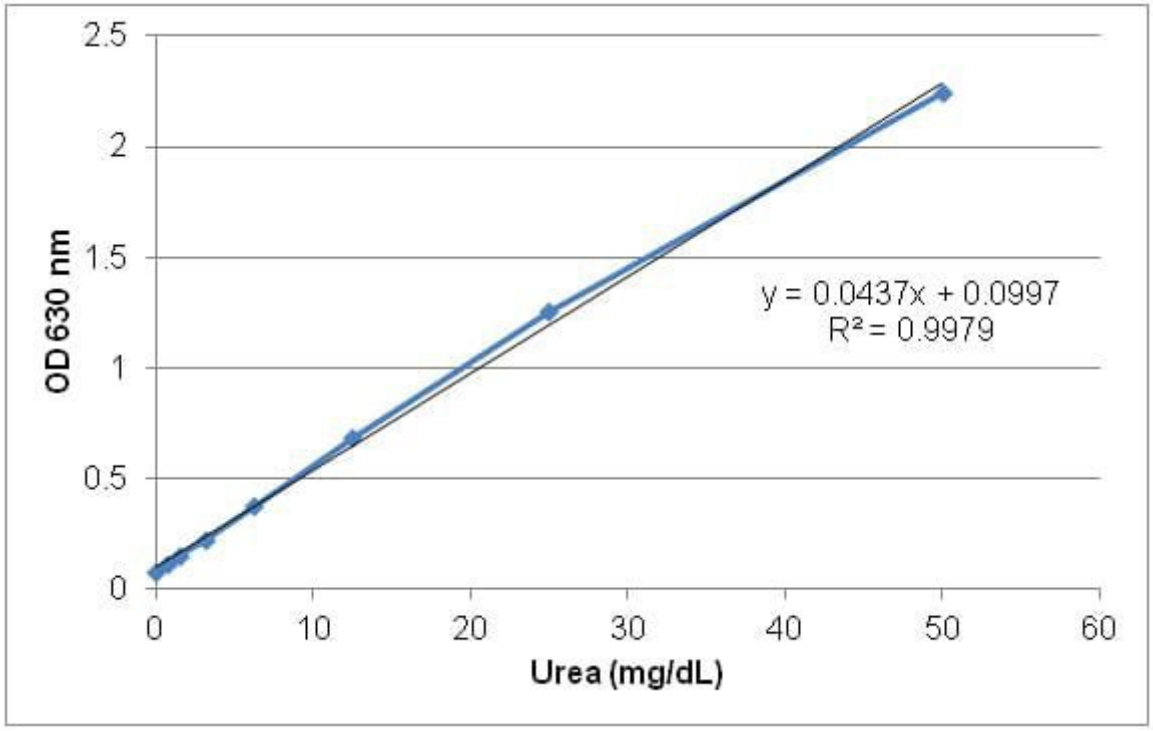


Fig (2.8): standard curve of determination of urea concentration.

2.7.7.1 Assessment of creatinine concentration

Using a bio system kit, the concentration of creatinine was measured.

Principle

The urinary creatinine assess kit from Cell Bio Labs measures the amount of creatinine in urine samples on a microliter plate with 96 wells and compares it to a standard sample of creatinine at a specific concentration. The standards are incubated with a reaction reagent for 30 minutes, which turns yellow when it reacts with creatinine and produces the creatinine-picrate

complex. To read the plate at 490 nm, a standard 96-well spectrophotometric microplate reader is utilized. Elevated creatinine levels are associated with increased OD levels. The creatinine concentration in the samples are determined by comparing them to known creatinine standard. Non-specific chromogen interference can be examined using the creatinine quencher, which eliminates all creatinine absorbance by dissolving the creatinine-picrate complex. Non-specific chromogens are the source of the residual absorbance, which may be deducted from the total results.

Preparation of Reagents

Creatinine reaction reagent: combine three parts creatinine reaction buffer and one part acid solution; for instance, to prepare 15 milliliters of creatinine reaction buffer and 5 milliliters of acid solution for 100 trials. This creatinine reaction reagent should be well combined and stored at room temperature for up to one week.

Calculation

1. The initial average absorbance (Ai) values for each standard and sample were calculated.
2. Each sample and standard had its final average absorbance (Af) values calculated.
3. The final absorbance was subtracted from the initial absorbance to determine the adjusted absorption (Ac).

4-The optimal curve was created by plotting the absorbance of the creatinine standards against their concentration. Regression analysis software or log paper can be used to linearize the data.

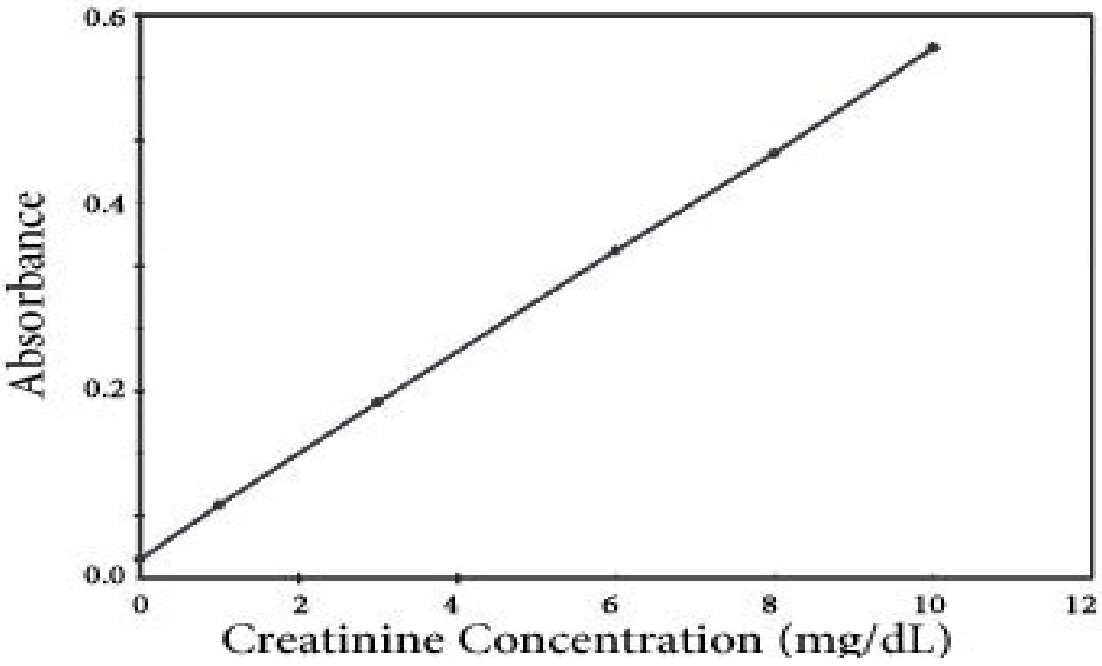


Fig (2.9): standard curve of determination of creatinine concentration.

2.8 Data Analysis

Statistical analysis was carried out using SPSS version 27. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (Means ± SD). T-Test was used to find the p value ≤ 0.0001 by comparison between groups. Correlation coefficient (r) was used to assess the relationship between two continuous variables. A p-value of ≤ 0.05 was considered as significant. Roc analysis was used to find the sensitivity of inflammatory biomarkers.

Chapter Three

Results and Discussions

3.Results

3.1 Comparison of the lipid profile, urea and creatinine in hypertension patients.

Table 3.1: Comparison of the lipid profile, urea and creatinine, between patients and the control group.

Parameter	Subject	Means ± S.D	P value
Age(years)	Patient	55.00 ± 5.11	**N.S**
	Control	52.00 ± 6.30	
Cholesterol(mg/dl)	Patient	197.00 ± 55.10	**0.0001**
	Control	132.48 ± 18.69	
Triglycerides(mg/dl)	Patient	175.73 ± 73.88	**0.0001**
	Control	97.11 ± 22.19	
VLDL(mg/dl)	Patient	34.93 ± 14.72	**0.0001**
	Control	19.73 ± 5.22	
LDL(mg/dl)	Patient	196.61 ± 68.06	**0.0001**
	Control	77.57 ± 39.01	
HDL(mg/dl)	Patient	40.62 ± 6.47	**0.0001**
	Control	76.37 ± 36.21	
Creatinine(mmol/L)	Patient	0.88 ± 0.41	**0.0001**
	Control	0.70 ± 0.27	
Urea(mmol/L)	Patient	33.27 ± 11.33	**0.0001**
	Control	22.68 ± 5.66	

Table 3.2: Comparison of the lipid profile, urea and creatinine, between male patients and female patients(No. of man=28 No. of woman=22)

Parameter	Subject	Means ± S.D	P value
Triglycerides (mg/dl)	Man	173.26 ± 79.07	**0.0001**
	Woman	103.48 ± 22.44	
Cholesterol(mg/dl)	Man	195.68 ± 55.46	**0.0001**
	Woman	133.05 ± 20.64	
VLDL(mg/dl)	Man	34.21 ± 15.68	**0.0001**
	Woman	21.26 ± 5.62	
LDL(mg/dl)	Man	208.03 ± 67.17	**0.0001**
	Woman	97.13 ± 37.95	
HDL(mg/dl)	Man	38.63 ± 6.19	**0.0001**
	Woman	59.94 ± 34.26	
Creatinine(mmol/L)	Man	1.01 ± 0.48	**0.0001**
	Woman	0.73 ± 0.31	
Urea(mmol/L)	Man	36.73 ± 10.30	**0.0001**
	Woman	22.47 ± 6.38	

Table 3.3: Comparison of the lipid profile, urea and creatinine, between patients aged 40-55 and patients aged 56-70.

Parameter	Subject	Means ± S.D	P value
Triglycerides(mg/dl)	40 – 55	164.91 ± 71.34	**N.S**
	56 – 70	190.35 ± 76.89	
VLDL(mg/dl)	40 – 55	32.61 ± 14.11	**N.S**
	56 – 70	38.61 ± 15.37	
LDL(mg/dl)	40 – 55	207.26 ± 67.85	**N.S**
	56 – 70	182.20 ± 67.65	
HDL(mg/dl)	40 – 55	42.39 ± 7.16	**0.05**
	56 – 70	38.23 ± 4.60	
Cholesterol(mg/dl)	40 – 55	197.00 ± 61.95	**N.S**
	56 – 70	197.00 ± 40.06	
Creatinine(mmol/L)	40 – 55	0.83 ± 0.40	**N.S**
	56 – 70	0.95 ± 0.43	
Urea(mmol/L)	40 – 55	32.60 ± 11.01	**N.S**
	56 – 70	34.14 ± 12.02	

Table 3.4: Comparison of the lipid profile, urea and creatinine, between patients with high blood pressure only and patients with other diseases.

Parameter	Subject	Means ± S.D	P value
Triglycerides(mg/dl)	patients with Hypertension	161.43 ± 67.47	**0.02**
	patients Other diseases	215.92 ± 80.73	
VLDL(mg/dl)	patients with Hypertension	32.00 ± 13.32	**0.03**
	patients Other diseases	42.53 ± 15.66	
LDL(mg/dl)	patients with Hypertension	176.02 ± 63.51	**0.01**
	patients Other diseases	248.03 ± 53.19	
HDL(mg/dl)	patients with Hypertension	40.25 ± 6.06	**N.s**
	patients Other diseases	41.15 ± 7.35	
Cholesterol(mg/dl)	patients with Hypertension	184.86 ± 52.86	**0.01**
	patients Other diseases	229.08 ± 51.12	
Creatinine(mmol/L)	patients with Hypertension	0.79 ± 0.28	**0.04**
	patients Other diseases	1.06 ± 0.56	
Urea(mmol/L)	patients with Hypertension	31.17 ± 10.87	**0.05**
	patients Other diseases	38.46 ± 10.86	

* patient's Other diseases: diabetes, kidney disease, high lipid profile.

3.2 Comparison of the TNF- α, HSP-70 and HS CRP in hypertension patients.

Table 3.5: Comparison of the TNF- α, HSP-70 and HS CRP between patients and the control group.

Parameter	Subject	Means ± S.D	P value
HS CRP (mg/l)	Patient	0.68 ± 1.27	0.0001
	Control	0.37 ± 0.21	
TNF – α (pg/ml)	Patient	0.73 ± 9.77	N.S
	Control	1.38 ± 13.87	
HSP-70 (ng/ml)	Patient	3.21 ± 1.72	0.0001
	Control	1.76 ± 2.26	

Table 3.6: Comparison of the TNF- α, HSP-70and HS CRP between male patients and female patients. No.of man=28,No.of woman=22

Parameter	Subject	Means ± S.D	P value
HS CRP (mg/l)	Man	0.91 ± 1.75	N.S
	Woman	0.40 ± 0.21	
TNF – α (pg/ml)	Man	0.69 ± 8.57	N.S
	Woman	1.76 ± 8.35	
HSP-70 (ng/ml)	Man	3.64 ± 1.73	0.0001
	Woman	1.54 ± 1.88	

Table 3.7: Comparison of the TNF- α, HSP-70and HS CRP between patients aged 40-55 and patients aged 56-70.

Parameter	Subject	Means ± S.D	P value
HS CRP (mg/l)	40 - 55	0.88 ± 1.63	N.S
	56 - 70	0.41 ± 0.36	
TNF – α (pg/ml)	40 - 55	2.55 ± 8.40	N.S
	56 - 70	1.70 ± 11.13	
HSP-70 (ng/ml)	40 - 55	3.28 ± 1.81	N.S
	56 - 70	3.13 ± 1.63	

Table 3.8: Comparison of the TNF- α, HSP-70and HS CRP between patients with high blood pressure only and patients with other diseases.

Parameter	Subject	Means ± S.D	P value
HS CRP (mg/l)	patients with Hypertension	0.75 ± 1.44	N.S
	Patients with Other diseases	0.90 ± 0.60	
TNF - α (pg/ml)	patients with Hypertension	6.56 ± 8.08	N.S
	patients with Other diseases	6.07 ± 4.80	
HSP-70 (ng/ml)	patients with Hypertension	3.54 ± 1.19	N.S
	Patients with Other diseases	3.45 ± 1.49	

* patient's with Other diseases: diabetes, kidney disease, high lipid profile.

3.3 The ration between duration of hypertension and lipid profile, urea and creatinine.

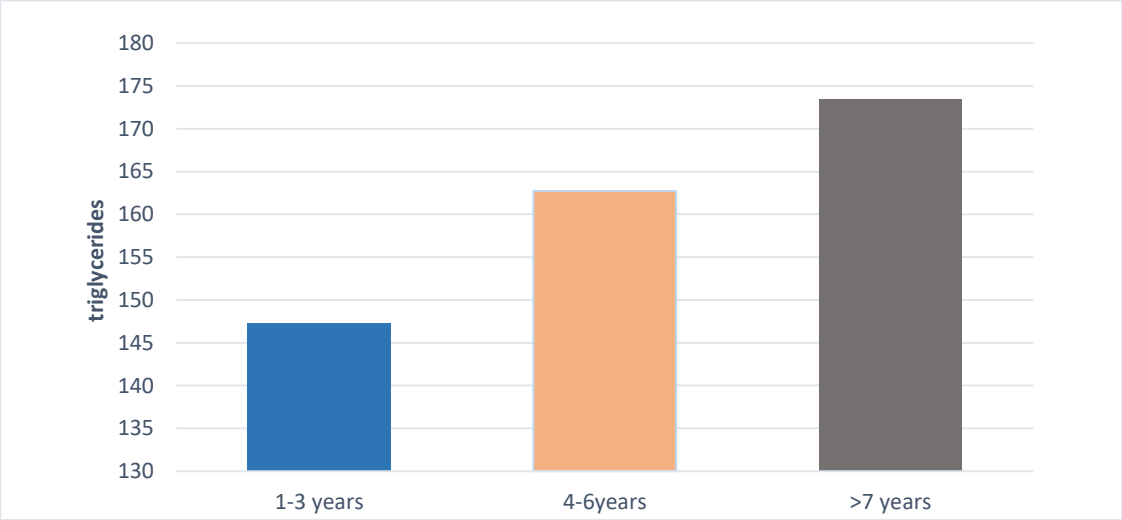


Fig (3.1): The relation between duration of hypertension and the level of triglycerides.

The relationship between triglycerides in patients with hypertension and the duration of their disease, is given in 1-3 years, 4-6 years, and older than 7 years. The measurement showed an increase in the percentage as the duration of illness in patients with hypertension increased.

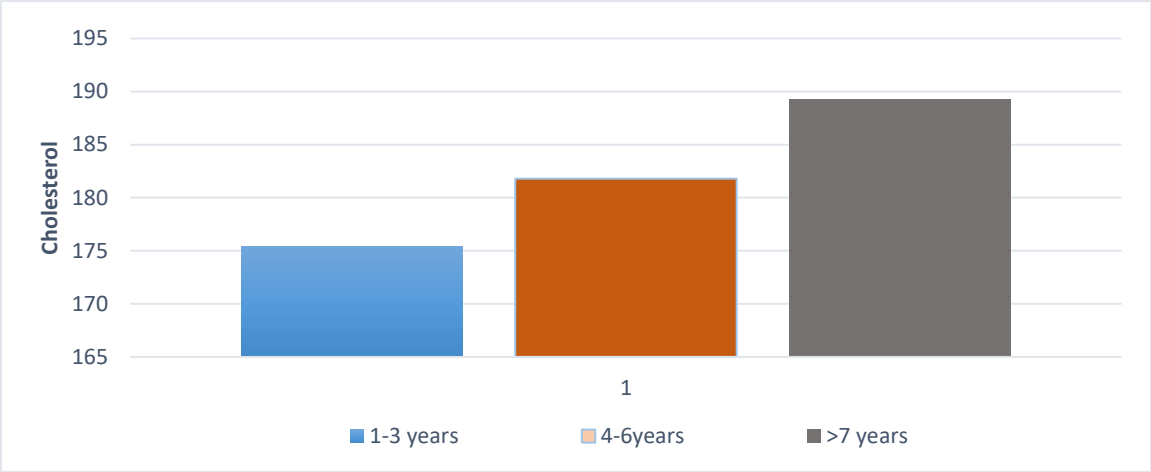


Fig (3.2): The relation between duration of hypertension and the level of Cholesterol.

The connection between Cholesterol in patients with hypertension and the length of their sickness, is were classified into 1-3 yrs, 4-6 yrs, and older than 7 yrs. The assessment showed an increase in the Proportion as the length of illness in those with hypertension escalated.

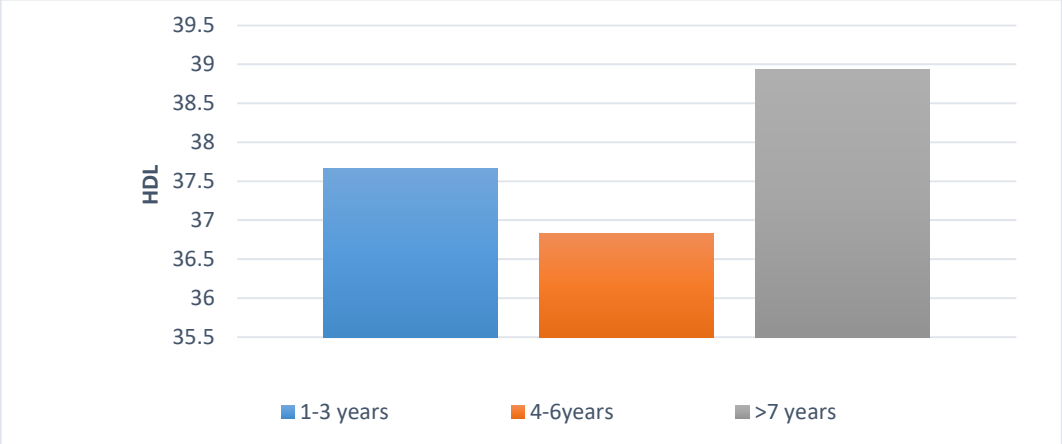
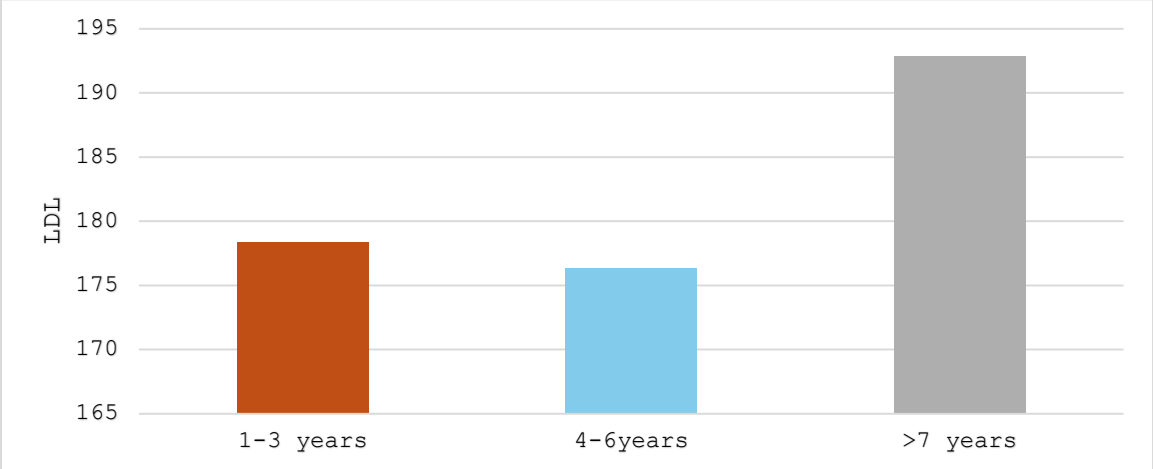


Fig (3.3): The relation between duration of hypertension and the level of HDL

The connection between HDL in individuals with hypertension and the length of their illness, which was separated into 1-3 yrs, 4-6 yrs, and more than 7

yrs. The observation revealed a rise in the proportion over 1-3 yrs, following which the proportion decreased over a period of 4-6 yrs and then increased again over a period of more than 7yrs in patients suffering from hypertension..



Fig(3.4): The relation between duration of hypertension and the level of LDL

The association between LDL in hypertensive patients and the length of their ailment, which was classified as 1-3 yrs, 4-6 yrs, and more than 7 yrs. The assessment revealed an increase in the proportion in 1-3 yrs, followed by a decline in 4-6 yrs, and then a large increase in visits in patients with hypertension in more than 7 yrs.

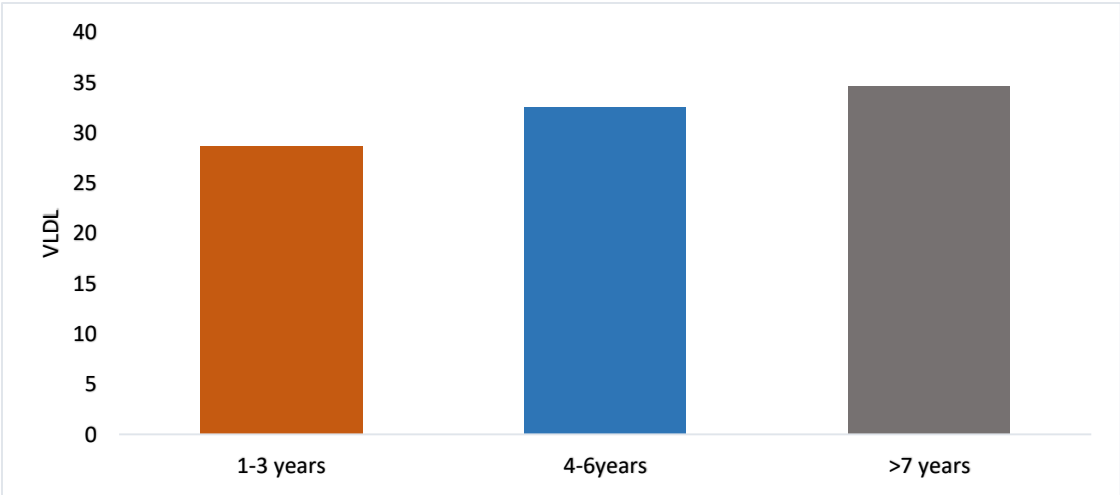


Fig (3.5): The relation between duration of hypertension and the level of VLDL

The association between VLDL in hypertension patients and the length of their condition, which was classified as 1-3 yrs, 4-6 yrs, and more than 7 yrs. The assessment revealed that the percentage increased with the duration of the ailment in hypertension patients.

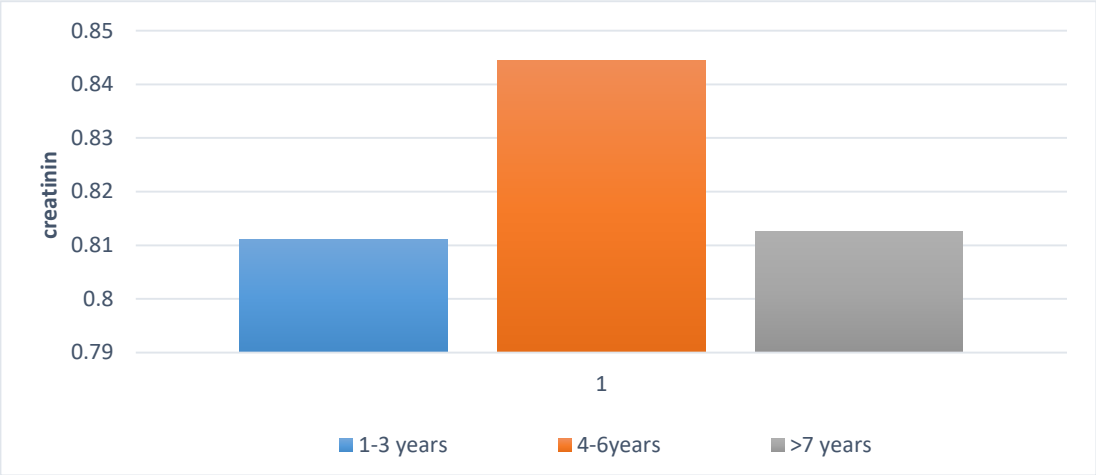


Fig (3.6): The relation between duration of hypertension and the level of creatinine.

The association between creatinine levels in hypertensive patients and the length of their ailment, was classified as 1-3 yrs, 4-6 yrs, or more than 7 yrs. The assessment revealed an increase in the percentage over a period of 4-6 yrs in individuals suffering from hypertension.

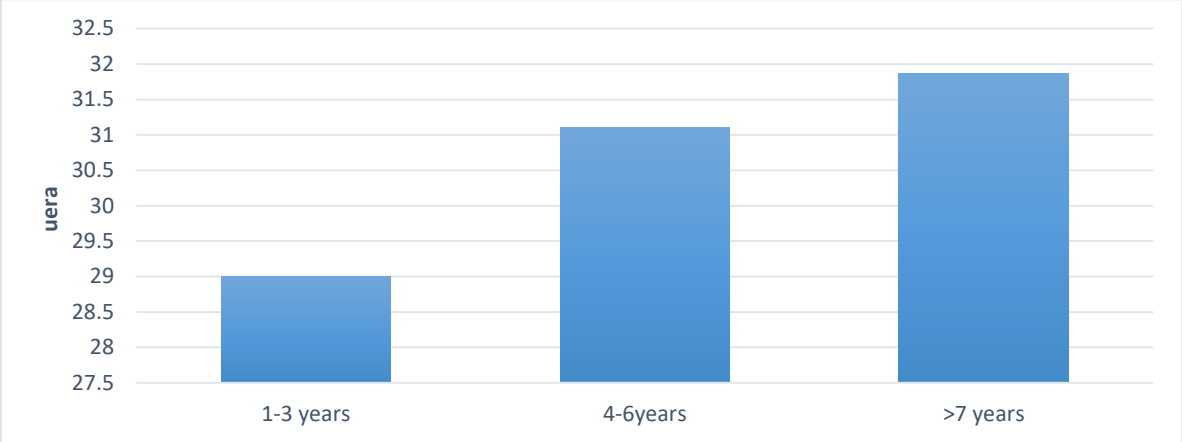


Fig (3.7): The relation between duration of hypertension and the level of urea.

3.4 The ration between duration of hypertension and TNF- α, HSP-70 and HS CRP.

The relationship between urea in hypertensive patients and the duration of their disease, was divided into 1–3 years, 4–6 years, and more than 7 years. The measurement showed an increase in the percentage with increasing duration of the disease in patients suffering from hypertensive.

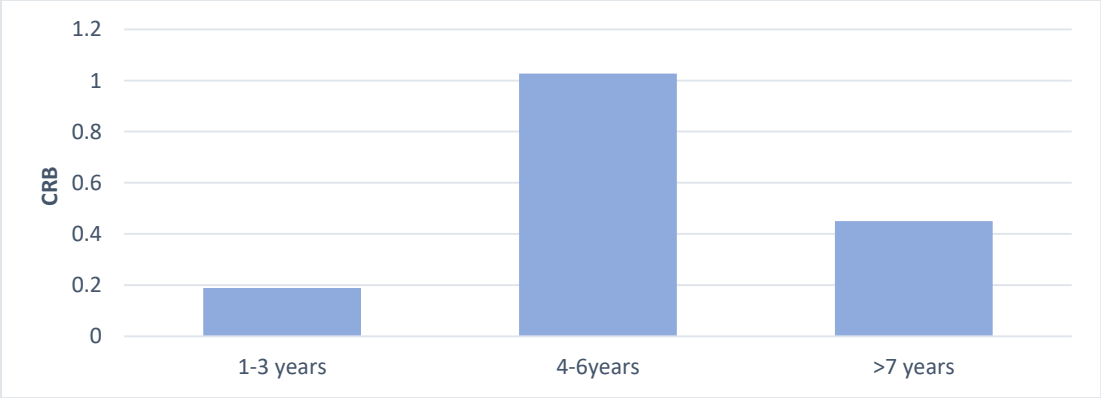


Fig (3.8): There ration between duration of hypertension and the level of HS CRP.

The relationship between HS CRP in individuals with hypertension and the duration of their disease, was separated into 1-3 yrs, 4-6 yrs, and >7 yrs. Monitoring revealed a significant increase in the rate over a period of 4-6 yrs in patients with high blood pressure.

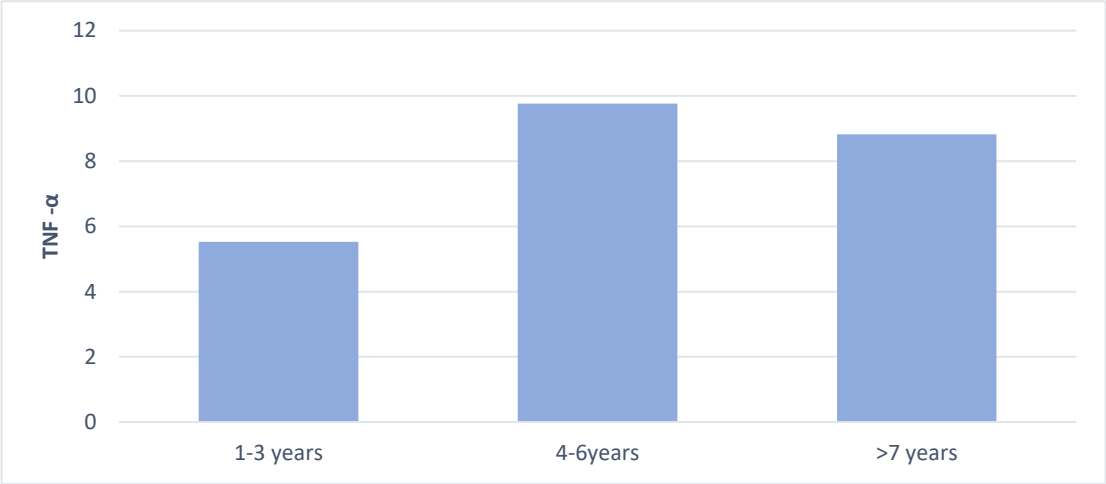


Fig (3.9) : There ration between duration of hypertension and the level of TNF- α.

The relationship between TNF- α in individuals with hypertension and the duration of their disease, was separated into 1-3 years, 4-6 yrs, and >7 yrs. Monitoring revealed a high percentage 1-3 yrs, after which the percentage increases significantly over a period of 4-6 yrs and then decreases slightly again over more than 7 years in patients with high blood pressure.

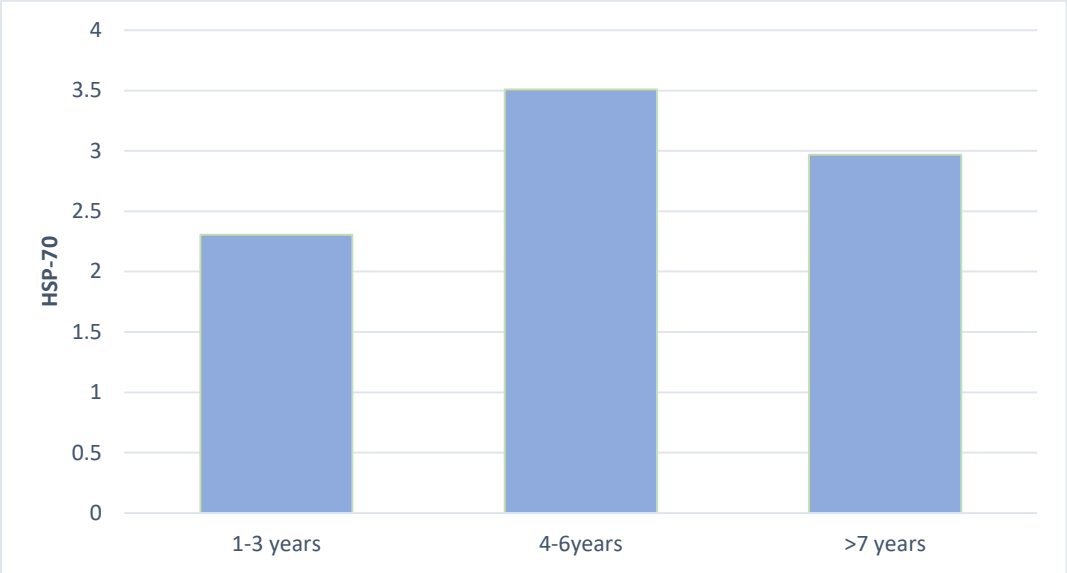


Fig (3. 10): There ration between duration of hypertension and the level of HSP-70

The relationship between Hsp-70 in individuals with hypertension and the duration of their disease, was separated into 1-3 yrs, 4-6 yrs, and >7 yrs. Monitoring revealed a high percentage 1-3 yrs, after which the percentage increases significantly over a period of 4-6 yrs and then decreases slightly again over more than 7 yrs in patients with high blood pressure.

3.5 Relationship of BMI ,HSP-70 and TNF-α with the obese group, the over-obese group, and the normal group in patients hypertension.

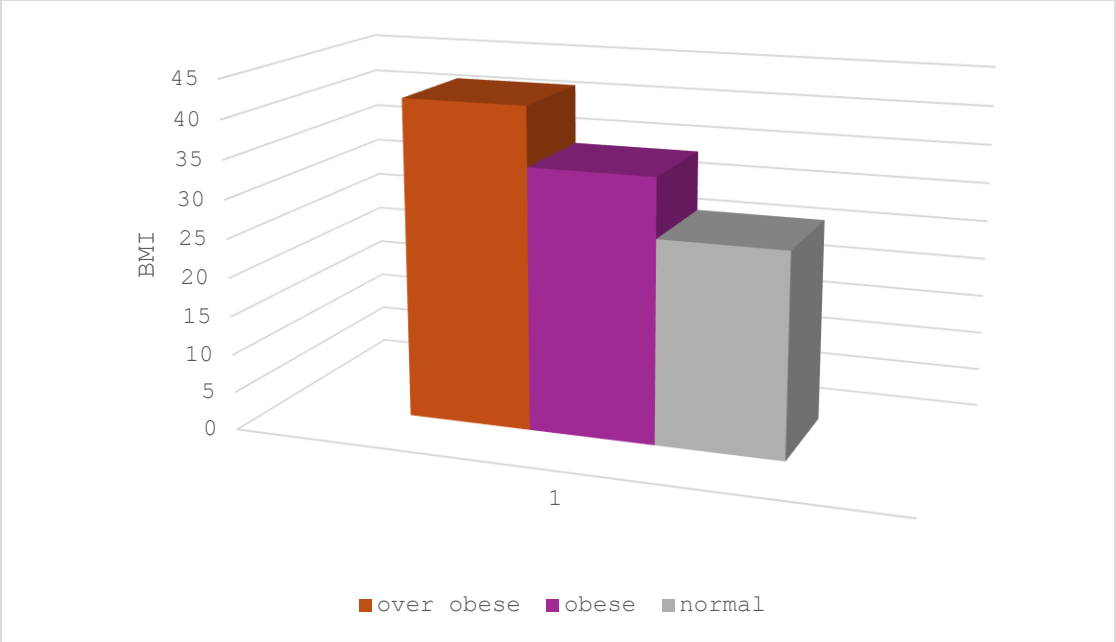


Fig (3.11): shows the relationship of BMI with the obese group, the over-obese group, and the normal group in patients with high blood pressure.

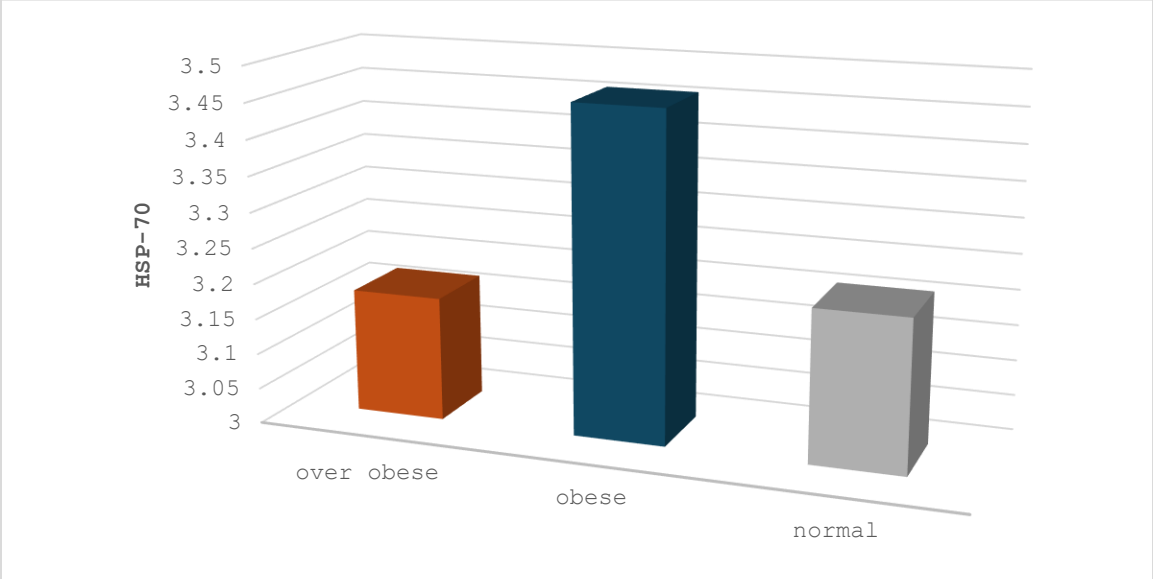


Fig (3.12): The relationship of HSP-70 with the obese group, the over-obese group, and the normal group in patients with high blood pressure.

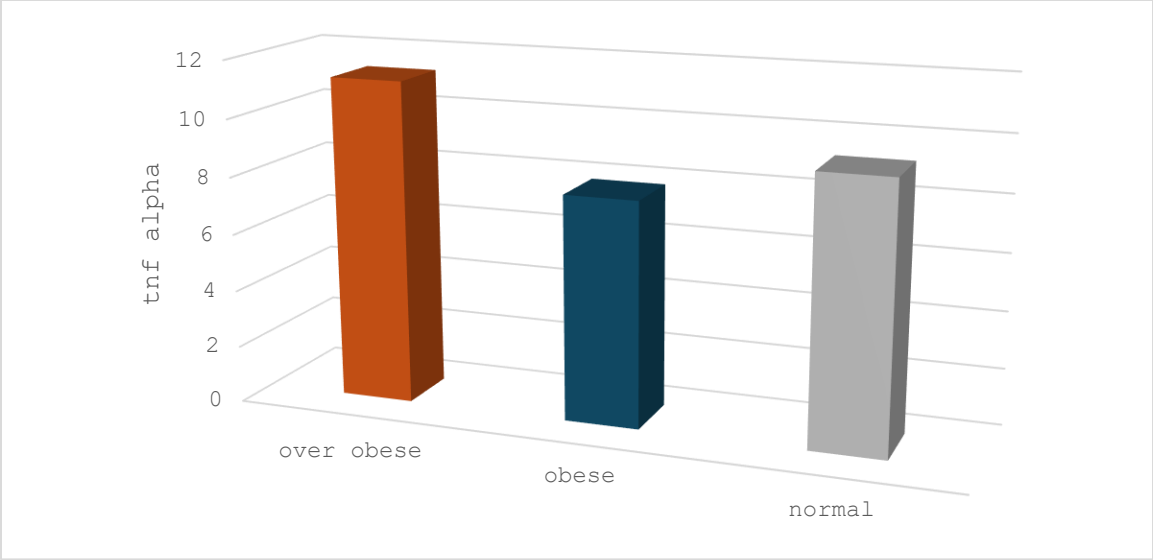


Fig (3.13): shows the relationship of TNF-α with the obese group, the over-obese group, and the normal group in patients with high blood pressure.

3.6 relationship ROC curve of TNF- α and HSP-70 in patients hypertensive.

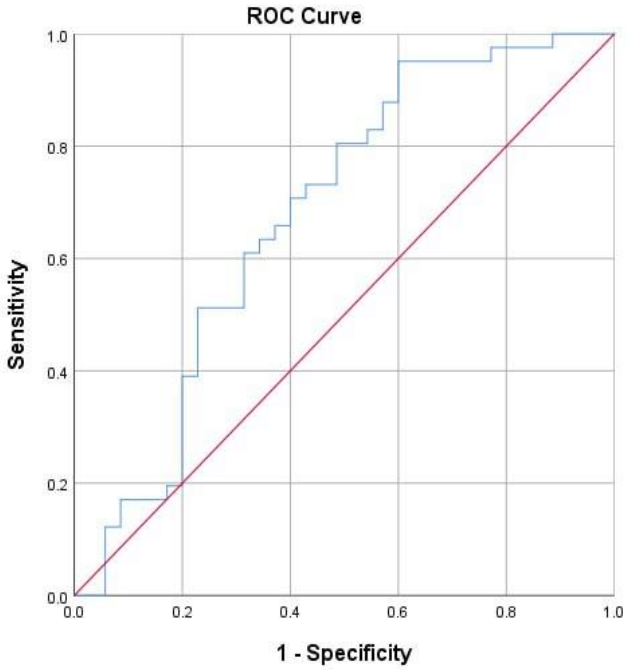


Fig (3.14): ROC curve of TNF- α in patients hypertensive compared to control group

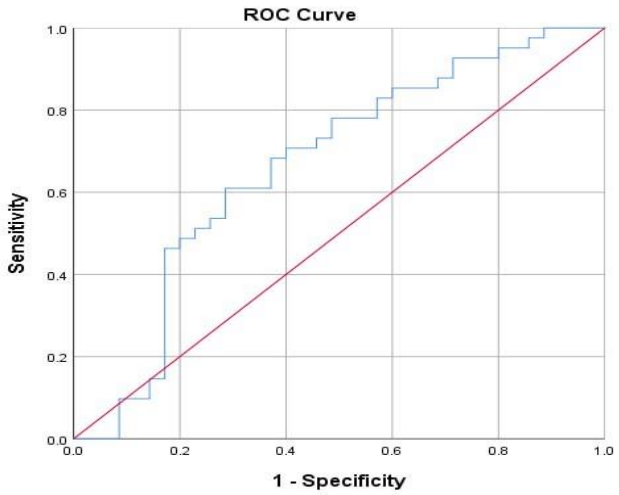


Fig (3.15): ROC curve of HSP-70 in patients hypertensive compared to control group.

3.7 The correlation between TNF-α ,HSP-70 and parameter in hypertension patients

Table 3.9: The correlation between TNF-α and parameter in hypertension patients.

Parameter	TNF-α R	P Value
HSP-70	0.607	Sig
HS CRP	0.50	Sig
TG	0.63	Sig
T CHOL	0.978	Sig
LDL	0.95	Sig
VLDL	0.50	Sig
HDL	0.72	Sig
BMI	0.39	No Sig
Creatinine	0.56	Sig

Table 3.10: The correlation between HSP-70 and parameter in hypertension patients.

Parameter	HSP-70 R	P Value
TNF- α	0.607	Sig
HS CRP	0.12	No Sig
TG	0.804	Sig
T CHOL	0.705	Sig
LDL	0.96	Sig
HDL	0.51	Sig
VLDL	0.82	Sig
BMI	0.25	No Sig
Urea	0.8	Sig

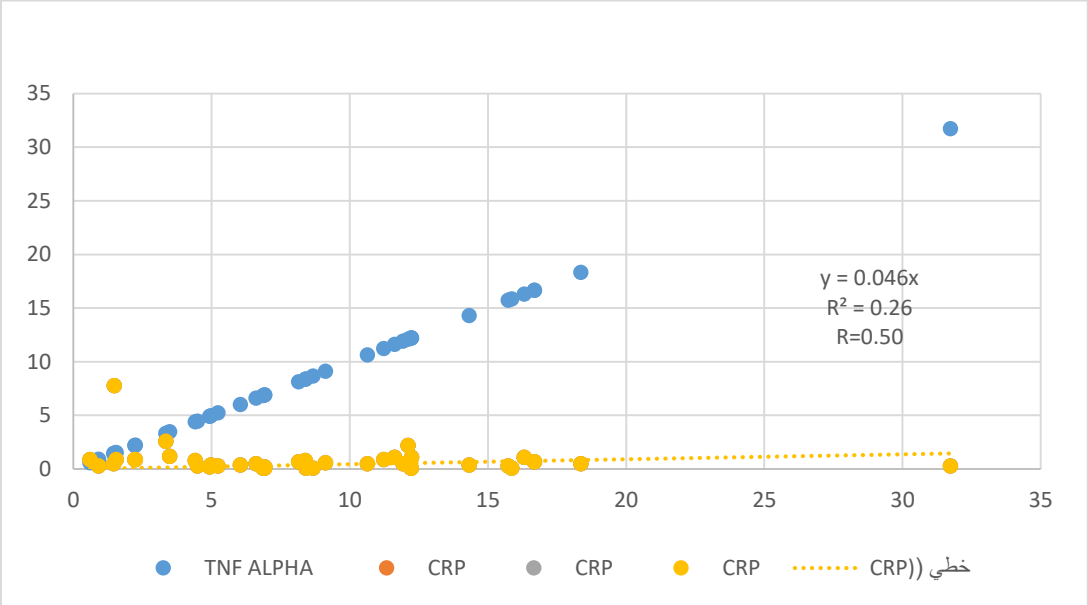


Fig (3.16): Correlation coefficient between TNF-α and HS CR

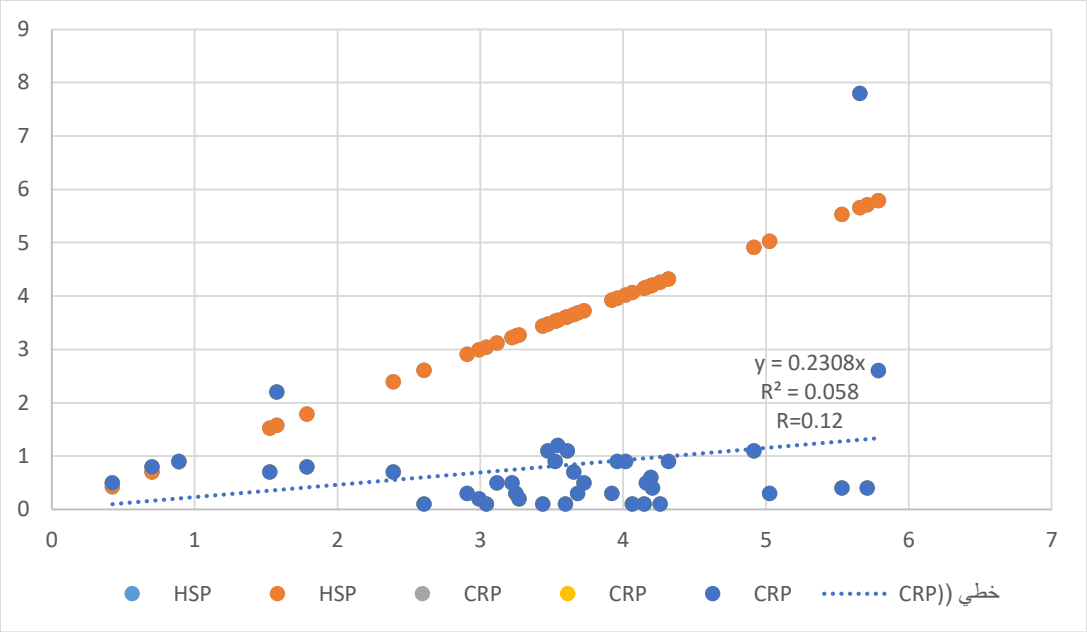


Fig (3.17): Correlation coefficient between Hsp-70 and HS CRP

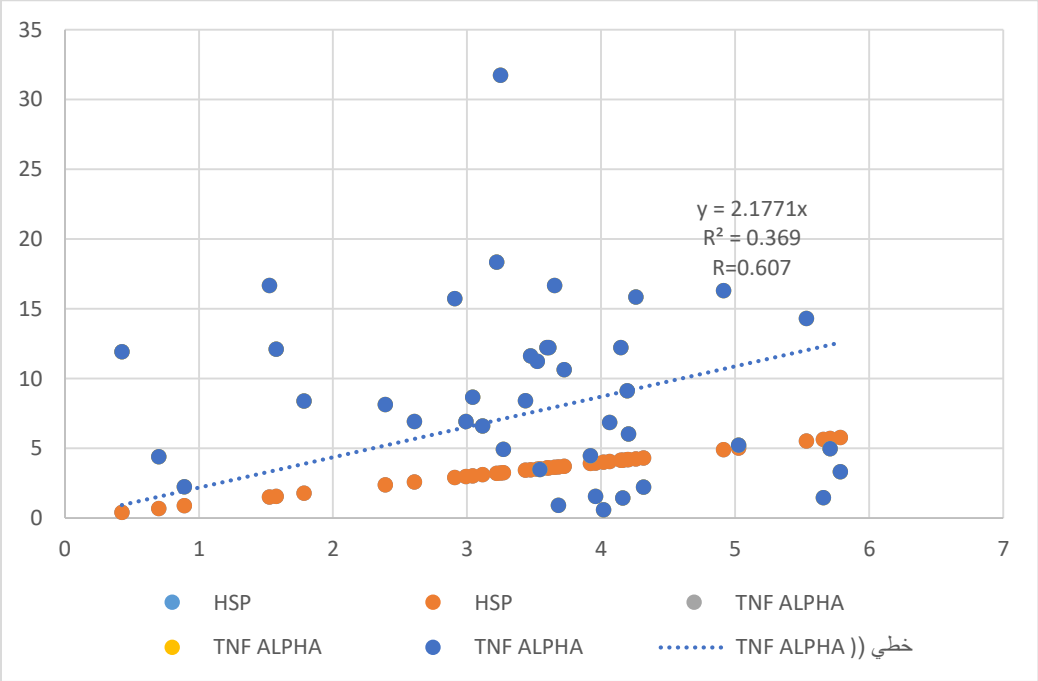


Fig (3.18): Correlation coefficient between TNF-alpha and HSP-70

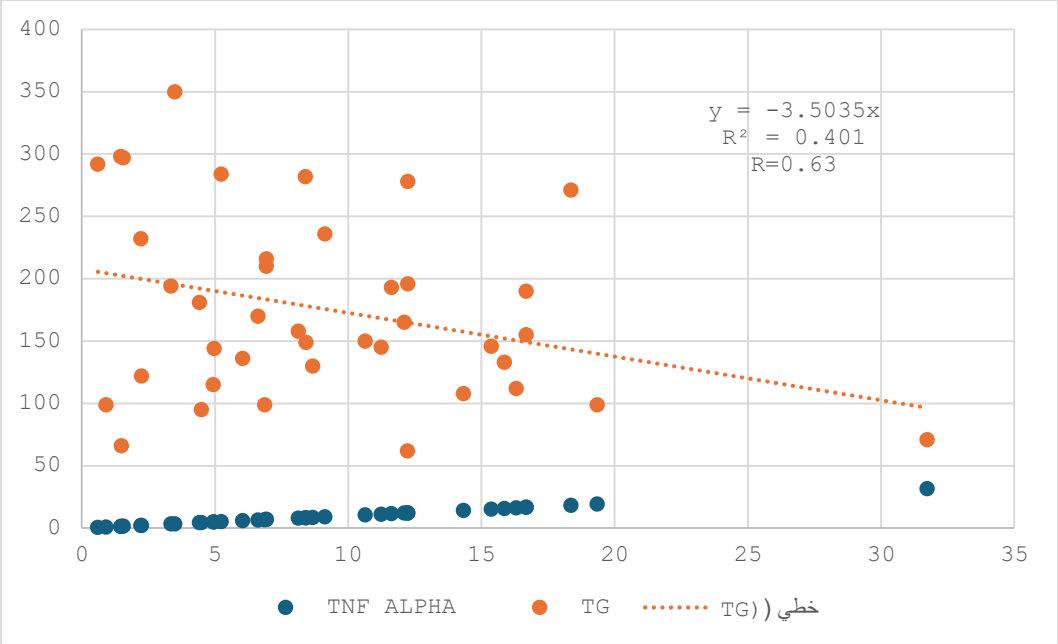


Fig (3.19): Correlation coefficient between TNF-α and Triglycerides

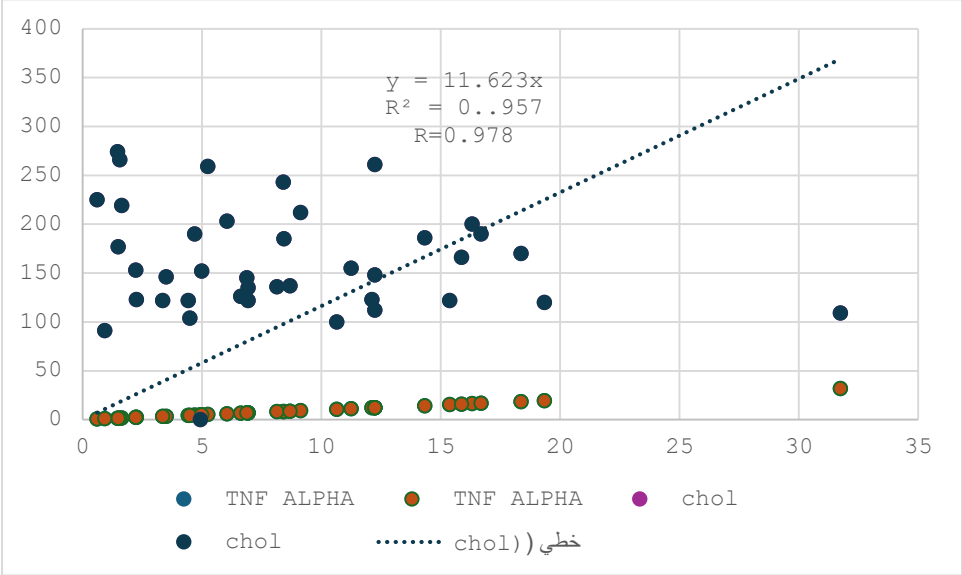


Fig (3.20): Correlation coefficient between TNF-α and cholesterol

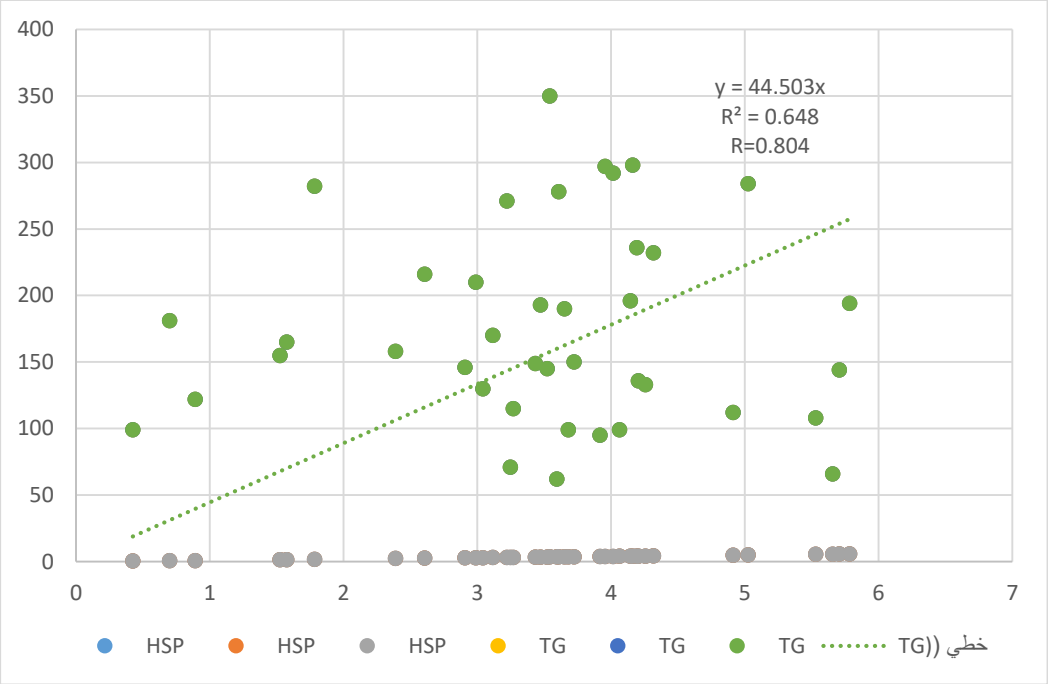


Fig (3.21): Correlation coefficient between Hsp-70 and Triglycerides

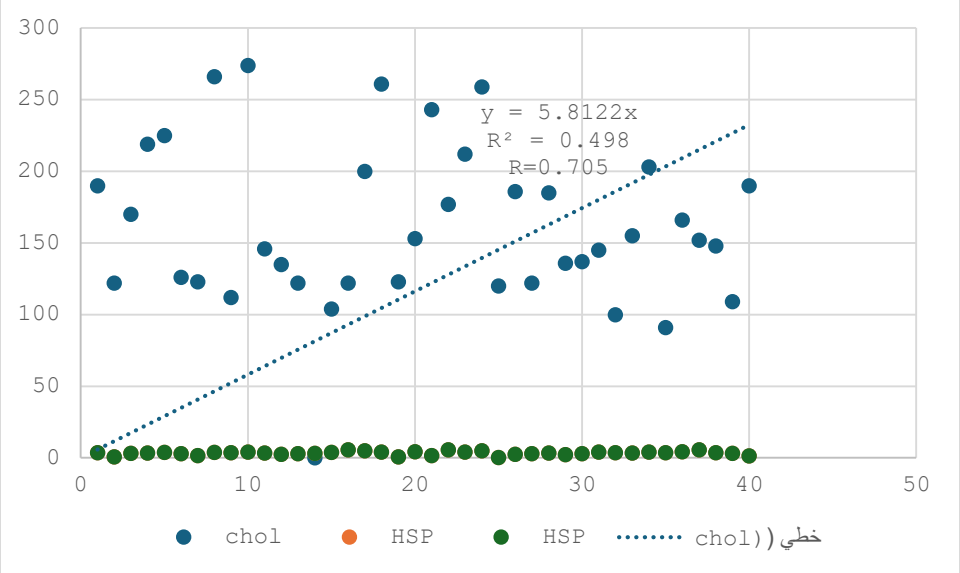


Fig (3.22): Correlation coefficient between Hsp-70 and cholesterol

4. Discussion

4.1 Relation between Patients of hypertension and Lipid Profile and (urea, creatinine)

The results of the Table(3.1) and Figures (3.2),(3.5) showed a significant difference (P value = ≤ 0.0001) in cholesterol and triglycerides compared to the control group. It also (LDL, HDL, and VLDL). In hypertension individuals, the mean blood levels of triglycerides, total cholesterol, and low-density lipoprotein were considerably higher than their threshold values. Furthermore, according to these findings, aberrant levels of low-density lipoprotein, total cholesterol, triglycerides, and high-density lipoprotein were increasing in hypertension patients [126,127].

The results also showed a significant difference (p=0.0001) in the percentage of urea and creatinine when compared with the control group. Patients with hypertensive suffer from high levels of Urea and creatinine result from fluid retention in the body due to kidney damage or improper functioning [128].

The results of the Table (3.2) and Figure (3.3) showed a significant difference (P = 0.0001) in cholesterol and triglycerides, (LDL, HDL, VLDL) between men and women . In addition there is a substantial difference (P = 0.0001) in creatinine and urea levels between men and women. Our findings concur with the findings of two Japanese research studies that showed a favorable correlation between high blood pressure and HDL values [129]. A research including over 190,000 French individuals under the age of 55 who had high blood pressure revealed that over 50% of them had dyslipidemia [130]. According to the results of hypertension screening conducted in the United States, dyslipidemia was present in 79% of white male and 65% of white female hypertension, which was higher than the percentages observed in black male and female hypertensive patients [131]. Nigerians had a 64% incidence of elevated lipid profiles among hypertension patients [132]. The average prevalence of lipid disorders in patients with hypertension in the Algerian population was 16.1%. [133]. The hypertensive population in this study had a high lipid profile prevalence, which was comparable to previous

research on the hypertensive population from rural northeastern China [134] and the rural Chinese community in Liaoning Province, China [135].

The results of the Table (3.3) and Figure (3.1),(3.4) showed that there was no significant difference in the percentage of cholesterol, triglycerides, and (LDL, VLDL) creatinine and urea according to the age group between 40-55 and 56-70, only a significant difference in the percentage of HDL ($p = 0.05$). These results are in agreement with other research showing that age is linked to increased blood pressure, carried out in both industrialized and developing nations [136]. Furthermore, this investigation showed that in hypertension patients, age was strongly correlated with serum LDL [137]. It is also supported by studies reporting a direct relationship between age and cholesterol levels [138]. Blood pressure naturally rises with age, possibly as a result of changes in atherosclerotic endothelium cells and increasing atherosclerosis in the blood arteries. Wen & Co. Additionally, stated that atherosclerosis advances with age. As people's age, there is a growing positive correlation between arterial stiffness and blood pressure [139] .The prevalence of atherosclerosis and hypertension rises with advancing age [140].

The results of Table (3.4) and Figure (3.6),(3.7) showed a significant difference between ($p = 0.02$) in triglycerides, ($p = 0.03$) VLDL, ($p = 0.01$) LDL and cholesterol, Obesity, diabetes, and dyslipidemia are among the additional cardiovascular risk factors that are frequently linked to hypertension. The pathogenesis of hypertension may involve endothelial dysfunction brought on by the presence of cardiovascular risk factors [141]. According to a research by Young et al., [142] insulin resistance has been shown to negatively affect blood pressure in older people and may have a bigger effect than aging. Additionally, a correlation between plasma insulin concentrations and hypertension was discovered ($r = 0.31$, $p < 0.01$) [143]. This study also revealed that hypertension individuals who consumed alcohol had higher average blood TC levels than those who did not. Furthermore, individuals with a smoking habit exhibited aberrant lipid levels, which is in line with a Greek research [144]. Worldwide, hypertension is recognized as a significant risk factor for diabetes, renal disease, heart disease, and stroke [145]. The results of the current study showed that there was significant difference in the percentage of ($p = 0.04$) with creatinine, ($p = 0.05$) with urea. as well as the absence of Significant difference with HDL compared to

patients hypertension with other diseases. End-stage renal disease (ESRD) is more common and its incidence is increasing [146]. Renal function will ultimately gradually deteriorate in around one-third of those afflicted [147]. According to worldwide data on the prevalence of hypertension worldwide, in 2005, 20.6% of Indian men and 20.9% of Indian women reported having high blood pressure. By 2025, it is anticipated that these rates would increase to 22.9% and 23.6%, respectively, for Indian men and women [148]. Adequate blood pressure regulation is widely acknowledged to be crucial in avoiding cardiovascular disease and end-stage renal disease (ESRD) and reducing the course of chronic kidney disease (CKD) [149]. Long-term exposure to blood pressure increases, especially in normotensive settings, can cause early kidney injury since the kidneys are the first organ targeted for damage in hypertension [150]. The effect of duration of hypertension which increases the risk and heart disease(Hardening and blockage of the arteries) and kidney diseased[151].

4.2 Relation between Patients with hypertension and Inflammatory Factors (HS CRP, TNF-α, HSP-70)

The results of the Table (3.5) showed a significant difference (P value = ≤ 0.0001) in HSP-70 and HS CRP but there was no significant difference in TNF-alpha in patients with hypertension compared to the control group. Heat shock protein 70 has been linked to hypertension in a number of epidemiological and clinical studies [152]. Essential hypertension is a common medical disease whose etiology is unclear. Research has revealed a connection between cardiovascular diseases, specifically essential hypertension, and the HSP70 gene [153] . Some cross-sectional studies found that patients with essential hypertension have higher plasma levels of inflammatory markers such as (CRP), (TNF-alpha), and adhesion molecules than healthy people, indicating that inflammation plays a role in the pathogenesis of hypertension [154].

The results of the Table (3.6) and (3.7) showed a significant difference (P value = ≤ 0.0001) in HSP-70 of man and women but there was no significant difference in TNF-alpha and HS CRP compared between men and

women also there was no significant difference in all parameters according to the age groups.

The results can be explained Hsp-70 levels were significantly inversely correlated with age, but not with sex. The function and potential involvement of Hsp70, notably in cytoprotection against various stressors, might account for these observations[155] . Our findings from Kunming participants suggest that Hsp70 levels in lymphocytes decline with aging. Other studies have found that Hsp70 levels in human lymphocytes fluctuate with aging[156] . Tanno-Sobetsu, a prospective cohort research done in Japan, revealed no connection between raised HS-CRP alone with increased risk of developing hypertension in both men and women[157] . According to the present research, individuals with hypertension had elevated TNF-α levels in comparison to those with normal blood pressure at comparable ages. This implies that TNF-α may contribute to the development of hypertension via inflammatory responses and cellular immunity, among other pathways[158] .

The results of the Table (3.8) showed no significant difference in TNF-alpha and HS CRP and HSP-70 between patients with high blood pressure only and patients with other diseases, diabetes, kidney disease, high lipid profile. Increased levels of proinflammatory cytokines, such as tissue necrosis factor α and interleukin 6, are associated with obesity and elevate CRP levels in the blood. As a result, obesity may contribute to the link between CRP and blood pressure[159] . It previously reported that HSP70 was slightly elevated in patients with chronic kidney-related diseases, such as chronic kidney disease, immunoglobulin nephropathy, and diabetic nephropathy[160] . TNF-α levels in type 2 diabetes patients correlate with greater HbA1c values, suggesting that they potentially predict glycemic control in obese diabetics [161]. The relationship between HSP-70, HS CRP, and TNF-alpha in hypertensive patients and the duration of their disease, were classified as 1-3 years, 4-6 years, or more than 7 years.

The evaluation revealed an increase in the rate over a period of 4-6 years in individuals with high blood pressure, there ration between duration of hypertension and the level of HSP-70, HS CRP and TNF-alpha of Figure (3.8),(3.9) and (3.10). High blood Hsp70 levels have been linked to improved

survival in individuals who have had severe trauma[162] . It has been shown that older people with acute heat illness have lower Hsp70 levels than younger people[163] . Human serum Hsp70 (inducible) levels rise after exercise, indicating a possible systemic function for Hsp70 from other tissues or organs [164]. The links between the several inflammatory markers in hypertension have been studied in some detail. For example, after controlling other risk factors, Bautista et al.'s cross-sectional study of the connection between IL-6, TNF-alpha, and HS CRP and hypertension in a random sample of 196 healthy people revealed no significant link between the three variables and hypertension. Even with its small sample size of 79 hypertensive people, this brief research is the first one to investigate the potentially misleading relationship between several inflammatory markers and hypertension [165] .

The study showed a sensitivity between TNF-alpha and hypertension compared with the control group. Real-time PCR was used to analyze TNFα and receptor expression in the renal medulla of rats, which have lower blood pressure salt-sensitivity than rats, were employed as salt-insensitive controls [166]. A showed a sensitivity between HSP-70 in hypertension when compared with the control group, Different kinds of inflammation in human's lead phagocytes to produce more ROS, and alter the activities of anti-stress genes. Environmental influences can also alter the action of anti-stress genes [167], Microenvironment can induce oxidative stress [168]. Individual susceptibility to stress may represent the organism's immunological response [169]. In humans, traumatic tissue injuries cause changes in HSP expression and cytokine production, and HSPs may reflect trauma-associated immunomodulation. Mathematical study supports the concept that short-term stress reveals individual neutrophils' susceptibility to stress during the first minute following exposure. Long heat shocks, such as those lasting more than three minutes, do not reveal individual neutrophil susceptibility to stress. Individual sensitivity can be realized at the mRNA level of anti-stress neutrophils [170].

4.3 The Effect Body Mass Index (BMI) on Patients hypertension

Over the past 50 years, obesity has increased to epidemic levels on a global scale [171]. The World Health Organization reports that between 1980

and 2013, there was a 27.5% rise in the prevalence of individuals worldwide with a body mass index (BMI) more than 23.9 kg/m. Numerous studies have connected a high body mass index (BMI) to an increased chance of developing a number of illnesses, including diabetes [172], heart disease, cancer, and musculoskeletal problems [173], all of which have a detrimental effect on one's overall quality of life.

Notably, the incidence of high blood pressure worldwide was calculated at 25% among adults in 2020, with expectations indicating that it will rise to 29% by 2025 [174]. Furthermore, obesity has been observed to contribute to 60-70% of cases of hypertension, with the obese population facing a 3-4 times higher risk than people of normal weight [175].

In addition, obesity-related fat accumulation can lead to an increase in chest wall thickness, leading to increased respiratory resistance and impaired lung function, as evidenced by decreased vital capacity [176]. As such, an in-depth investigation into the complex and intricate relationship between BMI, blood pressure, and vital capacity is needed.

Figure (3.11) shows that it draws a positive correlation between the MBI with the obese group, the morbidly obese group, and the normal group in patients with hypertension. Previous systematic reviews and retrospective studies have consistently indicated that higher BMI values are associated with higher blood pressure in adults, a trend that has been widely confirmed [177, 178]. This is in line with our current results, which reveal a positive relationship between BMI and all blood pressure measurements.

4.4 The relationship of HSp-70 and TNF-a to the obese group, the morbidly obese group, and the normal group in patients with hypertension.

The functions of heat shock protein-70 (HSP-70) molecules vary based on whether they are expressed extracellularly or intracellularly. Their primary functions include the removal and breakdown of misfolded proteins, chaperone-mediated autophagy, mechanisms for protein quality control, cell signaling, the development of stress responses, and renal self-defense systems [179].

Previous research has looked at the connection between HSPs and metabolic syndrome and obesity. It has been suggested that the expression of

HSP-70 and HSP-27 intracellularly may be a significant factor in the development of metabolic syndrome in obese people [180]. The literature has demonstrated that intracellular HSP-70 expression is decreased in the muscle tissue of obese patients and that serum and liver HSP-70 levels are low in diabetic monkeys [181,182]. Although it has been suggested that intracellular HSP-70 molecules have a protective effect on insulin resistance and hyperinsulinemia, the effects of extracellular HSP-70 molecules on obesity are not yet fully known [183]. Sell et al. reported that HSP-60 levels were high in morbidly obese patients but that they decreased after bariatric surgery, and this decrease had a correlation with inflammatory markers and cardiovascular disease risk [184].

Inflation, inflation and inflammation of transcody cells cause many changes in fatty tissue structures and adaptation. Increase the levels of leptin hormone in patients with excessive obesity activates the friendly and cause sodium retention and high blood pressure. Moreover, the increase in leptin levels accelerate the development of kidney disease by increasing the virtue. The launch of inflammatory cytokines such as TNF-α in the fatty tissue of obese obesity causes detergent and oxidative stress [185,186]. The low levels of Adibonicat in patients with excessive obesity also contribute to kidney damage by reducing the organization of protection mechanisms [187].

Obesity, in turn, is associated with increased risks of cardiovascular disease, hypertension [188], metabolic syndrome [189], and mental health problems [190] such as depression [191]. In the context of immune-mediated inflammatory diseases (IMID), obesity has been associated with more severe disease activity [192], poorer quality of life, and treatment-dependent response [193]. Therefore, it would be invaluable for clinicians to have reliable information about whether TNF-α inhibitors systemically induce weight gain as a side effect and the extent to which weight gain is expected in a given period of time. If TNF-α inhibitors lead to an increase in body weight, blocking TNF-α signaling has become a new strategy for treating disorders with severely reduced weight loss such as cancer, cachexia, and anorexia nervosa.

4.5 Correlation between Study Biomarkers in Patients hypertension

Heat shock protein 70 and hypertension have been linked in a number of epidemiological and clinical investigations [194, 195]. Uncertainty surrounds the etiology and pathophysiology of essential hypertension, a prevalent health condition. There are reports that the HSP70 gene is associated with cardiovascular diseases including essential hypertension [196]. The involvement of pro-inflammatory processes in cardiovascular diseases such as hypertension is well accepted. Assessing cytokines and inflammatory markers might help lower the likelihood of developing critical hypertension by providing more insight into the genesis of cardiovascular illness [197].

Some cross-sectional studies have shown that plasma levels of inflammatory markers, such as C-reactive protein (CRP) and cytokines [TNF-alpha (tumor necrosis factor-alpha) and IL-6 (interleukin-6)] as well as adhesion molecules are increased in patients with high Baseline blood pressure compared to healthy individuals supports the role of inflammation in the etiology of hypertension [198,199]. High CRP level may lead to total stroke and high blood pressure; High CRP levels are also one of the main causes of high blood pressure [200]. Experimental data indicates that high blood pressure may Stimulate pro-inflammatory responses, leading to inflammation of the endothelium in the arterial walls and thus hypertension [201]. Empirical evidence suggests that it is high BP specifically stimulates endothelial expression of cytokines that promote inflammation in hypertension [202].

An experimental study conducted by Fernández Real et al. showed that the degree of activation of the TNF-α system was positively and significantly associated with systolic and diastolic blood pressure in patients with type 2 diabetes [203]. TNF-α has been shown to reduce endothelial function the mRNA level of nitric oxide synthase by shortening its half-life [204].This reduces bioavailable nitric oxide leading to endothelial dysfunction, followed by chronic vasoconstriction and hypertension. Additionally, polymorphisms in the promoter region of the TNF-α gene have been associated with increased TNF-α and systolic blood pressure [205].

4.6 The Effect of the kidney of the Disease hypertension

The kidneys and blood circulation depend on each other; as the kidneys help filter waste and excess fluids from the blood, using many blood vessels, high blood pressure can lead to narrowing, weakening, and hardening of the blood vessels, and reducing blood flow within them. This ultimately leads to weakening and damage throughout the body, including the blood vessels in the kidneys. If the blood vessels in the kidneys are damaged, they may not work properly and thus the kidneys cannot remove all waste and excess fluids from the body. Excess fluids in the blood vessels lead to increase blood pressure further; This creates a cycle of danger, causing further damage that leads to kidney failure (failure of kidney function).

The study showed a significant difference (p=0.0001) in the percentage of urea and creatinine when compared with the control group and the current study's results indicated a substantial difference (P = 0.0001) in creatinine and urea levels between men and women and no significant difference in the percentage of Creatinine, Urea according to the age group and the study showed that there was significant difference in the percentage of (p = 0.04) with creatinine, (p = 0.05) with urea compared to patients hypertension with other diseases.

These results are in agreement with Jabary et al., 2006[206], Vupputuri et al., 2003[207] and Bulpitt 1973[208]. This elevation may be relevant to the decrease GFR as a result of hypertension effect on renal function (decrease in renal blood flow as a sequence of increasing renal vascular resistance). A reduction in renal blood flow leads to a decrease of GFR, [209,210] this is lead to a decrease distal tubular flow rate which lead to increase of urea reabsorption and decreased secretion which may be the reason for elevated serum urea concentration [209,211]. The elevation of serum creatinine concentration may be attributed to the decrease in creatinine clearance due to the decrease in the GFR [212].

Chapter Four

Conclusions

And

Recommendation

5.1 Conclusions

The investigation came with the following findings:

1- High levels of lipid profile are an indicator of hypertension.

2-Elevation of the inflammatory factors HSP-70 and HS CRP is an important predictor for the risk factor in hypertension patients.

3-The greater body mass index which increases the risk of infections and heart disease.

4- The greater urea and creatinine increases hypertension.

5-No relationship was observed between TNF-α with hypertension.

6- There was sensitivity between HSP-70 and hypertension.

5.2 Recommendations

Taking into account all of our prior information, we can suggest the following:

1. Measuring the lipid profile of individuals with hypertension periodically.

2-Conducting continuous examinations for inflammatory factors, especially in patients over 30 years old.

3. It is advised to adopt healthy eating practices and engage in regular exercise to shed pounds and lower the risks of illnesses associated with obesity and its aftereffects.

4. Future research should evaluate the GOT and CPK enzymes in addition to all of the heart's enzymes.

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الخلاصة

ارتفاع ضغط الدم هو مرض شائع يمكن أن يكون خطيرًا إذا ترك دون علاج. كما أن العديد من العوامل يمكن أن تسبب ارتفاع ضغط الدم، بما في ذلك ارتفاع نسبة الدهون، يمكن أن تساهم الدهون العالية في تصلب الشرايين أو زيادة سماكة جدران الشرايين؛ مما يزيد من خطر الإصابة بتصلب الشرايين والسكتة الدماغية والنوبات القلبية وأمراض القلب. هناك علاقة قوية بين ارتفاع ضغط الدم وضعف الكلى، وذلك لأن ارتفاع ضغط الدم غير المنضبط هو سبب رئيسي لأمراض الكلى المزمنة، مرض الكلى المزمن (CKD)هو سبب رئيسي لارتفاع ضغط الدم، وارتفاع اليوريا والكرياتينين هي أهم العوامل التي تزيد من معدل ارتفاع ضغط الدم. يزيد ارتفاع ضغط الدم بشكل كبير من خطر الإصابة بأمراض القلب والأوعية الدموية وفشل الكلى والسكتة الدماغية. يمكن أن يحدث ارتفاع ضغط الدم بسبب عدة عوامل مثل الإفراط في تناول الملح أو الكحول، والإجهاد، والعمر، والوراثة. التاريخ العائلي، والسمنة، والحالة البدنية.

تم تصميم هذه الدراسة لتقييم مستويات بعض العلامات الالتهابية وهي بروتين الصدمة الحرارية-70 (HSP-70) وعامل نخر الورم البشري ألفا (TNF-α) وبروتين سي التفاعلي عالي الحساسية (HS CRP) بالإضافة إلى ملف الدهون واليوريا والكرياتينين في مرضى ارتفاع ضغط الدم. شملت الدراسة 50 مريضًا يعانون من ارتفاع ضغط الدم و40 فردًا من مجموعة التحكم الصحية. يتكون هؤلاء المرضى من 28 ذكرًا و22 أنثى، تتراوح أعمارهم بين 40 إلى 70 عامًا، تمت مقارنتهم بالمجموعة الصحية. تم قياس المعايير في هذه المجموعات وهي الكوليسترول والدهون الثلاثية و LDLو HDL و VLDLواليوريا والكرياتينين و HSP-70و TNF-αو .HS CRPتم تحليل النتيجة بفارق كبير قيمة $p \leq 0.0001$ عند مقارنتها بين بيانات مرضى ارتفاع ضغط الدم ومجموعة الأشخاص الأصحاء. لاحظ أن النتائج كانت أعلى من الحد الطبيعي للكوليسترول، أظهرت النتائج وجود فروق معنوية في مستويات كل من الدهون الثلاثية، LDL، HDL، VLDL، اليوريا والكرياتينين، Hsp-70، CR-proteinلدى مرضى ارتفاع ضغط الدم، بينما أظهرت النتائج عدم وجود فروق معنوية في TNF-α لدى مرضى ارتفاع ضغط الدم، كما ظهر تأثير الجنس على مستويات المعايير من خلال الاختلاف بين مجموعتي الذكور والإناث، حيث كان هناك فرق معنوي = p value 0.02في الدهون الثلاثية، p value = 0.03مع VLDL ، p value = 0.01 لـ LDL والكوليسترول، وعدم وجود فرق معنوي مع HDL مقارنة بمرضى ارتفاع ضغط الدم ومرضى ارتفاع ضغط الدم المصابين بأمراض أخرى، كما لم يظهر فرق معنوي في TNF-alphaو HS CRP و HSP-70 بين مرضى ارتفاع ضغط الدم فقط ومرضى أمراض أخرى، كما كان هناك فرق معنوي p value = 0.05 في نسبة اليوريا والكرياتينين لدى مرضى ارتفاع ضغط الدم المصابين بأمراض أخرى عند مقارنتهم بمجموعة مرضى ارتفاع ضغط الدم فقط. أظهرت نتائج تأثير العمر عدم وجود فروق معنوية في نسبة

الكوليسترول والدهون الثلاثية والكوليسترول الجيد والكوليسترول الضار والكوليسترول منخفض الكثافة في الفئة العمرية من 40-55 سنة ولكن في الفئة العمرية من 56-70 سنة، كما أظهرت عدم وجود فروق معنوية قيمة $P \leq 0.0001$ في HSP-70 والبروتين التفاعلي-سي و TNF-alphaوالكرياتينين واليوريا في المرضى حسب العمر. وأظهرت حساسية HSP-70 في ارتفاع ضغط الدم عند مقارنتها بمجموعة التحكم. كما أظهرت وجود علاقة بين مجموعات مؤشر كتلة الجسم من البدناء والسمنة المفرطة والطبيعيين في مرضى ارتفاع ضغط الدم مع مستويات المعايير. ويمكن إظهار دور مدة المرض من خلال تأثير المدة على مستويات المعايير.

جامعة كربلاء

كلية التربية للعلوم الصرفة

قسم الكيمياء

دور العلامات الالتهابية لدى مرضى ارتفاع ضغط الدم في مدينة كربلاء المقدسة

رسالة مقدمة إلى مجلس كلية التربية للعلوم الصرفة / جامعة كربلاء وهي جزء من متطلبات نيل درجة الماجستير في علوم الكيمياء

كُتبت بواسطة

رشا عباس عبد الحسين مجدي

بأشراف

الأستاذ المساعد الدكتور

رحاب جاسم محمد

دكتوراه في الكيمياء الحياتية

الأستاذ المساعد الدكتور

لمياء عبد الكريم درويش

دكتوراه في الطب الباطني

1446 هـ

2024م