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Assessment of Ischemic Modified Albumin Levels as an Early Marker for Acute Coronary Syndrome

A Thesis

Submitted to the Council of the College of Medicine, University of Karbala, as a Partial Fulfillment in the Requirements for the Degree of Master in Clinical Chemistry

By

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وَيَسْأَلُونَكَ عَنِ الرُّوحِ ۖ قُلِ الرُّوحُ مِنْ أَمْرِ رَبِّي وَمَا أُوتِيتُمْ مِنَ الْعِلْمِ إِلَّا قَلِيلًا ﴿٨٥﴾

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آية ٨٥

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We have examined the student **"Inaam Kadhoum Mohamed "** in its content and in our opinion; it meets the standard of a thesis for the degree of **"master in Clinical chemistry"** and it is adequate with **"Excellent"** degree.

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Finally, I thank all my colleagues in the Master Class 2022.

Dedication

With my gratitude to God

I would like to **Dedicate my thesis to** *the*

source of my ambition: father

and to my inspiration: mother

for all my lovely family

to everyone who stood with me

and I dedicate this work

for all patient in the world

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List of Abbreviations	
ACB	Albumin cobalt binding
ACC	American College of Cardiology
ACS	Acute Coronary syndrome
AHA	American Heart association
AMI	Acute Myocardial Infarction
ANOVA	Analysis of variance
ATP	Adenine triphosphate
AUC	Area under carve
BMI	Body Mass index
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
cAMP	Cyclic Adenosine Monophosphate
CBC	Complete Blood Count
CCU	Cardiac Care Unit
CCTA Coronary	CT Angiography
CHD	Coronary Heart Disease
CHE	Cholesterol Esterase
CHOD	Cholesterol Oxidase
CK	Creatine Kinase
CKMB	creatinine kinase muscle brain
CRP	C Reactive Protein

CVA	Cerebro/ Vascular Accident
CVD	Cardio/ Vascular Disease
DM	Diabetes Mellitus
ECG	Electro Cardio Graph
Echo	Echocardiography
ED	Emergency Department
EF	Ejection Fraction
ELISA	Enzyme linked immunosorbent assay
ESC	European Society of Cardiology
GK	Glucokinase
GPO	Glycerol 3 Phosphate Oxidase
GRACE	Global Registry of Acute Coronary Events
HDL	High-Density Lipoprotein
hs-cTn	High Sensitive cardiac Troponin
HRP	Horseradish peroxidase
HSA	Human Serum Albumin
HTG	Hypertriglyceridemia
ICAM-1	Intercellular Adhesion Molecule-1
IHD	Ischemic Heart Disease
IMA	Ischemia Modified Albumin
LBBB	Left Bundle Branch Block

LDL	Low Density Lipoprotein
LSD	Least Significant Difference
LV	Left Ventricle
LVEF	Left Ventricle Ejection Fraction
LVH	Left Ventricular Hypertrophy
MI	Myocardial Infarction
MI-	Myocardial Infraction with negative troponin test
MI+	Myocardial Infraction with positive troponin test
NACB	National Academy of Clinical Biochemistry
NADH	Nicotinamide Adenine Dinucleotide
NTS	N -Terminal Site
NSTEMI	Non ST- Elevation Myocardial Infarction
PAI-1	Plasminogen Activator Inhibitor-1
PCI	Percutaneous Coronary Intervention
POD	Peroxidase
RBC	Red Blood Cell
RWMAs	Regional Wall Motion Abnormalities
SA-HRP	Streptavidin-Horseradish Peroxidase
SD	Standard deviation
SN, SP	Sensitivity, Specificity
STEMI	ST- Elevation Myocardial Infarction

t-PA	Tissue Plasminogen Activator
TC	Total – Cholesterol
TEE	Trans Esophageal Echocardiography
TG	Triglycerides
TnC	Troponin C
TnI	Troponin I
TnT	Troponin T
TMB	TetraMethylBenzidine
UA	Unstable Angina
VLDL	Very Low-Density Lipoprotein
WBC	White Blood Cell
WHO	World Health Organization

Summary

Acute coronary syndrome (ACS) is the clinical manifestation of the critical phase of coronary artery disease. Based on ECG and biochemical markers classified as ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina. The common underlying pathophysiology is related to plaque rupture or erosion with subsequent thrombus formation. Despite the decreasing age-adjusted mortality for myocardial infarction, the disease prevalence for non-fatal components of ACS remains high and the economic costs are immense. The effective treatment of ACS is guided by early diagnosis and risk stratification, and is based on the ECG and biochemical markers.

This study aimed to Investigate the role of biochemical marker; Ischemia modified albumin (IMA) as an early diagnostic tool of ACS. Study the role of these biochemical markers in differentiation between pathological chest pain causes; UA, NSTEMI and STEMI. Identify the cutoff values of these biochemical markers in early diagnosis of ACS.

Case - control study approach was conducted on four groups of participants, MI- , MI+ , UA and Control in Kerbala and Baghdad Governorates.

All patient are examined for signs and symptoms of any cardiac disorders. manifest such as Troponin with electrocardiographic patterns by specialist doctor. Serum biomarkers level were measured for the following parameter: IMA levels were measured using ELISA technique.; Measurement of Iipid profile levels in Human serum was performed using Spectrophotometric Technique; biochemical analysis of Complete blood count was done by XP-300™ Automated hematology analyzer Sysmex. The association between biochemical markers and disease severity was

evaluated. The efficiency of the predicting value was assessed using receiver operating characteristic (ROC) curve.

Results were indicated that IMA levels were shown a significant increased range levels in the negative troponin MI cases compared to the positive troponin MI and unstable angina. The range levels were (3.12-6.41); (3.1-5.66) and (3.17-5.56) respectively. On the other hand, unstable angina cases were shown a decreasing level of Albumin and increasing levels of IMA/ Alb ratio. Results were also illustrated the receiver operating curve (ROC) and AUC analysis for the Ischemic Modified Albumin, IMA/Albumin ratio as possible diagnostic parameters. IMA level was shown a good diagnostic performance for prediction ACS Patients compared to control group.

the optimal diagnostic points for predicting ACS by IMA were (sensitivity = 90%, specificity = 80%) at a level = 3.59, while IMA/ Alb ratio levels: (sensitivity = 92%, specificity = 67%) at a level = 0.072. Only p-values of the AUC for IMA were <0.001 and statistically significant.

Serum IMA appears to be a sensitive biomarker of myocardial ischemia in MI patients. Data analysis confirmed the ability to detect ischemia prior to myocyte death.

CHAPTER ONE

Introduction and literature review

1. Introduction

1.1. Definition of Acute Coronary Syndrome:

Acute Coronary Syndrome ACS is one of the most dangerous types of ischemic heart disease (IHD) ACS represents a life- threatening manifestation; like cardiac arrest, electrical or hemodynamic instability with cardiogenic shock (CS) due to ongoing ischemia or mechanical complications such as severe mitral regurgitation **[1].**

The main symptom of patient with suspected ACS is acute chest discomfort described as pain, pressure, tightness, and burning. Symptoms equivalent to chest pain may include dyspnea, epigastric pain, and pain in the left arm. Acute myocardial infarction (AMI) defines necrosis of Cardiomyocyte in a clinical setting consistent with acute myocardial ischemia. **[2].**

Non-ST-elevation myocardial infarction (NSTEMI), ST-elevation MI (STEMI), and unstable angina are the three traditional types of ACS. However, the widespread use of the high-sensitivity troponin test has changed the diagnosis of unstable angina to NSTEMI in almost all patients formerly diagnosed with unstable angina. This has occurred because those patients formerly unstable angina actually have abnormally elevated high-sensitivity troponin values. Traditionally, unstable angina was defined as clinical and electrocardiographic (ECG) findings in the absence of an elevated biomarker level. Indeed, they demonstrate elevated levels of this biomarker, thus confirming the presence of myocardial cell death induced by ischemia. Almost all of these patients do not show a STEMI pattern on their ECG, and so they should be diagnosed as an NSTEMI **[3]** .

1.2. Differentiated patients group by electrocardiogram

Based on the electrocardiogram (ECG), two groups of patients should be differentiated:

STEMI:

Patients with acute chest pain and persistent (>20 min) ST-segment elevation. This condition is termed ST-segment elevation ACS and generally, reflects an acute total or subtotal coronary occlusion. Most patients will ultimately develop ST-segment elevation myocardial infarction (STEMI). The mainstay of treatment in these patients is immediate reperfusion by primary percutaneous coronary intervention (PCI) or, if not available in a timely manner, by fibrinolytic therapy **[4]**

NSTEMI:

Patients with acute chest discomfort but no persistent ST-segment elevation [non-ST-segment elevation ACS (NSTE-ACS)] exhibit ECG changes that may include transient ST-segment elevation, persistent or transient ST-segment depression, T-wave inversion, flat T waves, or pseudonormalization of T waves; or the ECG may be normal **[1]**

1.3. Universal Definition of Myocardial Infarction

Acute myocardial infarction (AMI) defines cardiomyocyte necrosis in a clinical setting consistent with acute myocardial ischemia **[5]**. A combination of criteria is required to meet the diagnosis of AMI, namely the detection of an increase and/or decrease of a cardiac biomarker, preferably high-sensitivity cardiac troponin (hs-cTn) T or I, with at least one value above the 99% of the upper reference limit and at least one of the following:

- Symptoms of myocardial ischemia.
- New ischemic ECG changes.

- Development of pathological Q waves on ECG.
- Imaging evidence of loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology.
- Intracoronary thrombus detected on angiography or autopsy**[5].**

1.3.1. Type 1 myocardial infarction

Type 1 myocardial infarction (MI) is characterized by atherosclerotic plaque rupture, ulceration, fissure, or erosion with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow and/or distal embolization and subsequent myocardial necrosis. The patient may have underlying severe coronary artery disease (CAD). There may be non-obstructive coronary atherosclerosis or no angiographic evidence of CAD, particularly in women **[6]** . Show in figure (1.1)

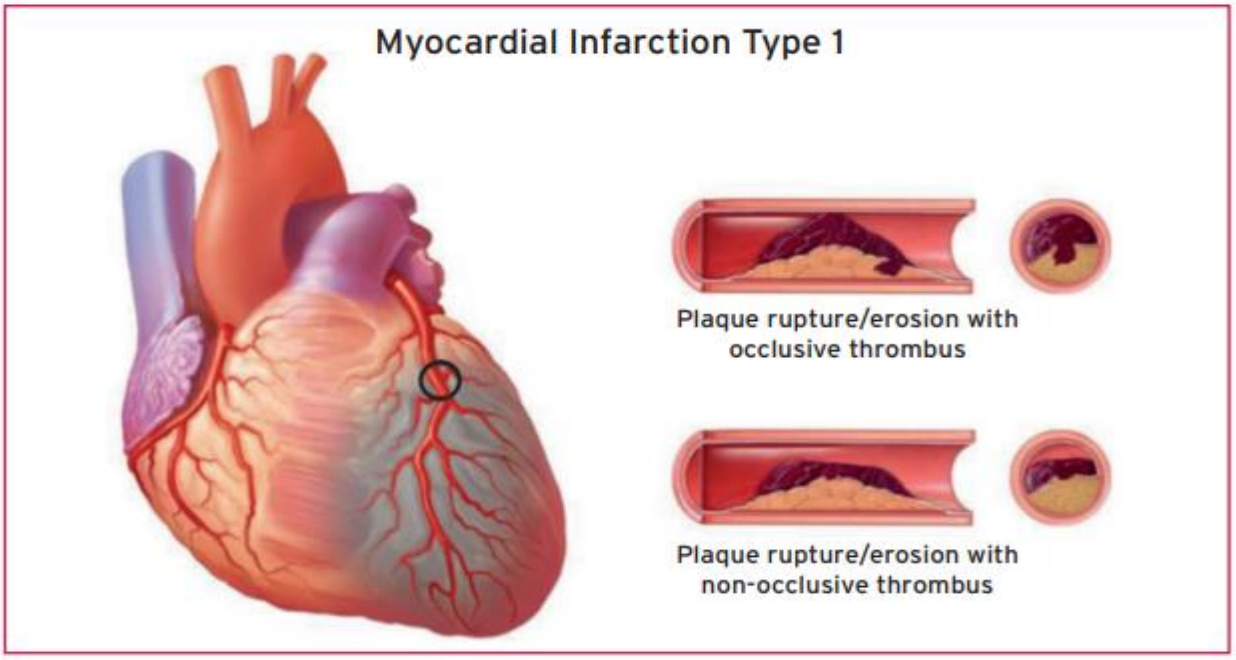


Figure 1.1: myocardial infarction Type 1 [7]

1.3.2. Type 2 myocardial infarction

Type 2 MI is myocardial necrosis in which a condition other than coronary plaque instability causes an imbalance between myocardial oxygen supply and demand **[8]**. Mechanisms include hypotension, hypertension, tachyarrhythmias, bradyarrhythmias, anaemia, hypoxaemia, coronary artery spasm, spontaneous coronary artery dissection (SCAD), coronary embolism, and coronary microvascular dysfunction **[9]** as shown in figure (1.2).

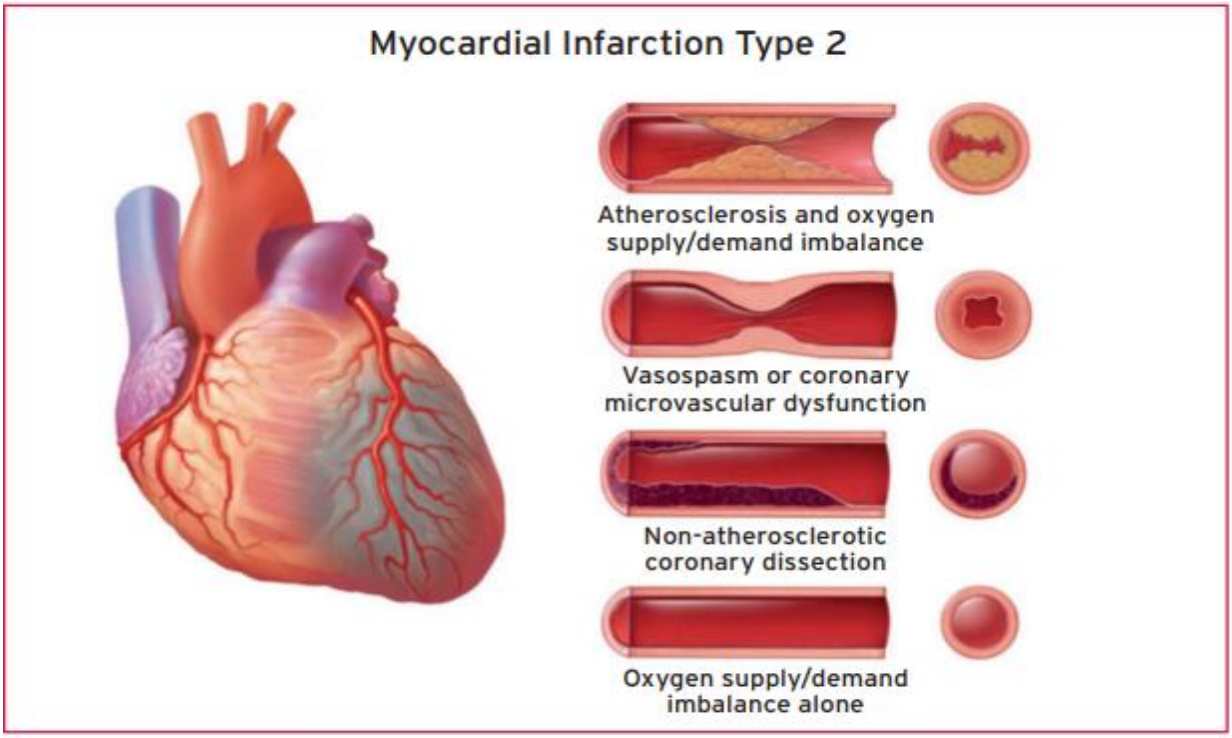


Figure 1.2: myocardial infarction type 2 [9].

1.3.3. Types 3 - 5 myocardial infarction

The universal definition of MI also includes type 3 MI (MI resulting in death when biomarkers are not available) and types 4 and 5 MI related to PCI and coronary artery bypass grafting (CABG), respectively **[6]**.

1.4. Unstable angina in the era of high-sensitivity cardiac troponin assay

Unstable angina is defined as myocardial ischemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis. Among unselected patients presenting to the emergency department with suspected NSTE-ACS, the introduction of hs-cTn measurements in place of standard troponin assays resulted in an increase in the detection of MI (4% absolute and 20% relative increases) and a reciprocal decrease in the diagnosis of unstable angina **[8]**. Compared with NSTEMI patients, individuals with unstable angina do not experience acute cardiomyocyte injury/necrosis, have a substantially lower risk of death, and appear to derive less benefit from intensified antiplatelet therapy, as well as an invasive strategy within 72 hr **[10]**. Unstable angina is defined as angina pectoris (or equivalent type of ischemic discomfort) with at least one of three features.

1. Occurring at rest (or minimal exertion) and usually lasting >20 minutes (if not interrupted by the administration of a nitrate or an analgesic).
2. Being severe and usually described as frank pain.
3. Occurring with a crescendo pattern (i.e., pain that awakens the patient from sleep or that is more severe, prolonged, or frequent than previously).

Previously two thirds of patients with unstable angina have evidence of myocardial necrosis. As troponin measurements become progressively more sensitive, an increasing fraction of patients with NSTE-ACS exhibit some release of troponin, and therefore these should be considered cases of NSTEMI with a reciprocal reduction in the fraction with unstable angina **[11]**.

1.5. Pathophysiology of ACS

Extensive research has focused on the fibrous cap of the plaque because of its importance in the majority of fatal ACS. Since inflammatory cells accumulate at the site of ruptured plaques, and biomarkers of inflammation predict acute coronary syndromes. Studies have focused on the hypothesis that macrophages, and the mediators that they produce and that regulate their function, disrupt the collagen in the plaque in a manner that may risk the integrity of the fibrous cap, thus precipitating an acute coronary syndrome. Plasma low-density lipoprotein can enter the arterial wall and phagocytes engulf LDL via scavenger receptors. Lipid-laden macrophage foam cells can die, contributing to the accumulation of extracellular cholesteryl ester and cholesterol monohydrate crystals in the lipid-rich necrotic core of the plaque. The dying macrophages can also release apoptotic bodies and microparticles that contain the potent procoagulant tissue factor (TF+). The cholesterol crystals can coactivate the inflammasome, an intracellular supramolecular structure that generates the biologically active forms of the proinflammatory cytokines interleukin (IL)-1β and IL-18. Large crystals might also cause mechanical disruption of the fibrous cap. **[12]** as a show in figure (1.3).

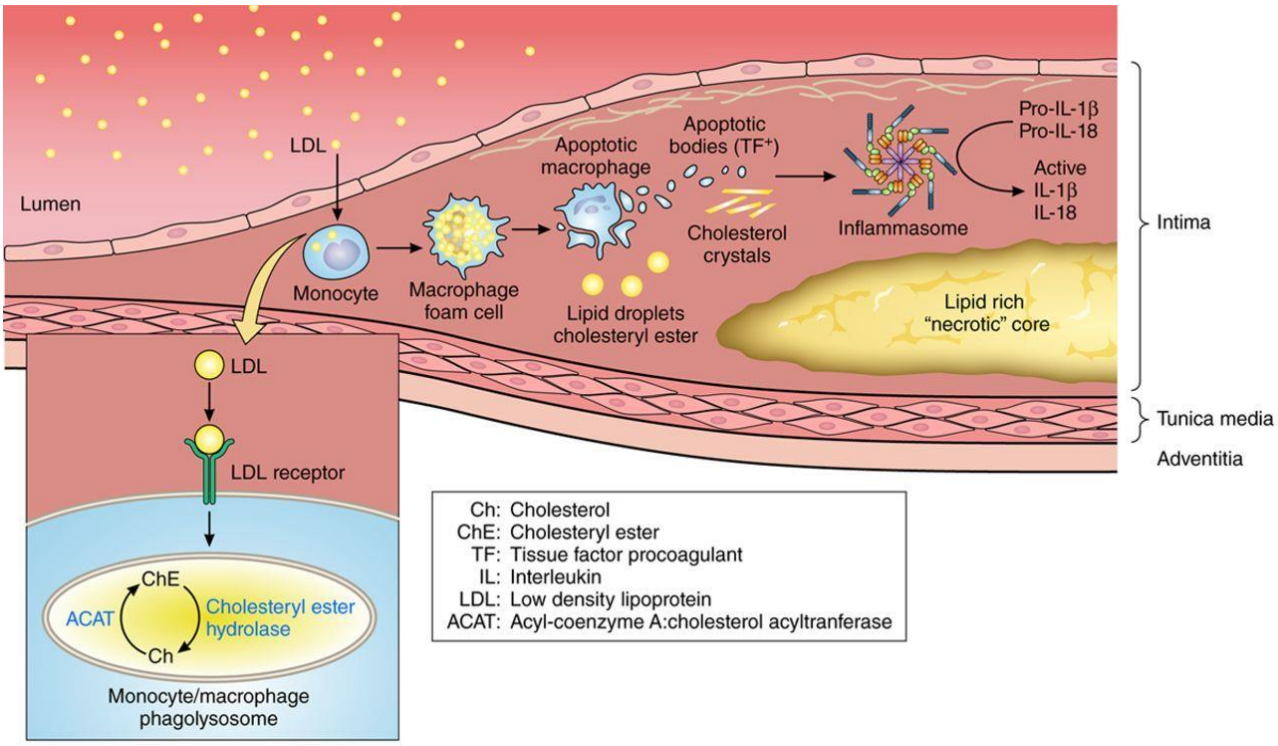


Figure 1.3 . Cholesterol crystals activate local innate immune pathways in the atherosclerotic plaque. **[12]**

The usual cause of acute occlusion is coronary artery thrombosis caused by rupture or erosion of a high-risk, lipid-laden, atheromatous plaque **[7].**This sudden, reduced blood flow to the heart results in an imbalance between myocardial metabolic demands and blood supply, leading to myocardial ischemia, which is the hallmark of ACS **[13]** .The imbalance may also be caused by several other cardiac abnormalities, including coronary artery embolism, coronary spasm, coronary dissection, severe anemia, and calcific aortic valve stenosis **[14] .** Depending upon the range of ischemic state, location of the occlusion, cardiac biomarker levels (e.g., troponin), and ST-segment elevation on the electrocardiogram (ECG), ACS is mainly categorized into three types (figure 1.4), namely unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) **[15].** Typically, a complete coronary artery

occlusion leading to myocardial tissue injury and elevated cardiac troponin level results in STEMI. Partial occlusion or occlusion with collateral circulation may lead to NSTEMI or UA **[15] .**

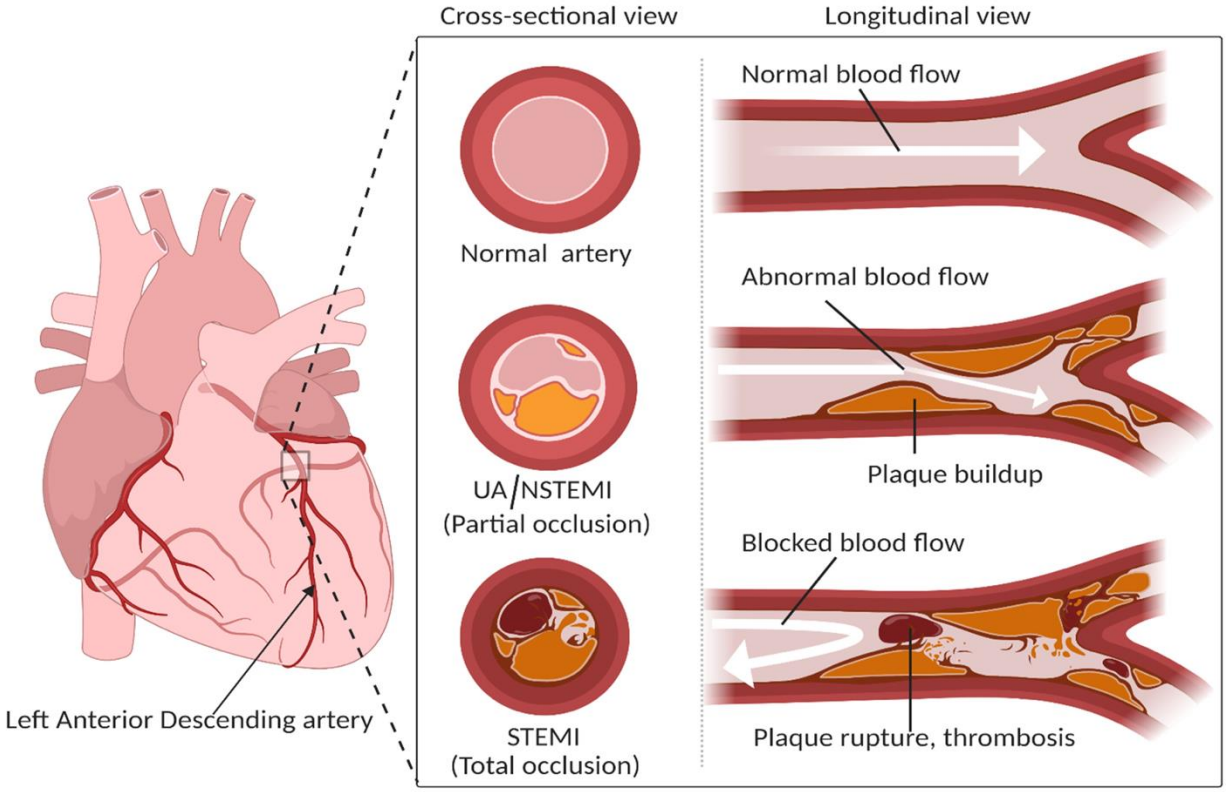


Figure 1.4: Classification of acute coronary syndromes.[15].

Epidemiology:

Acute coronary syndrome (ACS) has been reported to be one of the common reasons for deaths in Iraq and most important reason for morbidity and mortality according to Annual statistical report in 2020. The percentage of each subclass of ACS is as follows: UA (38%), ST EMI (30%), NST EMI (25%), and (7%) of other cardiac and non-cardiac final diagnoses **[16]**.Atherothrombosis can no longer be considered a disease of the developed world, because myocardial infarction and stroke are increasingly prevalent worldwide, across all socioeconomic strata. By 2025, cardiovascular mortality on a worldwide scale will likely surpass that of every major disease group, including infection, cancer, and trauma **[17]**.

1.6. Risk Factors:

Acute coronary syndrome is a serious health problem results from many risk factors which remains a significant cause of morbidity and mortality worldwide, the risk factors summarized in Figure (1.5) followed by a brief details about the main factors.

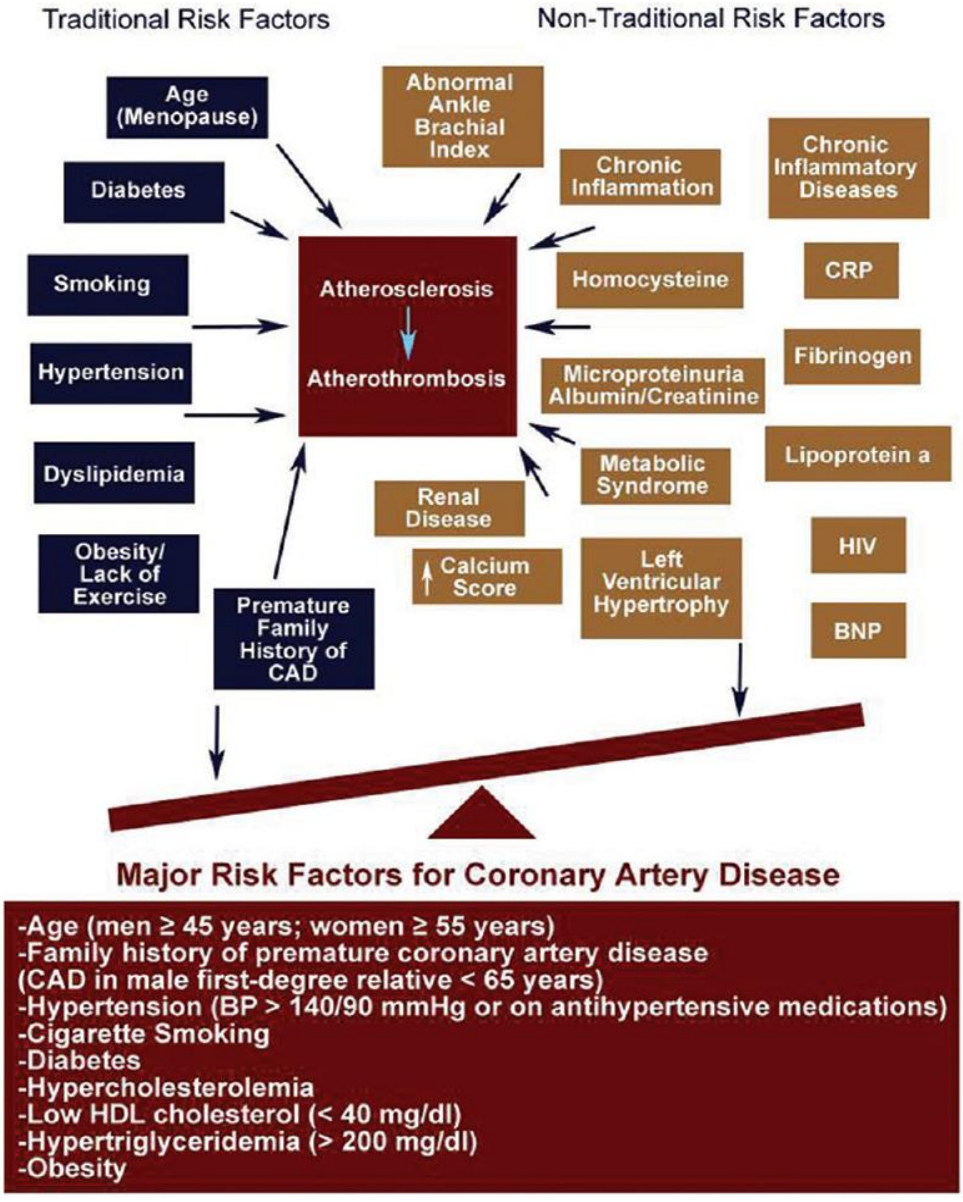


Figure 1.5 : Risk factors of acute coronary syndrome. [18]

Gender:

Male tend to have heart attacks earlier in life than female. Female rate of heart attack increases after menopause but does not equal males rate. Even so, heart disease is the leading cause of death for both men and women **[19]**.

Age:

Older patients have poorer outcomes than younger counterparts following an ACS **[20]**. This is related to a multitude of factors. Older age is a recognized risk factor not only for the development of coronary heart disease (CHD), but also highlighted in many ACS risk models to predict "short" and "long" term mortality **[21]**.

The elderly with ACS are at high risk for adverse outcomes, but those at high risk have the most to gain from ACS therapies **[20]**. However, older patients have greater frequency of physiological impairment (frailty), psychological and cognitive impairment, physical disability and co-morbidity which enhance their age-related risk **[22]**.

Smoking:

Smoking effects blood pressure sympathetic tone, and a reduction in myocardial oxygen supply, also, it affects atherothrombosis through several other mechanisms **[23]**. In addition to accelerating atherosclerotic progression, long-term smoking may enhance the oxidation of (LDL) cholesterol and impair endothelium-dependent coronary artery vasodilation. smoking has adverse inflammatory effects, including increased levels of C reactive protein (CRP), soluble intercellular adhesion molecule-1 (ICAM-1), fibrinogen, and homocysteine. Smoking may provoke spontaneous platelet aggregation, increased monocyte adhesion to endothelial cells, and adverse alterations in endothelial-derived fibrinolytic and antithrombotic factors, including tissue plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1). Compared with nonsmokers, smokers have an increased

prevalence of coronary spasm and reduced thresholds for ventricular arrhythmia. evidence suggests that insulin resistance represents an additional mechanistic link between smoking and premature atherosclerosis **[24]**.

Hypertension:

High blood pressure often confers silent cardiovascular risk, and its prevalence is steadily increasing. Part of the complexity of hypertension as a risk factor relates to changing definitions of risk and an understanding that systolic blood pressure and pulse pressure may have greater importance than diastolic blood pressure. Most epidemiologic studies now recognize the joint contributions of systolic and diastolic blood pressure to the development of cardiovascular risk, an issue that has influenced strategies for risk detection. Isolated systolic hypertension, in particular, has at least as much importance as diastolic blood pressure for the outcomes of total cardiovascular mortality and stroke. Evidence supports the treatment of systolic hypertension, even in older adult **[25]**.

Hyperlipidemia and Lipid Profile:

High-Density Lipoprotein (HDL) Cholesterol:

High-Density Lipoprotein (HDL) The smallest, densest, and more soluble lipoproteins, they are produced by the hepatocytes and intestinal mucosal cells by a process analogous to very low-density lipoprotein (VLDL) and chylomicron synthesis. High density lipoprotein (HDL) collects cholesterol from the body tissues and brings it back to the liver **[26]**. In general, each increase of HDL cholesterol by 1mg/dL is associated with a 2% to 3% decrease in risk of total cardiovascular disease. Patients with angiographically proven coronary artery disease more often have low levels of HDL and high levels of LDL, as defined by current criteria. The process of reverse cholesterol transport may explain in part the apparent protective role of HDL

against coronary death. According to this concept, HDL could ferry cholesterol from the vessel wall, augmenting peripheral catabolism of cholesterol. HDL can also carry antioxidant enzymes that may reduce the levels of oxidized phospholipids in atheromatous lesions, which could enhance atherogenesis **[27]**.

Low- Density Lipoprotein Cholesterol and VLDL:

Very low-density lipoprotein is a dense class of lipoprotein which carry triacylglycerol from the liver to adipose tissue. The endogenously synthesized triglyceride and cholesterol are packed in secretary vesicles in Golgi apparatus transported by exocytosis into the extracellular space **[28]**. LDL cholesterol as a CHD risk factor meets most of the criteria to establish a causative agent in a disease. High cholesterol levels consistently predict the risk of future cardiovascular events in human populations. Interventions in large clinical trials to lower LDL cholesterol levels by various approaches (e.g., bile acid-binding resins, intestinal bypass surgery and statins) have shown a reduction in cardiovascular events. Thus, LDL cholesterol fulfills the criteria of modified Koch's postulates as one causative agent in atherosclerosis **[29]**.

Triglyceride (TG)- Rich Lipoprotein and Cardiovascular Risk:

Excess triglyceride in plasma is called hypertriglyceridemia, It is linked to the occurrence of coronary artery disease. It transported by chylomicron which are lipoprotein particles that consist of triglycerides (85-92%), phospholipids (6-12%), cholesterol (1-3%), and proteins (1-2%). They transport dietary lipids from the intestines to other locations in the body **[30]**. elevated plasma TG level is an independent risk factor for CHD, hypertriglyceridemia (HTG) is often secondary to obesity-related insulin resistance **[31]**

Metabolic Syndrome, Insulin Resistance, and Diabetes Mellitus:

Insulin resistance and diabetes rank among the major cardiovascular risk factors; in one major survey, the presence of diabetes conferred an equivalent risk to aging 15 years, an impact higher than that of smoking. Patients with diabetes have two- to eightfold higher rate of future cardiovascular events as compared with age- and ethnicity-matched non-diabetic individuals, and 75% of all deaths in diabetic patients result from CHD. Insulin resistance alone confers an elevated risk of heart failure and probably explains the association of obesity with this diagnosis **[32]**.

1.7. Diagnosis of ACS:

Early diagnosis of AMI is of critical importance to save as much myocardium at risk as possible **[33]** . The initial assessment is based on the integration of low likelihood and high likelihood features derived from the clinical setting. ECG, and the cardiac troponin concentration determined at presentation to the emergency department and serially thereafter. Cardiac troponin and its change during serial sampling should be interpreted as a quantitative marker: the higher the 0 hr level or the absolute change during serial sampling, the higher the likelihood for the presence of MI. In patients presenting with cardiac arrest or haemodynamic instability of presumed cardiovascular origin, echocardiography should be performed/interpreted by trained physicians immediately following a 12-lead ECG. If the initial evaluation suggests aortic dissection or pulmonary embolism, D-dimers and CCTA are recommended according to dedicated algorithms figure (1.6) demonstrated the Diagnostic algorithm and triage in acute coronary syndrome **[34].**

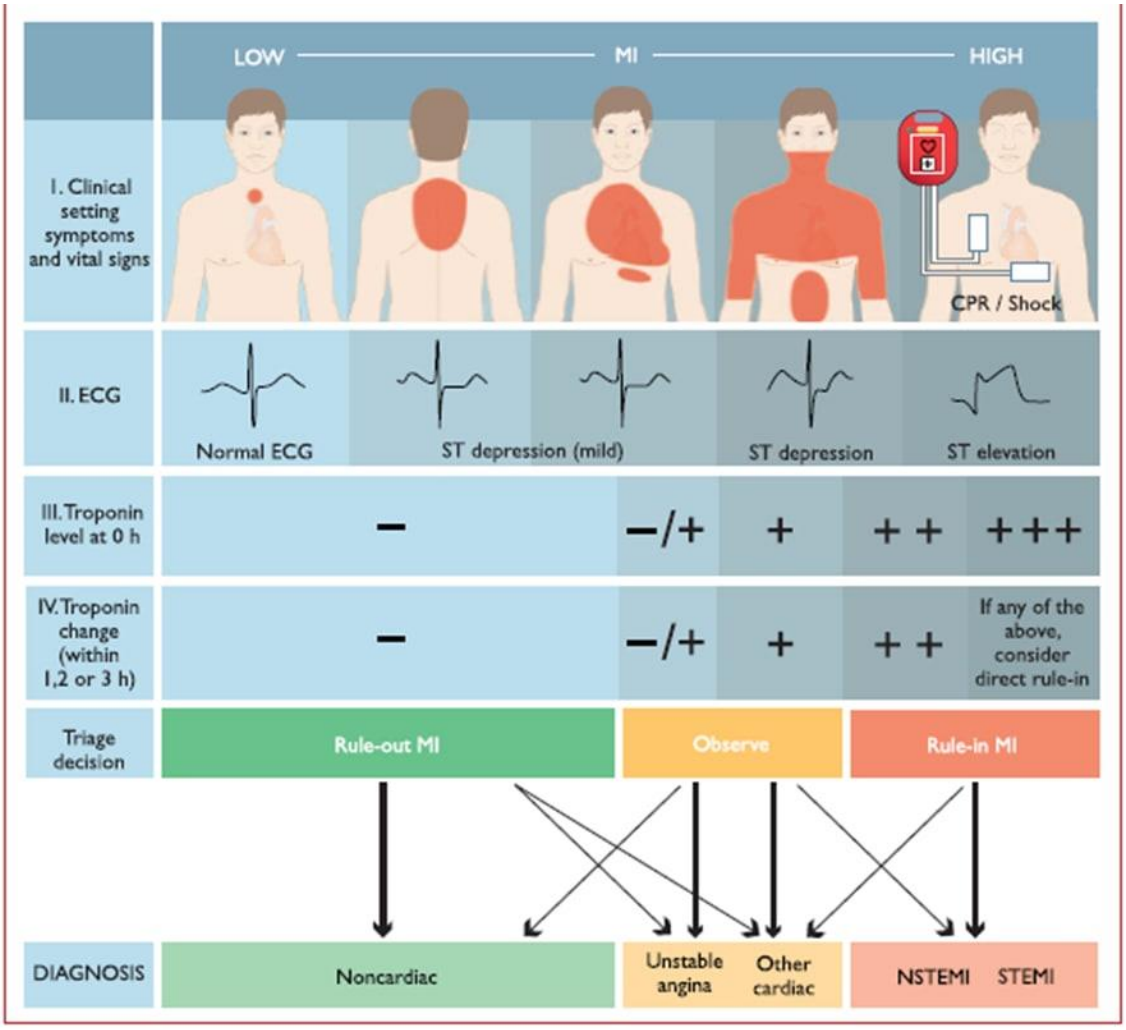


Figure 1.6: Diagnostic algorithm and triage in acute coronary syndrome.[35]

1.7.1. Non-biomarkers for diagnosis ACS

Electrocardiography:

The resting 12-lead ECG is the first-line diagnostic tool in the assessment of patients with suspected ACS., characteristic abnormalities include ST-segment depression, transient ST-segment elevation, and T-wave changes**[36].**

Echocardiography:

Echocardiography uses ultrasound beams reflected by cardiovascular structures to produce characteristic lines or shapes caused by normal or altered cardiac anatomy

in one, two, or three dimensions by M (motion)-mode, two-dimensional, or three-dimensional echocardiography, respectively. Doppler examination and color flow imaging provide reliable assessment of cardiac hemodynamics and blood flow**[37].**

Ejection Fraction (EF):

Ejection fraction is the fraction of outbound blood pumped from the heart with each heartbeat. It is commonly measured by echocardiogram and serves as a general measure of a person's cardiac function **[38]**.

1.7.2. Biomarkers for diagnosis ACS

The availability of serum cardiac markers with markedly enhanced sensitivity for myocardial damage enables clinicians to diagnose MI in approximately an additional one third of patients who would not have fulfilled criteria **[39]** The increased use of more sensitive biomarkers combined with more precise imaging techniques, has necessitated the establishment of new criteria**[40].**

1.7.2.1. Cardiac-Specific Troponin:

The troponin complex consists of three subunits that regulate the calcium-mediated contractile process of striated muscle. These include troponin C (TnC), which binds Ca^{2+}, troponin I (TnI), which binds to actin and inhibits actin-myosin interactions, and troponin T (TnT), which binds to tropomyosin, thereby attaching the troponin complex to the thin filament, (Figure 1.7) **[41].**

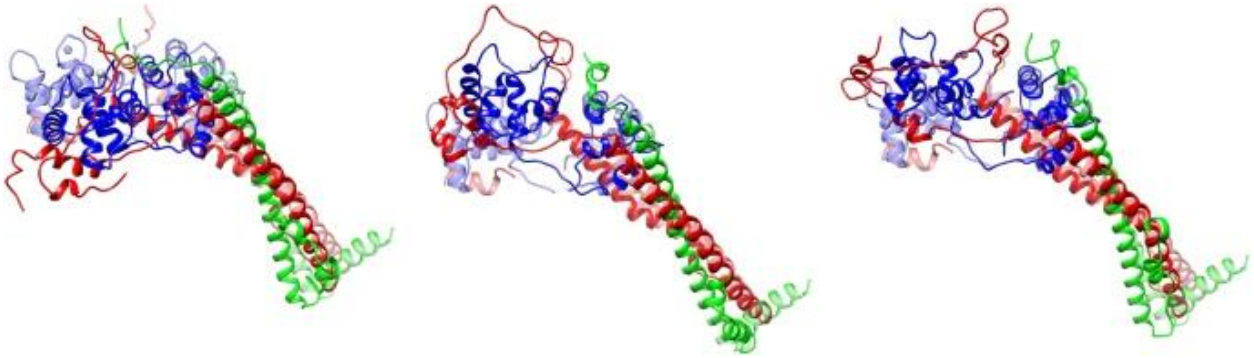


Figure 1.7: The three most populated structures of human cardiac troponin determined by molecular dynamics simulations overlaid over the Takeda et al. structure of hcTn (pale structure) TnC is depicted in blue, TnT in green and TnI in red [41].

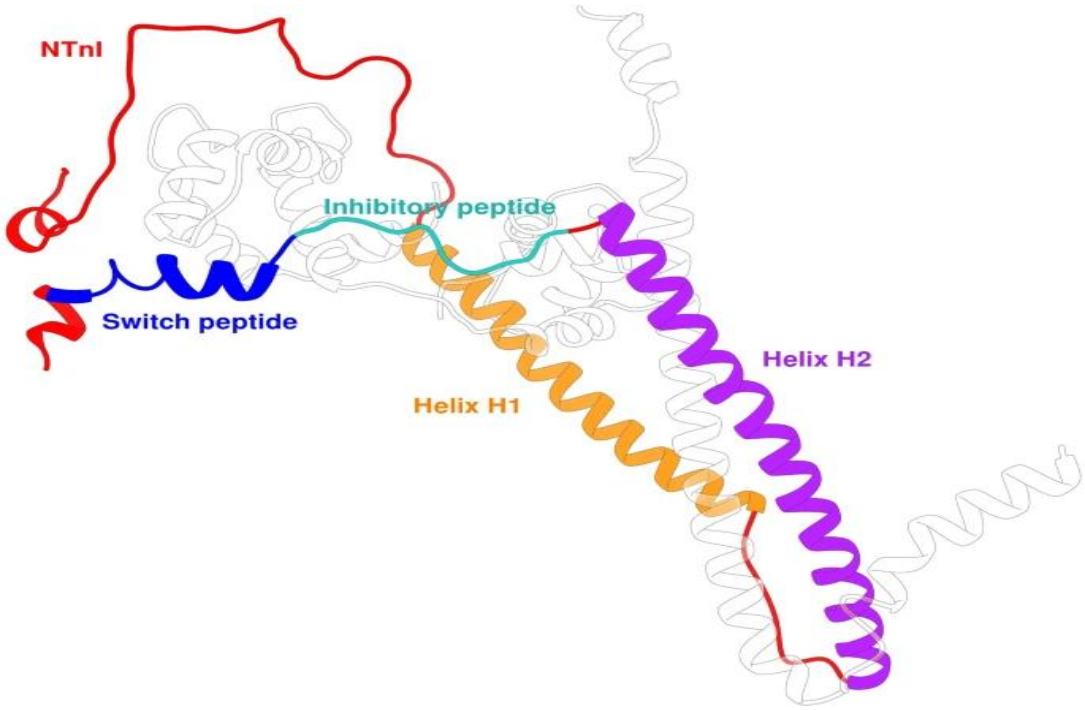


Figure 1.8: The cTnI molecule with its relevant structural regions highlighted. [42].

Following myocyte injury, the initial release of cTnT and cTnI is from the cytosolic pool, followed subsequently by release from the structural (myofilament-bound) pool. Different genes encode TnT and TnI in cardiac and skeletal muscle, thus permitting the production of specific antibodies for the cardiac form (cTnT and cTnI) that enable their quantitative assay **[43].** The measurement of cTnT or cTnI is now at the center of the new diagnostic criteria for MI. When interpreting the results of assays for cTnT or cTnI, clinicians must be cognizant of several analytic issues **[44]** Furthermore, cTnT and cTnI typically increase more than 20 times above the reference range, enabling the detection of even minor degrees of myocardial necrosis. In patients with MI, cTnT and cTnI levels first begin to rise above the upper reference limit by 3 hours from the onset of chest pain. Patients with STEMI and NSTEMI who undergo successful recanalization of the infarct-related artery have a rapid release of cardiac troponins, which can indicate reperfusion **[45].**

1.7.2.2. Ischemia-Modified Albumin (IMA):

Ischemia-modified albumin (IMA) is a "N-terminal modified" albumin which is generated immediately following myocardial ischemia.

The N-terminal portion of human serum albumin (HSA) is a binding site for transition metal ions such as cobalt, copper and nickel **[46].** It is currently not known if there are significant changes in total human serum albumin between ischemic and non-ischemic patients in the general chest pain population, figure (1.9) show generation of IMA **[47].**

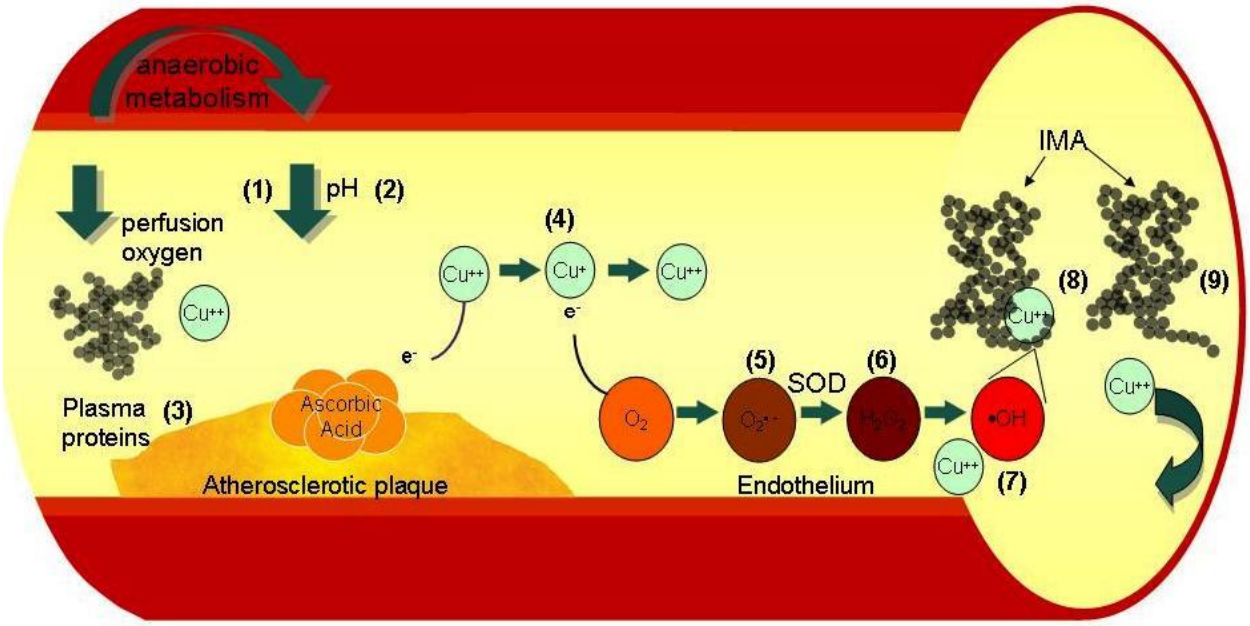


Figure 1.9: Postulated mechanism of IMA generation [48].

In ischemia of the myocardium within seconds of vascular obstruction, aerobic glycolysis ceases in the myocytes, leading to inadequate production of adenosine triphosphate and depletion of creatine phosphate resulting in the accumulation of lactic acid, NADH. Cellular proteins and enzymes become progressively more dysfunctional as the pH falls. Depletion of ATP leads to reduction in the activity of the plasma membrane dependent sodium pump resulting in intracellular accumulation of sodium and efflux of potassium. Failure of the calcium pump leads to influx of calcium and its damaging effects **[49]**. Reduced pH leads to release of bound copper and iron from protein and intracellular stores. Carriers of electron transport chain, thereby the formation of reactive oxygen species like super oxide anions **[50]**.These free radicals oxidatively damage the histidine present in the amino terminal region of albumin. This albumin which has a damaged amino terminal is called Ischemia Modified Albumin**[51].**

1.8. Clinical Studies using Ischemia Modified Albumin

Clinical validation of any test for ischemia is difficult as there is no accepted diagnostic gold standard. In addition, there is no predicate test which can be used against which initial validations can be performed. Initial studies on IMA were based on the ability of early measurements to predict a final diagnosis of AMI as defined by cardiac troponin. Two studies utilized the pre-release ACB test, the third an in-house method. The first study examined acute coronary syndrome (ACS) patients and utilized serial sampling on admission and two subsequent samples **[52]**.

Diagnostic sensitivity of the admission sample for a final diagnosis of AMI was 23.9% for cardiac troponin I (cTnI) alone, 39.1% for IMA alone and 55.9% for the two combined **[53]**. The second study examined 256 ACS patients. The area under the curve (AUC) of the receiver operator characteristic (ROC) curve for the ACB test was 0.78 with a sensitivity and specificity of 83% and 69% respectively at the optimised decision threshold for AMI. The third study was conducted on 75 patients with ischemia and 92 non-ischemic patients **[54]**. IMA had poor predictive power in discriminating between AMI and non-AMI in patients with underlying ischaemic heart disease (AUC of 0.66). However, the test gave good discrimination between patients with or without ischemia. AUC for the ROC curve for diagnosis of ischemia was 0.95 with a sensitivity of 94% and specificity of 88%. This made the method unsuitable for routine analysis and the assay was reformulated. Most patients brought to the hospital with chest pain and suspected of ACS are eventually ruled out for acute myocardial infarction and active unstable coronary disease. A study on ED presentations examined 208 patients and the diagnostic sensitivity of IMA measurement alone was 82% at 46% specificity in samples taken within the first 3 hours. A combination of ECG, cardiac troponin T (cTnT) and IMA showed 95% sensitivity for diagnosis of ACS at presentation **[55]**. One year follow up on this population demonstrated a survival disadvantage in patients with IMA greater than

the median concentration of the study group **[56]**.In a subsequent study on 538 patients admitted for chest pain evaluation admission measurement of IMA plus cTnT indicated 100% sensitivity for prediction of a final diagnosis of AMI **[57]**. IMA measurement appears to work best as part of other tests or a test sequence **[58]**. Admission measurement of IMA has been found superior to biomarkers of necrosis and to show 97% sensitivity when combined with them. Not all investigators consider the diagnostic performance of IMA either alone or in combination with cardiac troponin, or other biomarkers of necrosis, to be adequate. Conversely, another study found elevated IMA to predict long-term cardiac events **[59]**.

1.9. Half-life and Clearance of Ischemia Modified Albumin

The half life of human serum albumin is 19–20 days. If a slightly truncated form is responsible for generating IMA, it would presumably have similar stability properties. IMA however returns to the baseline rapidly after an ischaemic cardiac event. This indicates that alteration in albumin is possibly transient and reversible, rather than a definitive chemical alteration. However IMA may possibly undergo preferential proteolytic degradation **[60].**

1.10. Knowledge gap

Early diagnosis of AMI is of critical importance to save as much myocardium at risk as possible **[61]**.

Sensitivity and specificity of troponin less than IMA **[53]**. It is important to highlight that more than 50% of patients presenting with acute chest pain or LBBB to the emergency department pain unit will ultimately be found to have a diagnosis other than MI **[62]** and should, await the result of the hs-cTn T/I measurement at presentation **[63]** While the ECG in the setting of NSTE-ACS may be normal in

more than 30% of patients, characteristic abnormalities include ST-segment depression, transient ST-segment elevation, and T-wave changes **[64]**.

The hypothesis of the current study was that, IMA might indicate cardiac ischemia before cardiac myocyte injure and release troponin to blood circulation. also its important in the reinfarction.

1.11. Aims of the study:

1- To investigate diagnostic value of ischemia-modified albumin (IMA) levels in patients applying to emergency department with symptoms of acute coronary syndrome (ACS)

2- Study the role of these biochemical markers in differentiation of ACS chest pain causes; UA, NSTEMI and STEMI.

3- Identify the cutoff values of these biochemical markers in early diagnosis of ACS cases.

CHAPTER TWO

Materials and Methods

2. Materials and methods

2.1.Study design

The present work included a case control study for a group of (120) individuals: (90) patient with ACS, and are (30) apparently healthy control individuals.

Patients with Acute coronary syndrome cases were selected from the CCU of Karbala cardiac diseases centre, Ibn alnafees/ Baghdad and Baghdad Hospital in Medical city of Baghdad. The questionnaire used in this study was developed based on literature review and discussion within the researcher and supervisors' team.

They were also exposed to medical examination for signs and symptoms of any cardiac disorders manifest such as Troponin with electrocardiographic patterns by specialized doctor.

The questionnaire was structured into different sections. The sociodemographic characteristics of the participants were obtained and represented by the Baseline characteristics. Additionally, participants were asked to report their history with chronic conditions.

Also, the questionnaire was involved in a section for collecting data about Comorbidities at sudden cardiac arrest, Baseline electrocardiographic parameters, Medication, Etiology and Blood biochemical tests.

2.2.Instruments:

Table 2.1: The instruments used in the study

Instrument	Suppliers
Centrifuge	HETTICH/ Germany
Deep Freeze	COOLTECH/ China
ELISA system	UNO/HUMAN/ Germany
Roller Mixer	China
Biobase BK500	China
UV-spectrophotometer	UV-1800 Shimadzu /Japan

Tools, materials and Kits

The Tools, materials and kits with their supplier which were used in this study are listed in table (2.2) .

Table 2.2: Tools and materials used in the study

Tools and Materials	Suppliers
Pipette(100-1000µl)	DRAGON MED/ USA
Micropipette(10-100 µl)	DRAGON LAB/ USA
Gilson Tips,1000µl (blue)	China
Gilson Micro-tips, 100µl	China
Eppendroff Tubes	China
Gel tubes	China
EDTA tubes	China
Gloves	China
Syringe 5cc	China

Table 2.3: kits which are used in this study

kits	Suppliers
Lipid profile Kits	Bioteck/ China
IMA Kit	Bioteck/ China
Troponin I Kit	Bioteck/china
Albumin kit	Biobased bk500

2.3. Inclusion and Exclusion criteria:

2.3.1. Patients' inclusion Criteria

All patients were subjected to the full clinical history, clinical examination, and relevant laboratory investigations. The diagnosis of the Acute coronary syndrome (unstable angina, myocardial infraction) clinical conditions was established according to the latest clinical practice guidelines by the ACC, ESC. The etiologiy of cases was identified based on signs and symptoms, evaluation of ECG and laboratory measurements.

Patients Exclusion criteria:

Patients with presence of renal diseases, cirrhosis, stroke, skeletal muscle injury, malignancy, ongoing infectious diseases were excluded of this study

2.3.2. Control Criteria:

Control group of an apparently healthy subjects were chosen randomly. Blood samples were drawn from the volunteers, participants had no history of heart diseases. The ages of the participants were also convergent in the whole study group.

Demographic information of the participants was also collected through the self-reported technique (student questionnaire).

2.4.Study variables:

- **Dependent Variable**

IMA, Troponin and Albumin

- **Independent Variable**

Age, Gender, BMI, Lipid profile, CBC, Demographic factors.

2.5.Approval of the Ethical Committee

The protocol of the study was approved by Ethical Committee of Karbala Medical College, and committee of heart disease unit in karbala cardiac center and Ibn Alnafes cardiac center and CCU of Baghdad hosbital . Serum sample were obtained after consent from patients or the patients relatives.

2.6.Measurement and Data collection

2.6.1. Blood Collection and Storage

Blood samples were collected from the above mentioned centers. Five ml of blood samples were drown by venipuncture using 5ml disposable syringes using gel tube for biochemical test and EDTA tube for CBC test and blood was left for (15 min) at room temperature in gel tube. Serums were separated by centrifuging for 10 minutes at approximately 4000 xg. Serum samples were aliquot into three to foure Eppendorf and store at -20°C to avoiding multiple freezing-thawing cycles and used for the

further measurement. Blood collection tubes were be disposable, non-pyrogenic, and non-endotoxin.

2.7. Methods:

2.7.1. Measurement of IMA levels in Human serum by using Sandwich-ELISA Technique:

Principle

This ELISA kit uses Sandwich-ELISA as the method. The Micro Elisa strip plate provided in this kit has been pre-coated with an antibody specific to IMA Standards or samples are added to the appropriate Micro Elisa strip plate wells and combined to the specific antibody. Then a Horseradish Peroxidase (HRP)-conjugated antibody specific for IMA is added to each Micro Elisa strip plate well and incubated. Free components are washed away. The TMB substrate solution is added to each well. Only those wells that contain IMA and HRP conjugated IMA antibody will appear blue in color and then turn yellow after the addition of the stop solution. The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is proportional to the concentration of IMA You can calculate the concentration of IMA in the samples by comparing the OD of the samples to the standard curve.

Materials provided with the kit

Table 2.4: Materials provided with the ELISA kit

	Materials provided with the kit	96 determinations	Storage
1	User manual	1	
2	Closure plate membrane	2	R.T.
3	Sealed bags	1	R.T.

4	Micro Elisa strip plate	1	2-8℃
5	Standard：90 U/ml	0.5ml×1 bottle	2-8℃
6	Standard diluent	1.5ml×1 bottle	2-8℃
7	HRP-Conjugate reagent	6ml×1 bottle	2-8℃
8	Sample diluent	6ml×1 bottle	2-8℃
9	Chromogen Solution A	6ml×1 bottle	2-8℃
10	Chromogen Solution B	6ml×1 bottle	2-8℃
11	Stop Solution	6ml×1 bottle	2-8℃
12	Wash Solution	20ml (30X)×1bottle	2-8℃

Preparation of reagents:

Stock solutions were prepared according to the procedure of the kit. All reagents were prepared freshly at room temperature before using.

1. **Dilution of Standards**: Dilution of Standards

Dilute the standard by small tubes first, then pipette the volume of 50ul from each tube to microplate well,each tube use two wells, total ten wells.

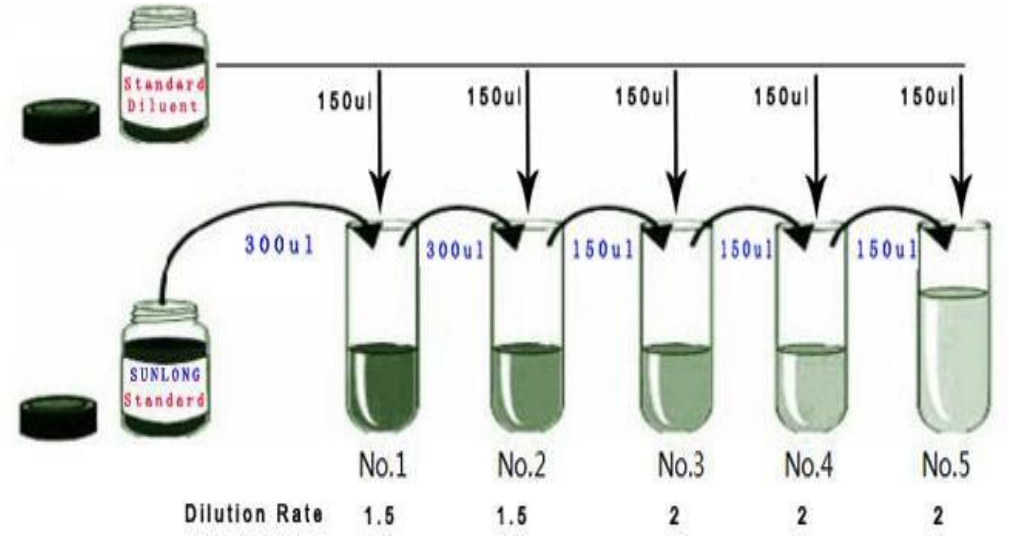


Table 2.5: Dilution of Standards

60 U/ml	Standard No.1	300µl Original Standard + 150µl Standard diluents
40 U/ml	Standard No.2	300µl Standard No.1 + 150µl Standard diluents
20 U/ml	Standard No.3	150µl Standard No.2 + 150µl Standard diluent
10 U/ml	Standard No.4	150µl Standard No.3 + 150µl Standard diluent
5 U/ml	Standard No.5	150µl Standard No.4 + 150µl Standard diluent

Procedure: Dilute the standard by small tubes first, then pipette the volume of 50ul from each tube to microplate well, each tube use two wells, total ten wells.

1. In the Micro ELISA strip plate, leave a well empty as blank control. In sample wells, 40µl Sample dilution buffer and 10µl sample are added (dilution factor is 5). Samples should be loaded onto the bottom without touching the well wall. Mix well with gentle shaking. Incubation: incubate 30 min at 37℃ after sealed with Closure plate membrane.
2. Dilution: dilute the concentrated washing buffer with distilled water (30 times for 96T)
3. Washing: carefully peel off Closure plate membrane, aspirate and refill with the wash solution. Discard the wash solution after resting for 30 seconds. Repeat the washing procedure for 5 times.

4. Add 50 µl HRP-Conjugate reagent to each well except the blank control well.
5. Incubation as described in Step 1.
6. Washing as described in Step 3.
7. Colouring: Add 50 µl Chromogen Solution A and 50 µl Chromogen Solution B to each well, mix with gently shaking and incubate at 37°C for 15 minutes. Light is avoided during colouring.
8. Termination: add 50 µl stop solution to each well to terminate the reaction. The colour in the well should change from blue to yellow.
9. Read absorbance O.D. at 450nm using a Microtiter Plate Reader. The OD value of the blank control well is set as zero. Assay was carried out within 15 minutes after adding stop solution.

Calculation of results: A standard curve was constructed by plotting the average OD for each standard on the vertical (Y) axis against the concentration on the horizontal (X) axis and a best fit curve was drawn through the points on the graph. These calculations can be best done with computer-based curve-fitting software and the best fit line can be determined by regression analysis. The result was expressed in U/ml.

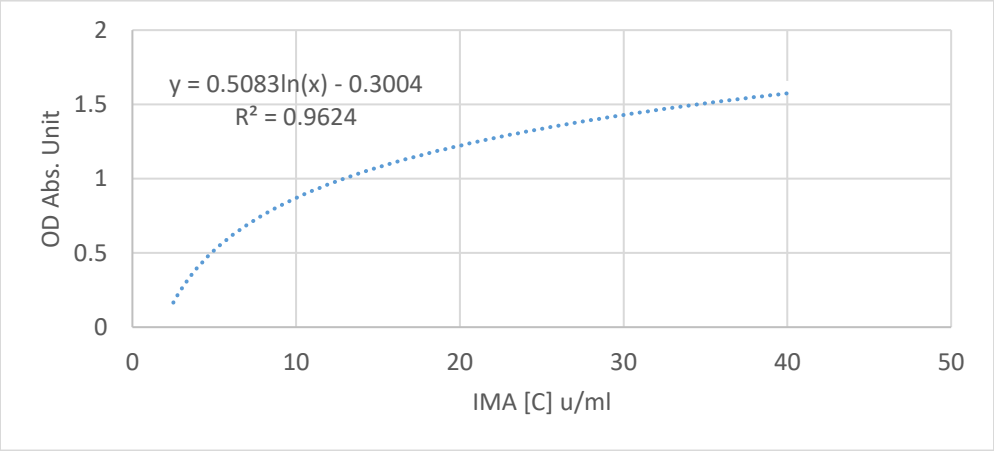


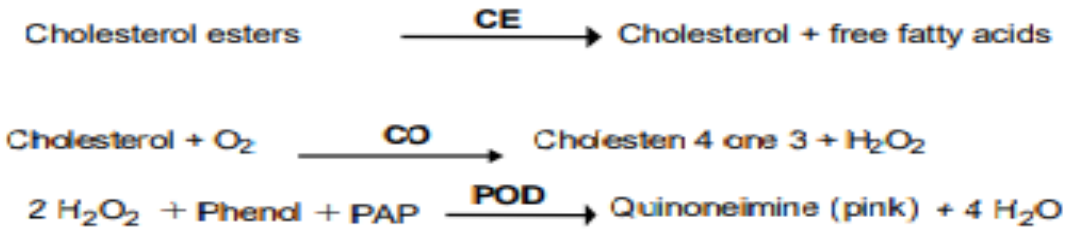
Figure (2.1) Standard Curve of the Human IMA concentration which plotted by the scale of OD Vs. the scale of a known concentration. The original concentration is calculated by multiplying the dilution factor.

2.7.2. Measurement of lipid profile

2.7.2.1. Measurement of Cholesterol levels in Human serum by using Spectrophotometric Technique:

Principle : Esterified cholesterol is hydrolized into free cholesterol and fatty acid by cholesterol esterase (CHE). Cholesterol oxidase (CHOD) oxidizes the free cholesterol into cholestene-3-one with formation of hydrogen peroxide. In presence of peroxidase (POD), hydrogen peroxide reacts with a derivative of phenol and 4-aminoantipyrine to produce a colored complex whose color intensity is directly proportional to the total cholesterol concentration in the sample.

Enzymatic method described by Allain and al., which reaction scheme is as follows:



Kit components:

R1: 2*100 ml

R2: 2*100 ml

R3: 1*5 ml standard

Procedure:

pipette	blank	Sample	standard
Reagent (A)	1000 µl	1000 µl	1000 µl
Water	10 µl		
Sample		10 µl	
Standard			10 µl

It was mixed and left for 5 min at 37°C after which the absorbance at 500 nm was recorded against a blank reagent

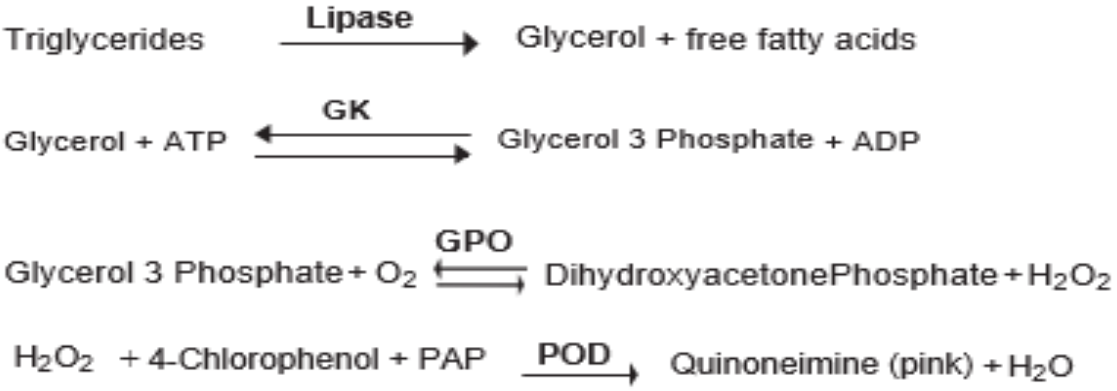
Calculation:

Cholesterol mg/dl = Absorbance sample/Absorbance standard x 200 (concentration of standard)

2.7.2.2. Measurement of Triglycerides levels in Human serum by using Spectrophotometric Technique:

Principle: Fossati and Prencipe method Associated with Trinder reaction.

Reaction scheme is as follows:



The absorbance of the coloured complex (quinoneimine),is proportional to the amount of triglycerides in the specimen, is measured at 500 nm.

Kit components:

R1: 2*50 ml

R2: 2*50 ml

R3: 1*5 ml standard

Procedure:

pipette	blank	Sample	standard
Reagent (A)	1000 µl	1000 µl	1000 µl
Water	10 µl		
Sample		10 µl	
Standard			10 µl

It was mixed and left for 10 min at room temperature after which the absorbance at 500 nm was recorded against a blank reagent.

Calculation: The result was calculated as follows:

Result = A sample/A standarad x concentration of Standard (200 mg/dl)

2.7.2.3. Measurement of HDL-Cholesterol levels in Human serum by using Spectrophotometric Technique:

Principle:this reagent is only for treatment of speciments before determenation of HDL-cholesterol with areagent for total cholesterol.

Low density lipoproteins (LDL), very low density (VLDL) and chylomicrons from specimens are precipitated by phosphotungstic acid (PTA) and Magnesium chloride. HDL-Cholesterol obtained in supernatant after centrifugation is then measured with Total Cholesterol reagent.

Kit components:

R1: percipitant

R2: standarad (100 mg/dl)

Procedure: reagents and supernatants were placed at room temperature.

	Micro- method
specimen	0.5 ml
precipitant	50 µl

It was mixed and left for 10 min at room temperature centerfuge 15 min at 3500-4000 xg then take supernatent from procedure above

pipette	blank	Sample(supernantent)	standard
Reagent (A)	1000 µl	1000 µl	1000 µl
Water	10 µl		
Sample		10 µl	
Standard			10 µl

mixed and left for 10 min at room temperature after which the absorbance at 500 nm (480-520) was recorded against a blank reagent

reagent stable for 1 hour.

Calculation: The result was calculated as follows:

Result = A sample/ A standarad x Standard concentration (100 mg/dl)

Refrence range :

<40 mg/dl Risk factor

>60 protective factor

2.7.2.4. Measurement of LDL Cholesterol levels in Human serum by full automated biochemical analyser

Principle

The principle of this method is that each lipoprotein reacts differently with surfactants depending on its physicochemical properties. Therefore, two different surfactants are employed. Surfactant 1 is added in the first reaction. It can change the structure of lipoproteins other than LDL, including chylomicron (CM), very VLDL and HDL. In the presence of this surfactant, lipoproteins other than LDL are eliminated by the action of cholesterol oxidase and cholesterol esterase. Surfactant 2, which promotes the enzymatic reaction of all types of lipoproteins, is used in the second reaction. The enzymatic reaction with LDL-cholesterol left from the first reaction is initiated to produce color development.

Kit Components

Ingredients Enzyme Solution: 4-Aminoantipyrine Cholesterol Oxidase Cholesterol Esterase Peroxidase Coloring Solution: N, N-bis (4-sulfobutyl)-m-toluidine disodium (DSBmT)

Procedure:

Preparation of reagents:

Reagent (1): Enzyme Solution is ready to use.

Reagent (2): Coloring Solution is ready to use

Assay Procedure:

This product is compatible with various types of automated analyzer. An example of the assay procedure is indicated below.

Sample 3 µL + Reagent (1) 300 µL 37°C Measurement (Absorbance I)

Reagent (2) 100 µL 37°C Measurement (Absorbance II) Calculation of concentration Absorbance I and II: The difference in absorbance between 660 nm and 546 nm.

Normal rang: <128 mg/dl

2.7.3. Measurement of Complete blood count

The measures of CBC were done by XP-300™ Automated hematology analyzer.

Principle:

- DC detection method for WBC.
- DC detection method for RBC/PLT.
- Non-cyanide haemoglobin analysis method for HGB.
- **Parameters:** WBC, RBC, HGB, , PLT, LYM%, NEU%, LYM#, NEU#, and MPV.

Sample volume:

- Whole blood (WB) mode: Approximately 50µL.

- Pre-diluted (PD) mode: Approximately 20µL.

2.7.4. Measurement of Albumin levels in Human serum by full automated biochemical analyser

Assay Principle for a number of years the standard method for albumin determination was measurement of protein remaining in solution following salt precipitation of globulin fractions . Electrophoresis has also been widely used. Measurement of albumin has been greatly simplified by the introduction of dye binding methods. The method using bromcresol green (BCG) is more specific, sensitive, and less prone to pigment interference than the earlier dye binding methods, and has been improved by reduction of the reaction pH. Albumin at pH 4.2 is sufficiently cationic to bind the anionic dye bromcresol green (BCG) to form a blue-green colored complex. The intensity of the blue-green color is directly proportional to albumin concentration in the specimen. It is determined by measuring the increase in absorbance at 580 - 630 nm.

2.8. Statistical Analysis:

Information from the questionnaire and all test results from study groups samples were entered in a data sheet. The data analysis for this work was generated using the Statistical Package for the Social Sciences software, version 28.0 (IBM, SPSS, Chicago, Illinois, USA) and the Real Statistics Resource Pack software for Mac (Release 7.2) of the resource pack for Excel 2016. Copyright (2013 – 2020).

Descriptive statistics were performed on the data of each group. Values were illustrated by n (%) for categorical, scale variables were presented by mean ± standard deviation for normal data while non-normal data, continuous variables were

presented by interquartile range (IQR) and median. The distribution of the data was checked using Shapiro-Wilk test as numerical means of assessing normality.

For abnormal distribution, the univariate analysis was performed using an independent Kruskal Wallis Test for continuous variables. Biomarkers were compared using Spearman rank test to evaluate the relationship within the case study.

Significant differences in categorical variables among the parameters were confirmed through analytical statistical tests. Results of all hypothesis tests with p-values <0.05 (two-side) were considered to be statistically significant.

The optimal threshold with high specificity and sensitivity for critical cases was detected using receiver operating characteristic (ROC) analysis. It was found out that all the values of P were two-sided, and a $P < 0.05$ was considered to be statistically significant.

CHAPTER THREE

Results& Dissections

3. Results and Discussion:

This study was examined the characterization of the IMA test for early identification of ischemic patients of Acute coronary syndrome. Prolonged ischemia can lead to myocardial cell death and is a pre-condition to infarction.

Identification of Myocardial Ischemia at the earliest stage would prevent the devastating consequences of the disease. Currently available biochemical markers don't seem to serve this requirement, they have to leak out of the myocytes, which becomes possible only when sufficient amount of cell death has already taken place.IMA is being thoroughly researched as a prospective option for the goal of meeting the global requirement for a cardiac marker that can serve the aforementioned function.

3.1 Demographic and clinical characteristics:

The clinical demographic characteristics of patients & control groups were summarized in Figure (3.1). The mean age of ACS patients group was (53.6) Years old and for control group (50.3) Years old. Overall, results indicated that most of the ACS patients samples were obese. Gender distribution among the studied groups were: 70% male, 30% female, and about 60 % of the participants were heavy smokers in patient . The disease history of the patients was collected through a student self-report questioner, patients were indicated that about 79% of them have a duration of the ACS less than four years and 83% reported to have more than five attacks since diagnosis, base to the repeated attacks, about 42% of the patients groups were undergone a percutaneous coronary intervention. 64% were pointed to have elevate heart pulse rate and more than two third were reported to have high in the diastolic and systolic pressure.

Table (3.1) Baseline clinical characteristics of the study population in cases of ACS patients (n=90)

Biomarkers		-MI Group		+MI Group		UA Group		Normal Values
		Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	
Lipid Profile	Cholesterol	95.09±29.92	90(80-236)	95.71±25.48	90(71-213)	85.25±5.74	86(74-94)	<200 mg/dl
	Triglyceride	136.73±24.46	138(90-180)	154.53±31.62	164(92-206)	124.75±27.20	131(90-164)	35-160 mg/dl
	LDL	68.50±27.57	64(46-197)	67±17.83	63(50-149)	60.71±4.67	62(52-70)	<128 mg|dl
	HDL	40.2568±5.34	40(32-50)	42.70±4.89	43(35-55)	41.76±4.29	42(34-48)	>40 mg/dl
CBC	HB	13.61±1.62	14(10-15)	13.05±2.15	13(9-18)	13.82±1.50	14(11-18)	12-16.5 g/dl
	WBC	10.59±3.45	10(6-21)	9.87±3.78	9(6-20)	7.85±2.00	7(5-12)	4-10 10 ^9
	RBC	4.58±0.45	5(4-5)	4.49±0.72	4(3-6)	4.84±0.54	5(4-6)	3.5-5.5 *10 ^12
	Platelet	250.10±38.74	233(218-370)	259.94±94.79	250(75-457)	229.31±78.95	212(153-428)	150-350 * 10^9
Diagnostic Markers	IMA	5.26±3.50	4(3-19)	4.18±1.18	4.04(3.10-6.66)	5.16±2.82	5(3-16)	/
	Albumin	42.79±4.85	41(36-55)	44.57±8.42	47(22-58)	37.16+8.57	37(12-49)	39-53 g/l
	Troponin	100% Troponin Negative		100% Troponin Positive		100% Troponin Negative		/

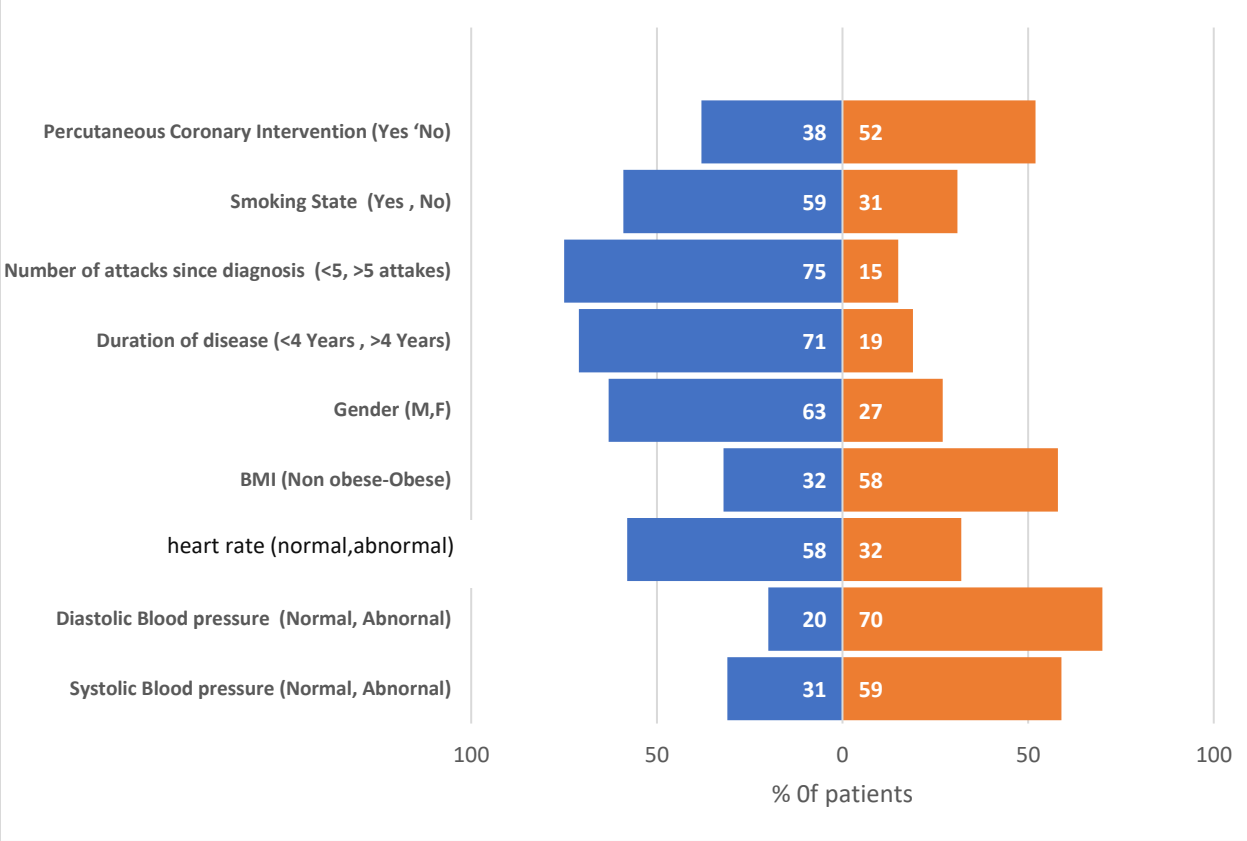


Figure (3.1) Demographic statistical Descriptive of the study population in cases of ACS patients group (n= 90)

3.2 Examination the distribution of data in the studied groups:

3.2.1 Distribution of serum level of Lipid profile panel

A box plot was used to visually show the distribution of data through displaying the data quartiles and averages. Figure (3.2) demonstrated a across distribution of serum level of lipid profile panel in ACS patients groups and healthy control group. ACS Patients were divided into three subgroups (MI with negative troponin test, MI with positive troponin test and unstable angina), the main endpoint was discriminating

patient's subgroup throughout clinical history, electrocardiography and laboratory abnormality (troponin).

The quartiles and range levels of serum total cholesterol and LDL were decreased markedly in group of unstable angina, while TG was estimated to have great variability in patients compared to control. The mean levels of cholesterol in patients group were (95.1,95.89 and 84.5 mg/ml ±29.92) respectively, while in control group, mean level of cholesterol was (122.48mg/dL±22.41). on the other hand, LDL in the (negative troponin MI, positive troponin MI and unstable angina) groups were (68.5, 67.12 and 60.89 mg/dL±27.57) compared to (77.2 mg/dL±15.91) in healthy control group.

Furthermore, the mean differences of TG were also examined, results were indicated that, there was a massive increased in the TG levels in ACS patients compared to healthy control group. The mean of TG in control group (116.24) mg/dl ±25.69 was significantly lower than in ACS subgroups, (136.73±24.46 , 154.53±31.62 and 124.75±27.20 mg/dL) in MI-, MI- , UA respectively. The distribution of serum level of lipid profile in ACS patients compared to healthy control group was presented in Figure (3-2).

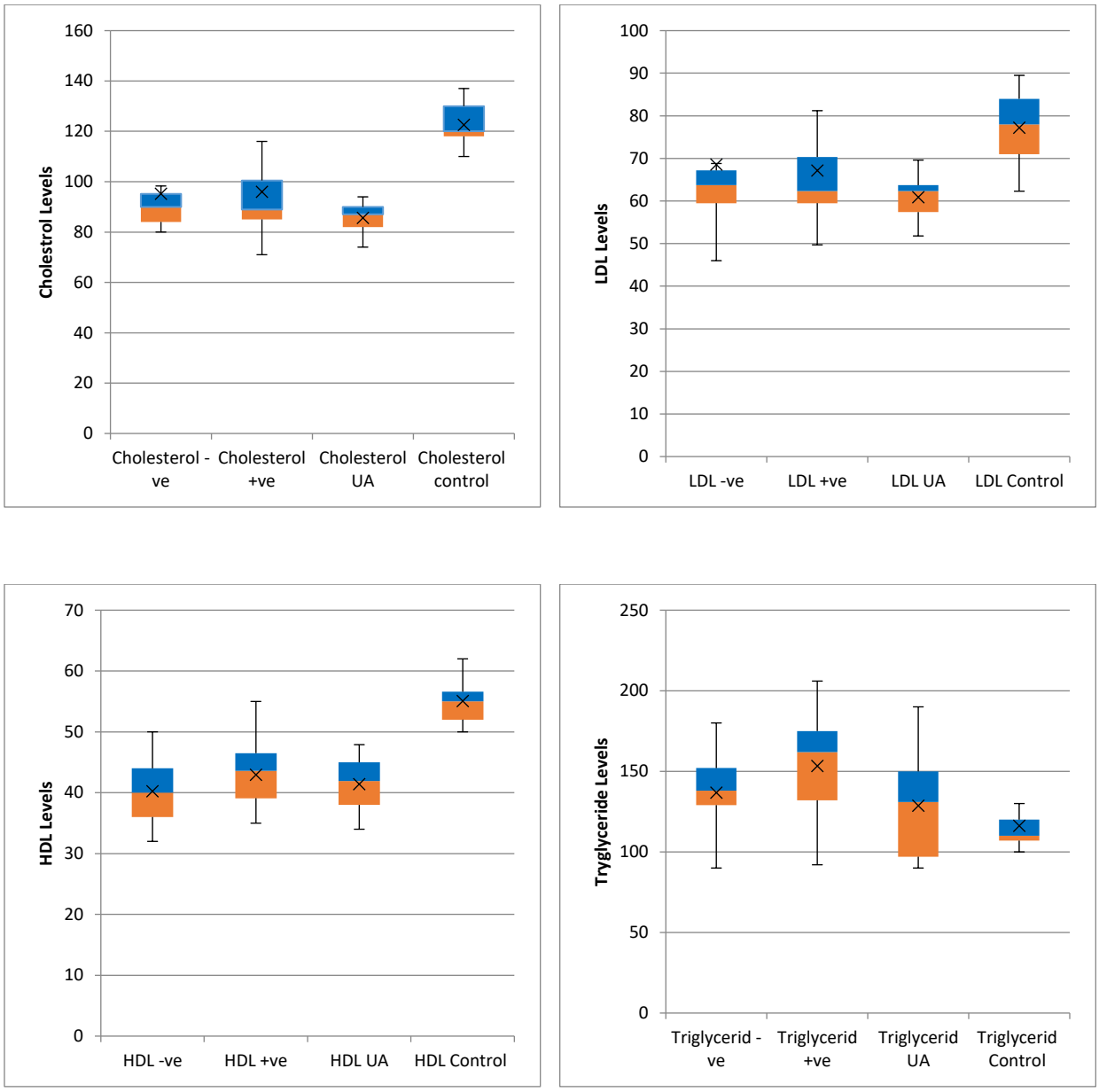


Figure (3.2): Boxplot of the Distribution of serum lipid profile panel in ACS patients: Negative Troponin MI; Positive Troponin MI ; Unstable angina group; and Healthy control group

ACS pathology characterized by different grade vascular inflammation rather than a mere accumulation of lipids. Inflammation is central at all stages of ischemia. Acute coronary syndrome significantly affects the concentration and composition of the lipids and lipoproteins in plasma. Plasma triglyceride and very low-density lipoprotein levels increase, while high density lipoprotein, low density lipoprotein and total cholesterol levels decrease. Early treatment of hyperlipidemia provides potential benefits. However, post-event changes in lipid and lipoproteins lead to delays in the choice of the treatment. **[65]**

Different mechanisms have been reported, one of them, since 1957, Biorck *et al*. first reported that serum cholesterol levels decrease during myocardial infarction **[66]**. A wide range of changes in the serum lipid and lipoproteins following ACS have been reported. A reduction in the magnitude of these changes is seen over time **[67] .**In early relevant studies, it was noted that although the levels of TC, LDL and HDL decrease by up to 47%, 39% and 11%, respectively, TG levels rise by up to 50% **[68]**. These inconsistent data may be associated with factors such as the changing nature of therapeutic interventions **[69]**. It is thought that these changes become manifest within 24-48 hours after ACS, reach maximum levels within approximately 4-7 days and are present for a few months. Although the changes in the lipids and lipoproteins depend on the extent and the severity of myocardial necrosis and the serum lipid levels, they are not associated with thrombolytic treatment and percutaneous interventions **[70]**.

During the inflammation in ACS cases, the level of HDL would decrease by increasing the activity of endothelial lipase and soluble phospholipase A2 and replacing the Apo-A1 in the HDL with serum amyloid A. In addition, significant changes are seen in the protein and lipid composition of HDL **[71]**

On the other hand, inflammation associated with hypertriglyceridemia which caused by an increase lipoprotein production and a decrease in lipoprotein clearance.

Increase in TG-rich lipoproteins is secondary to the re-esterification of plasma fatty acids. Clearance decreases mainly secondary to the inhibition of lipoprotein lipase activity. **[72]**

After that, drugs used in hospital have a role in these modifications. Heparin activates the lipoprotein lipase, so that the internalization of the LDL and VLDL through LDL receptors increases **[73].**

Later, McCann et al., were reported that Myocardial damage-induced stress which increases the adrenergic-mediated lipolysis of the adipocytes. That might be lead to an increase in free fatty acids, TGs and lipoproteins. The mobilization of free fatty acids and hepatic secretion of VLDLs increase and lead to the elevation of TG levels. **[74]**

in this study, Fisher's LSD method was used in ANOVA to create confidence intervals for all pairwise differences between Lipid profile panel and ACS subgroups while controlling the individual error rate to a significance level that specify. Fisher's LSD method was used to calculate the simultaneous confidence level for all confidence intervals. This simultaneous confidence level is the probability that all confidence intervals contain the true difference. There homogeneity of variances was assessed by Levene's test ($p = 0.493$), data was presented as mean differences in the tables Table (3.2).

Cholesterol level was statistically significantly different between negative troponin MI cases compared to control group ($p < 0.001$). LSD post hoc analysis revealed statistically significant decreased, as present in Table (3.2).

Table (3.2) : Multiple Comparisons of Dependent Variable and Least Significant Difference-Post Hoc Test for (Cholesterol) level with Study groups.

Dependent Variable: Cholesterol					
(I)	(J)	Mean Difference (I-J)	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
1	2	-0.6171	0.918	-12.5445	11.3103
	3	9.8472	0.162	-4.0305	23.7249
	4	-27.3790*	<0.001	-40.2099	-14.5481

1:MI-ve group 2:MI+ve group 3:UA group 4:control group

Furthermore, there was a statistically significant difference in HDL and TG level between negative troponin MI cases compared to positive troponin MI and control group. LSD post hoc test differences in the HDL level was statistically significant ($p < 0.05$), as shown in Table (3.3) & (3.4)

Table (3.3) : Multiple Comparisons of Dependent Variable and Least Significant Difference-Post Hoc Test for (High density Lipoprotein) level with Study groups.

Dependent Variable: HDL					
(I)	(J)	Mean Difference (I-J)	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
1	2	-2.44	0.054	-4.974	0.077
	3	-1.511	0.309	-4.451	1.42
	4	-14.79*	<.001	-17.51	-12.08

1:MI-ve group 2:MI+ve group 3:UA group 4: control group

Table (3.4) : Multiple Comparisons of Dependent Variable and Least Significant Difference-Post Hoc Test for (Triglyceride) level with Study groups.

Dependent Variable: Triglyceride					
(I)	(J)	Mean Difference (I-J)	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
1	2	-17.804*	.015	-32.074	-3.534
	3	11.982	.155	-4.621	28.585
	4	20.494*	.009	5.143	35.845

1:MI-ve group 2:MI+ve group 3:UA group 4: control group

Interestingly, the multiple comparisons of LDL levels among the patients groups were not illustrated any significant differences compared to control group. The means differences and p value were presented in Table (3.5).

Table (3.5) : Multiple Comparisons of Dependent Variable and Least Significant Difference-Post Hoc Test for (Low density Lipoprotein) level with Study groups.

Dependent Variable: LDL					
(I)	(J)	Mean Difference (I-J)	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
1	2	1.5032	.765	-8.473	11.480
	3	7.7844	.186	-3.823	19.392
	4	-8.692	.111	-19.424	2.0406

1:MI-ve group 2:MI+ve group 3:UA group 4: control group

3.2.2 Association between hematological parameters and ACS subgroups

Acute coronary syndrome is an essentially inflammatory disease and, depends on the extent of cardiac damage, with hemodynamic repercussion. These inflammatory and hypoxemic processes have been associated with the presence of hematological markers in the peripheral blood **[75]**.

The distribution of the main involved hematological parameters was examined as demonstrated in Figure (3.3). Generally, patients with ACS were shown an increasing range level of white blood cells count, hemoglobin and platelet when comparing with the healthy control groups. Positive troponin MI was shown a wide range of variability in the range levels of the markers.

The range levels of these markers in patients' subgroups were shown the following distribution: WBC range count was (6-20.7); (5.78-20.11); (5.2-12.5) in MI- ,MI+ ,UA respectively compared to control groups (6-9). The range levels of platelet were (218-370); 75-457); (153-428) in MI- ,MI+ ,UA respectively, while in control group was (116-251). And the range levels of HB were (10-15.3); (8.5-17.7); (11-17.6) compared in MI- ,MI+ ,UA respectively to control levels (11-13).

On the other hand, only red blood cells count were shown a decreased in the range levels in ACS patients subgroups (4-5.31); (3.07-5.6); (4-5.8) compared to control group (4-6) .

Only four CBC variables were considered in this study. The excess mortality associated with high hemoglobin concentration has been shown in STEMI patients with high WBC count, whereas the association did exist in those with low WBC count **[76]**. The interaction between hemoglobin level and WBC count was also observed in previous study. The combined use of the WBC count, hemoglobin, and MPV levels may represent a biochemical-integrated assessment of inflammatory status, thrombotic risk, and the extent of myocardium at risk **[77]**

The elevated WBC count was associated with worse outcomes in patients with STEMI **[78]**

Patients were also shown a wide range variability in the platelet count specially in the positive MI and unstable angina. That might be related to the presence of thrombocytopenia which reflects a complex underlying etiology such as immune- or drug-induced platelet destruction. According to published studies, the prevalence of baseline thrombocytopenia is about 3–11% in ACS patients **[79].**

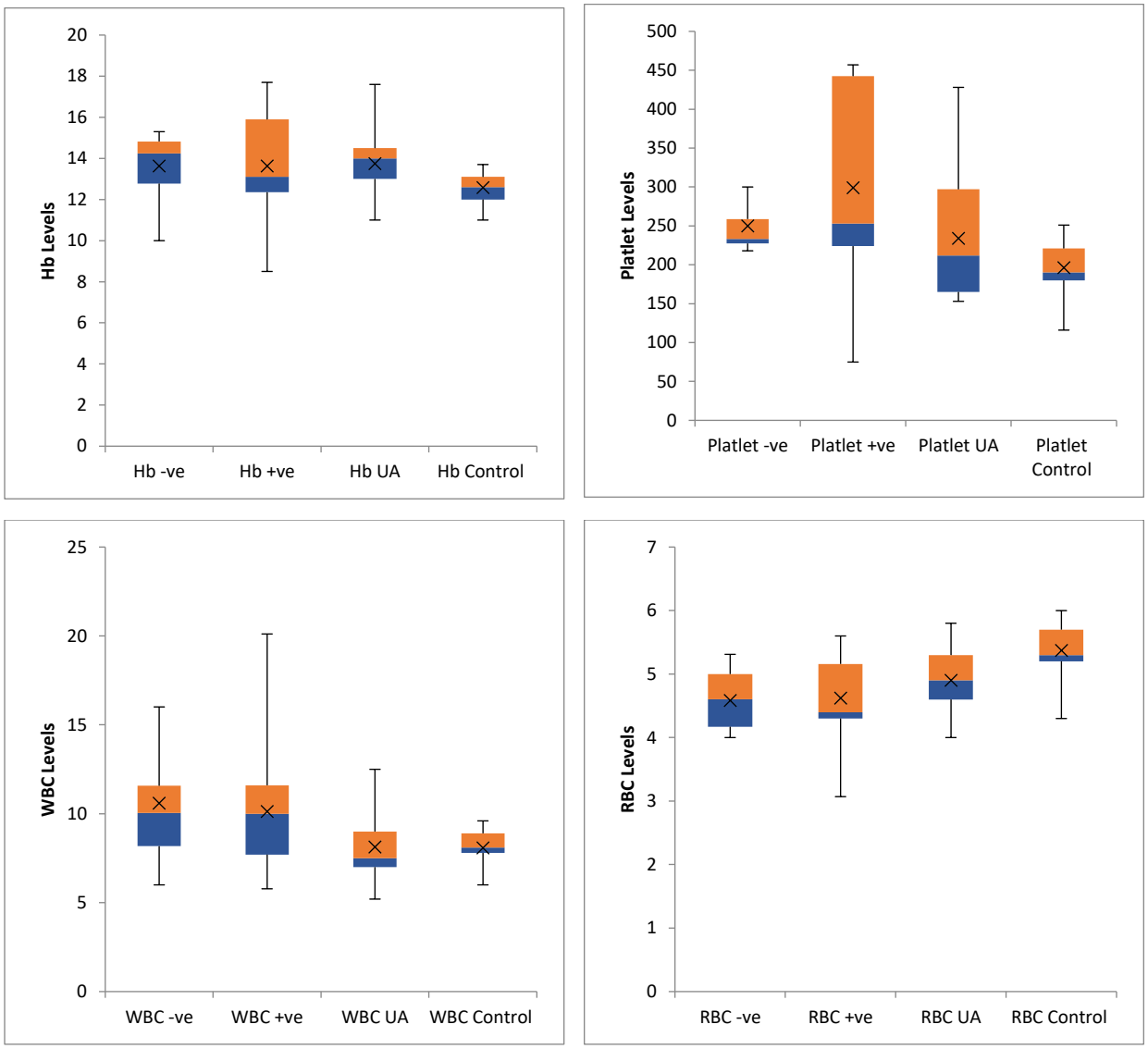


Figure (3.3): Boxplot of the Distribution of CBC test in ACS patients: Negative Troponin MI; Positive Troponin MI ; Unstable angina group; and Healthy control group

3.3 Association between ischemia-modified albumin and ACS subgroups

Knowledge about the role of oxidative stress in human diseases, including cardiovascular system disorders, emphasizes the need for reliable markers of oxidative stress. Evaluation the levels of the novel marker ischemia-modified albumin (IMA) was highlighted in the updated research. Serum IMA levels as an oxidative stress index, their ratio to Albumin and IMA were estimated in this study among three subgroups of ACS patients.

Results were indicated that IMA levels were shown a significant increased range levels in the negative troponin MI cases compared to the positive troponin MI and unstable angina. The range levels were (3.12-6.41); (3.1-5.66) and (3.17-5.56) respectively. On the other hand, unstable angina cases were shown a decreasing level of Albumin and increasing levels of IMA/ Alb ratio. Figure (3.4) demonstrated the distribution of Ischemic Modified Albumin, IMA/Albumin ratio and Albumin Levels in Acute coronary syndrome groups.

Albumin synthesis or changes of functional activity can destabilize oncotic blood pressure. Albumin properties incur some changes under ischemic attacks associated with oxidative stress, production of reactive oxygen species (ROS), and development of acidosis

During ischemia, the mechanism of IMA formation driven by oxidative stress. Tissue hypoxia and activation of anaerobic glycolysis induce acidosis and release copper ions from copper-containing proteins, such as ceruloplasmin. In the presence of reducing agents Cu^{2+} is reduced to Cu+, followed by the formation of superoxide

anion O^{-2}. Superoxide dismutase (SOD) catalyzes the dismutation of superoxide O^{-2} to hydrogen peroxide H_2O_2, which, in the presence of Cu2+, undergoes the Fenton reaction with the formation of hydroxyl radicals ·OH. These radicals contribute to the degradation of NTS and IMA formation **[80]**

Also many studies reported that , IMA has been proposed as an early biomarker for various diseases associated with ischemia and oxidative stress, **[81]**. The N-terminal sequence of HSA (Asp1-Ala2- His3-Lys4) is very susceptible to biochemical modifications and degradation induced by oxidative stress. Consequently, the affinity of NTS to transition metals, especially to cobalt, is reduced. This variant of albumin was called ischemia- modified albumin (IMA) **[82].**

It seems to be in case of negative troponin, as an early stage of ischemia, IMA could be used as an early diagnostic marker better than even troponin. The Posttranslational changes might be result in a wide range of albumin variants that appear or become more abundant in the blood as a result of metabolic changes associated with various diseases. **[83].**

Ischemic Modified Albumin

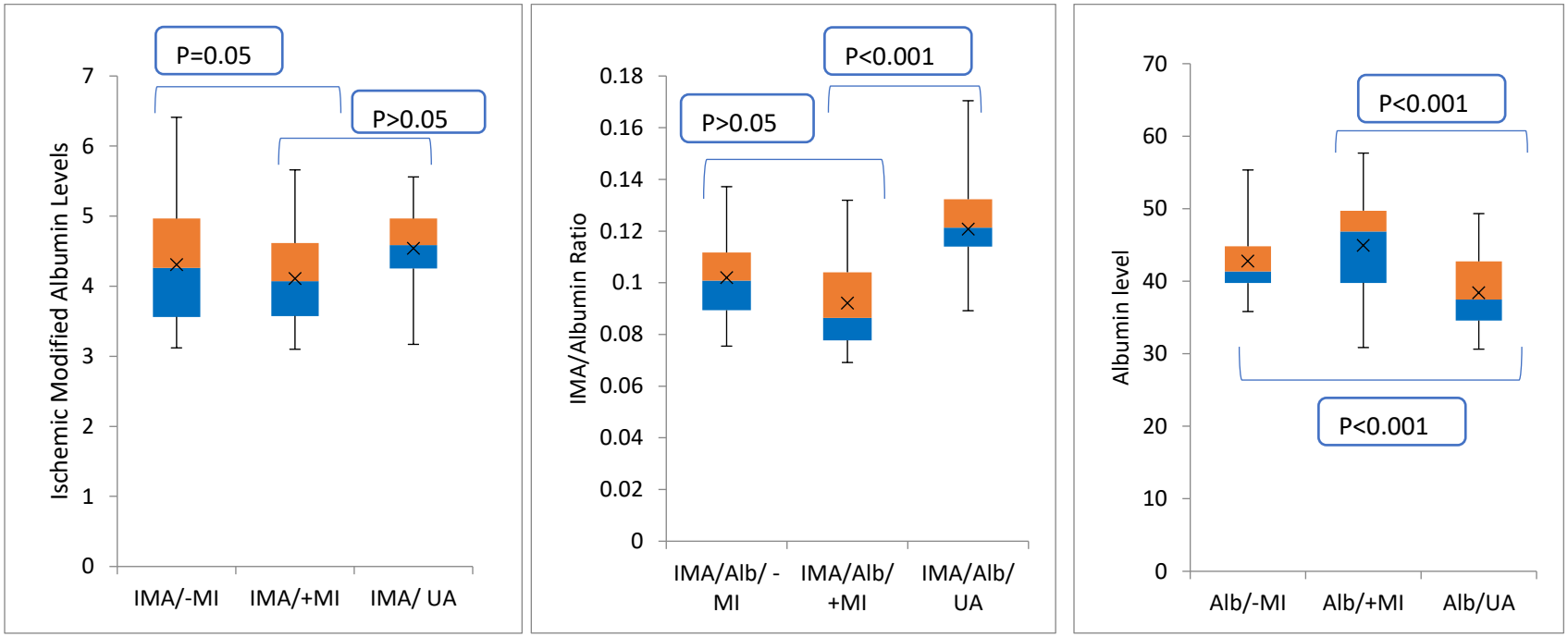


Figure (3.4) Boxplot of Distribution Ischemic Modified Albumin, IMA/Albumin ratio and Albumin Levels in Acute coronary syndrome groups

3.4 Examination the sampling time of ischemia-modified albumin in ACS subgroups.

The present study was also examined time of IMA sampling. The duration of sampling was divided into subgroups: samples that withdraw during less than 90min and more that 90min from their presence in the CCU. The impact of serum albumin on IMA levels is still an important factor, even within the normal range. It has been demonstrated that each 1 g/dl change in albumin produces an opposite change of 2.6% in IMA levels, resulting in a negative correlation. This indicates a need to evaluate IMA values together with those of albumin using their ratio to avoid possible false-positive or -negative values **[84]**

Results were confirmed that serum IMA and their ratio to albumin that measured in less than 1.5 hour of chest pain in ACS patients who were administrated to CCU has higher levels and reflected their ability in differentiation the early ischemia episode. The mean levels of IMA in early 90min of attack was (4.79) while in cases that measured after more than 90min the mean levels were (4.4). the IMA/Alb ratio was also increased positively with early measurement.

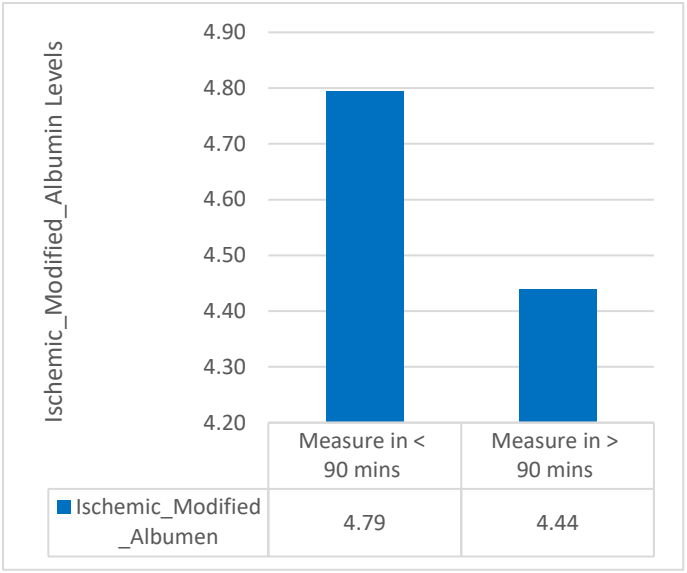
Figure (3.5) illustrated the mean Levels of IMA and Ischemic Modified Albumin/ Albumin ratio) in Acute coronary syndrome patients based on the sampling time of their duration staying in emergency and CCU **[85] .**concluded that serum IMA appears to be a sensitive biomarker of myocardial ischemia in MI patients. Research was confirmed the ability to detect ischemia before myocyte destruction. Furthermore, it was also indicated that assessment of concentrations of IMA were vastly superior to the assessment of cTn concentrations within the same time frame for early diagnosis of MI. In myocardial ischemia, a structural change in the N-

terminus of albumin occurred, and this albumin showed lower metal-binding capacity with cobalt on the albumin–cobalt binding test. IMA rise can be detected by this test 3 hours after the appearance of ACS symptoms **[86]**

It is well known that within minutes of onset of myocardial ischemia, there is hypoxia, free radical damage and acidosis followed by disruption of membrane sodium/calcium ion pumps. it has been indicated that mechanisms involved in ischemia / reperfusion are induced changes in albumin and may include exposure to endothelial and extracellular hypoxia, acidosis, free radical damage, ATP dependant sodium and calcium pump disruption resulting in exposure to free iron and copper ions **[87]**

An early study was shown that IMA levels rise within minutes after ischemia and return to baseline within 6 h **[88]** It has been reported that the sensitivity of IMA for the diagnosis of acute ischemic chest pain is significantly greater than that of ECG and cTn. In addition, in a human model of ischemia induced by balloon angioplasty, IMA rises early after balloon inflation and levels returns to baseline within 6–12 hours. **[89]**

On the other hand, utilization of IMA measurements in ACS patients was start to rise in the blood after a few minutes following ischemia when investigated in a number of trials. The results of trials indicate that the IMA levels show an early increase shortly after the onset of ischemia and maintain these high levels for 6-12 hours following ischemia **[90]**



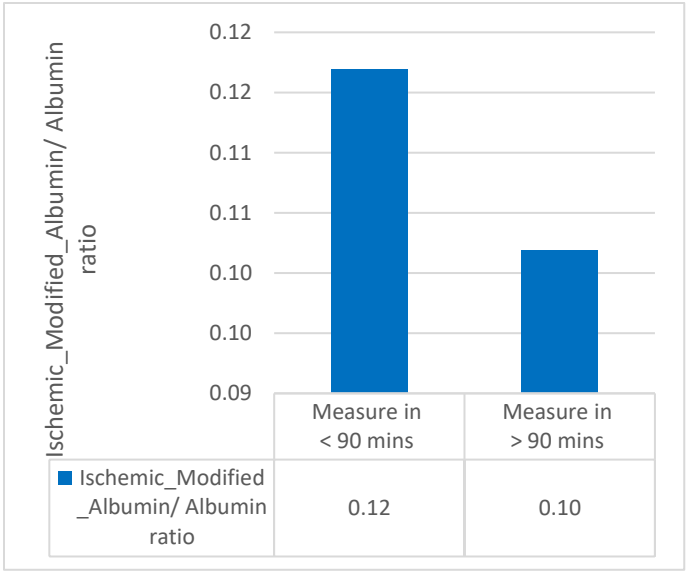


Figure (3.5): Biomarkers Levels (IMA and Ischemic_Modified_Albumin/ Albumin ratio) in Acute coronary syndrome patients based on the sampling time of their duration staying in emergency and CCU

3.5 Correlation of Ischemic Modified Albumin, IMA/Albumin ratio and Biochemical markers

Considering the important role of the measured biomarkers in the progression of ACS, the multivariable linear regression model was used to analyze the response relationship between parameters.

Serum IMA levels was positively significant correlated to their ratio with albumin. In addition, IMA was significantly associated with TG & LDL levels. On the other hand, serum IMA/Alb ratio was highly significant positively related to Albumin levels and TG (all $P < 0.05$). The relationship between the laboratory parameters and ACS cases was presented in Table (3.6 & 3.7). Their correlations would be confirmed the post translation modification of albumin due to oxidative stress process and acumaltion of lipid, since several works suggested the release of fatty acids in myocardial ischemia results in the binding of fatty acid to albumin, inducing a conformational change in albumin **[91]**

Table (3.6): Correlation coefficients by Spearman rank test for Ischemic Modified Albumin, IMA/Albumin ratio with the lipid profile and Albumin in all of them.

Variables	IMA	
	Correlation coefficient (r)	P value
IMA/Alb	0.8	**<0.001**
Albumin	0.2	0.103
HDL	0.3	0.47
TG	0.4	**0.01**
LDL	0.4	**0.026**
cholesterol	0.32	0.14

Table (3-7): Correlation coefficients by Spearman rank test for Ischemic Modified Albumin, IMA/Albumin ratio with the lipid profile and Albumin in ACS patients

Variables	IMA/Alb ratio	
	Correlation coefficient (r)	P value
IMA	0.8	**<0.001**
Albumin	0.5	**<0.001**
HDL	0.3	0.9
TG	0.4	**0.04**
LDL	0.2	0.128
Cholesterol	0.41	0.698

3.6 Receiver operating curve (ROC) curve of serum IMA levels for diagnosis of ACS

Results of the receiver operating curve (ROC) curve and AUC analysis for the Ischemic Modified Albumin, IMA/Albumin ratio as possible diagnostic parameters. IMA level was shown a good diagnostic performance for prediction ACS Patients compared to control group, data are presented in Figure (3.6) and Table (3.8).

For IMA levels: (sensitivity = 90%, specificity = 80%) at a level = 3.59 , while IMA/ Alb ratio levels: (sensitivity = 0.92%, specificity = 0.67%) at a level = 0.072. Only p-values of the AUC for IMA were <0.001 and statistically significant.

Previously, it has been demonstrated by Ertekin et al., 2013 that the high sensitivity and specificity rates of IMA make it the safe and promising method in diagnosing ACS at the emergency department along with its advantages in low cost, rapid results and easy measured indicate that this test may be used as a powerful marker in clinical practice in the near future. **[92]**

Also, Abdel Wahab. (2017) revealed that the diagnostic performance of the IMA level in the ACS patients was greater as compared to that of the TnI assay. The sensitivity and the specificity of IMA were significantly greater than those of TnI. The combination of the IMA and the TnI results improved the sensitivity of the detection of ACS to 98% with a negative predictive value of 92%. These authors also revealed that 71% of troponin negative patients have significant obstructive coronary artery disease while IMA could predict significant obstructive CAD in those troponin negative patients with sensitivity of 96.3%, specificity of 72.7%, PPV of 89.7%, NPV of 88.9% and accuracy 89.5%.**[93]**

Table (3.8): AUC, optimal threshold, Sensitivity and specificity of Ischemic Modified Albumin, IMA/Albumin ratio obtained by the ROC curves for prediction of ACS compared to control group

Test Variable	AUP	Sensitivity %	Specificity %	Cut-off points	P vale	CI (95%)
IMA	0.703	0.9	0.8	3.59	0.006	0.568-0.837
IMA/ Albumin	0.62	0.9	0.6	0.072	0.111	0.481-0.754

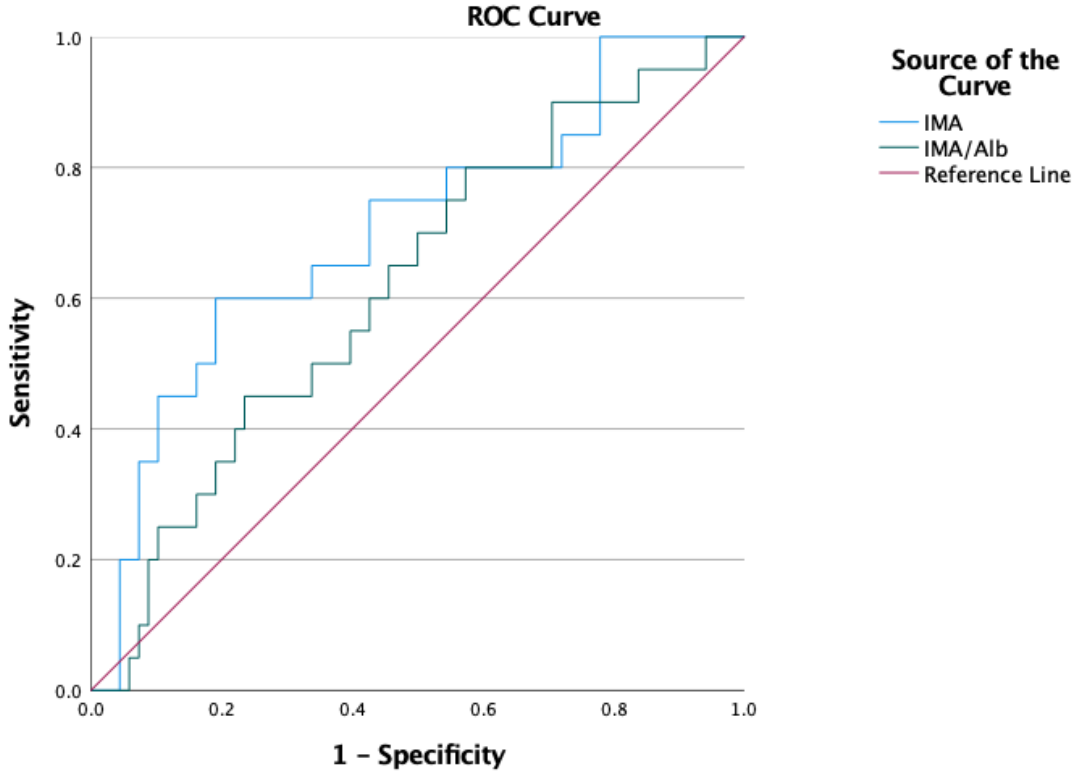


Figure (3.6) ROC curves for Ischemic Modified Albumin, IMA/Albumin ratio in ACS patients to analyse the optimal diagnostic points for predicting ACS cases compared to control group.

Furthermore, the analysis of the optimal diagnostic points for predicting negative troponin MI cases among ACS patients compared to positive troponin MI and unstable angina cases was also performed.

Results were indicated that IMA was shown an interesting prediction about negative troponin cases. The optimal threshold and diagnostic performance were presented in Table (3.9) and Figure (3.7)

Table (3.9): AUC, optimal threshold, Sensitivity and specificity of IMA level obtained by the ROC curves for prediction negative troponin MI cases among ACS patients

Test Variable	AUP	Sensitivity %	Specificity %	Cut-off points	P vale	CI (95%)
IMA	0.71	0.963	0.883	6.53	0.007	0.565-0.798

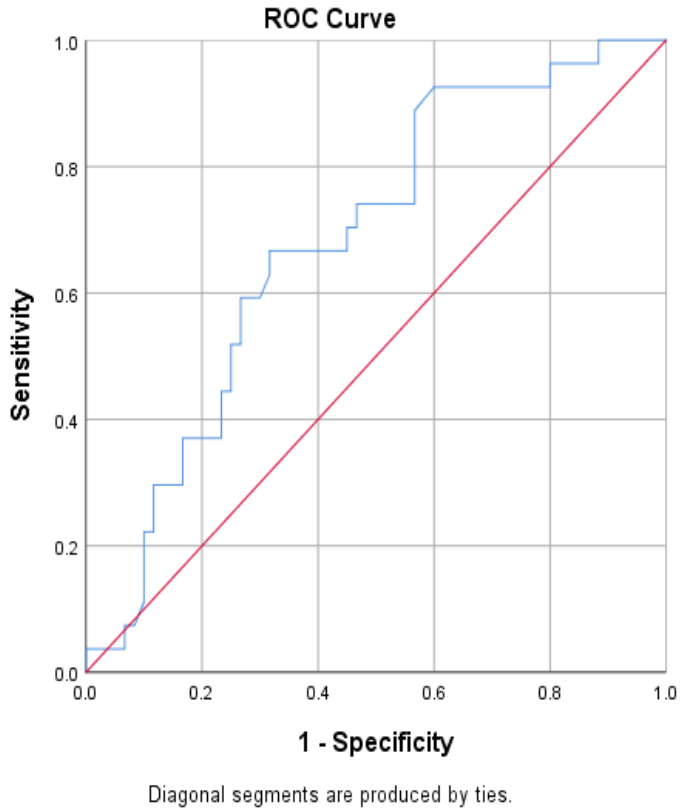


Figure (3.7): Receiver Operative Curve (ROC) plot serum IMA levels as discriminator of negative troponin cases among ACS patients.

The determination of biomarkers for myocardial injuries plays an important role in the diagnosis and the treatment of ACS. In the clinical practice, more attention has been paid to the determination of myocardial markers for the diagnosis of acute myocardial Ischemia, stratification of the ACS risk and the differential diagnoses of reversible versus irreversible myocardial ischemia and acute chest pain. The quantitative or qualitative determination of cardiac TnI has been well accepted as a marker of the myocardial damage. However, most of the biomarkers of Acute Myocardial Infarction (AMI) are the products of myocardial necrosis and thus are detected typically at a later stage of the myocardial damage **[94]**. Therefore, rapidly detectable, highly sensitive markers would be desirable for myocardial ischemia, to identify the patients with only ischemia and those who are early in the course of an acute coronary syndrome without the evidence of any myocardial necrosis.

The core of this study lay in the fact that the measurements of the serum IMA levels could aid in a diagnosis of ACS in patients with ongoing ischaemic pain, who presented to the emergency department. IMA can be used as an independent point of care test or an additional parameter along with TnI, to boost the confidence of the clinicians in ruling out cardiac ischaemia. This combination seems to have clear potentials of time saving, an early intervention and a shortened stay in the emergency department **[95]**.

IMA has confirmed to provide a valuable information regarding the duration of diseases and possible complications, and it can be used in the differential diagnosis of certain pathological conditions. IMA's advantage as a biomarker over other markers is its ability to detect ischemic conditions at earlier stages. The simplicity and availability of the techniques for its determination provide an opportunity to stratify patients and determine risk groups for adverse events after a stroke, heart

attack, traumatic brain injuries, and spinal injuries and assess the state of patients with neurological disorders, diabetes, pregnancy complications, and with gynecological and other ischemic-associated pathologies. **[96].**

Conclusion

&

Recommendations

Conclusion

- There was a statistically significant difference in Lipid profile levels between negative troponin MI cases compared to positive troponin MI and control group. LSD post hoc test differences in the HDL level was statistically significant.

- Patients with ACS were shown an increasing range level of white blood cells count, hemoglobin and platelet when comparing the healthy control groups. Positive troponin MI group was shown a wide range of variability in the range levels of the markers. Only red blood cells count was shown a decreased in the range levels in ACS patients

- Results were indicated that IMA levels were shown a significant increased range levels in the negative troponin MI cases compared to the positive troponin MI and unstable angina.

- Data analysis was confirmed that serum IMA and their ratio to albumin that measured in less than 1.5 hour of chest pain in ACS patients who were administrated to CCU has higher levels and reflected their ability in differentiation the early ischemia episode.

- Serum IMA levels was positively significant correlated to their ratio with albumin. In addition, IMA was significantly associated with TG & LDL levels. On the other hand, serum IMA/Alb ratio was highly significant positively related to Albumin levels and TG.

- Results of the receiver operating curve (ROC) curve and AUC analysis for the Ischemic Modified Albumin, IMA/Albumin ratio as possible diagnostic parameters. IMA level was shown a good diagnostic performance for prediction ACS Patients compared to control group. For IMA levels: (sensitivity = 90%, specificity = 80%) at a level = 3.59 , while IMA/ Alb ratio levels: (sensitivity = 0.92%, specificity = 0.67%) at a level = 0.072. Only p-values of the AUC for IMA were <0.001 and statistically significant.

Recommendations & Future work

- IMA levels might be check with other disease such as gynecological diseases included dysmenorrhea, ovarian torsion, endometriosis, PCOS, menopause and infertility, since these are a primarily caused by hypoxia/ischemia and postischemia reperfusion. In these commonly seen cases, there is noticeable rise in serum IMA level, which is a novel marker for ischemia. This promising marker – IMA – may be used gynecology practice such as early diagnosis and follow-up.

- IMA's has a wide range advantage as a biomarker over other markers reflected by the ability to detect ischemic conditions at earlier stages. This might be used as a simplicity and availability of the techniques for its determination provide an opportunity to stratify patients and determine risk groups for adverse events after a stroke, heart attack, traumatic brain injuries, and spinal injuries and assess the state of patients with neurological disorders, diabetes.

- There is a still needing for well-designed validation studies as a required for the development of blood biomarkers to improve the care of patients with ischemic stroke.

- We need to study the role of IMA in patient with reinfraction .

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Appendix

Appendix I

Questionnaire

Name:
Age:
Gender:

Temp	
BP	
O2	
Pulus	
A1c	
drugs	

BMI:

Weight :
Height :

Diagnosis:
Number of attack :
Duration of disease:
Family history of disease :
ECG :

PCI	:	Yes :	No:
Diagnostic cath	:		
Chif compdaint	:		
date of Admision	:		
Time Admision	:		
Time of sampling	:		
Troponin	:		
SOB	:		
Smoker	:	Yes:	No:

Passive smoker	Yes :	No:

Other chronic disease:

Phone N:

<u>Investigation</u>:

Cardiac Tests : Troponin: Ischemia Modified Albumin

الخلاصة

متلازمة الشريان التاجي الحادة هي المظهر السريري للمرحلة الحرجة لمرض الشريان التاجي. بناءً على ملخص, متلازمة الشريان التاجي الحاد هي المظهر السريري للمرحلة الحرجة لمرض الشريان التاجي. بناءً على تخطيط القلب الكهربائي والعلامات البيوكيميائية المصنفة على أنها احتشاء عضلة القلب بارتفاع ST (STEMI) واحتشاء عضلة القلب غير المرتفع ST (NSTEMI) والذبحة الصدرية غير المستقرة. يرتبط الفيزيولوجيا المرضية الأساسية الشائعة بتمزق اللويحة أو التآكل مع تكوين الجلطة اللاحقة. على الرغم من انخفاض معدل الوفيات المصححة بالعمر بسبب احتشاء عضلة القلب ، فإن انتشار المرض للمكونات غير المميتة لهذه المتلازمة لا يزال مرتفعاً والتكاليف الاقتصادية هائلة. يسترشد العلاج الفعال ل متلازمة الشريان التاجي الحاد بالتشخيص المبكر وتصنيف المخاطر ، ويستند إلى تخطيط القلب والعلامات الكيموحيوية.

هدفت هذه الدراسة إلى معرفة دور المعلمات البيوكيميائية. نقص التروية المعدلة من الألبومين كأداة تشخيصية مبكرة لمتلازمة الشريان التاجي الحاد .دراسة دور هذه الواسمات البيوكيميائية في التفريق بين أسباب آلام الصدر المرضية ؛ الذبحة الصدرية و احتشاء عضلة القلب غير مرتفع ST و و احتشاء عضلة القلب مرتفع مقطعST تحديد قيم القطع لهذه الواسمات البيوكيميائية في التشخيص المبكر للمتلازمة الشريان التاجي الحاد.

تم إجراء منهج دراسة الحالة والشواهد على أربع مجموعات من المشاركين ، مجموعة مرضى احتشاء عضلة القلب مع نتيجة التروبونين السالبة و مجموعة مرضى احتشاء عضلة القلب مع نتيجة التروبونين الموجبة ومجموعة مرضى الذبحة الصدرية الغير مستقرة ومجموعة الاصحاء في محافظتي كربلاء وبغداد.

يتم فحص جميع المرضى بحثًا عن علامات وأعراض أي اضطرابات قلبية تظهر مثل تروبونين مع أنماط تخطيط كهربية القلب بواسطة طبيب مختص. تم قياس مستوى المؤشرات الحيوية في المصل التالية: تم قياس مستويات الالبوميم المعدل الاقفاري باستخدام تقنية ELISA تم إجراء قياس مستويات مستوى الدهون في مصل الدم البشري باستخدام تقنية المطياف الضوئي. تم إجراء التحليل الكيميائي الحيوي لتعداد الدم الكامل بواسطة محلل الدم الآلي . تم تقييم العلاقة بين العلامات البيوكيميائية وشدة المرض. تم تقييم كفاءة قيمة التنبؤ باستخدام منحنى خاصية تشغيل المستقبل.ROC

أشارت النتائج إلى أن مستويات الالبومين المعدل الاقفاري أظهرت زيادة ملحوظة في مستويات النطاق في حالات تروبونين السلبية مقارنةً بالتروبونين الإيجابي والذبحة الصدرية غير المستقرة. كانت مستويات النطاق (6.41-3.12) ؛ (5.66-3.1) و (5.56-3.17) على التوالي. من ناحية أخرى ، أظهرت حالات الذبحة الصدرية غير المستقرة انخفاض مستوى الألبومين وزيادة مستويات النسبة .تم توضيح النتائج أيضًا منحنى تشغيل المستقبِل ((ROCوتحليل AUC لمعدل الألبومين الإقفاري المعدل ، ونسبة لألبومين الى الالبومين المعدل الاقفاري كمعلمات تشخيصية محتملة. أظهر مستوى الالبومين المعدل الاقفاري أداءً تشخيصيًا جيدًا لمرضى متلازمة الشريان التاجي الحاد للتنبؤ مقارنة بمجموعة التحكم.

كانت نقاط التشخيص المثلى للتنبؤ بـ متلازمة الشريان التاجي الحاد بواسطة الالبومين المعدل الاقفاري)الحساسية = 90٪ ، النوعية = 80٪) عند مستوى = 3.59 ، بينما مستويات نسبة الالبومين الى الالبومين المعدل الاقفاري الحساسية = 92٪ ، النوعية = 67٪) عند مستوى = 0.072 . فقط قيم p من AUC لـ الالبومين المعدل الاقفاري كانت <0.001 وذات دلالة إحصائية.

يبدو أن مصل الدم الالبومين المعدل الاقفاري هو علامة بيولوجية حساسة لنقص تروية عضلة القلب لدى مرضى احتشاء عضلة القلب. أكد تحليل البيانات القدرة على اكتشاف نقص التروية قبل موت الخلايا العضلية.

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة كربلاء

كلية الطب

فرع الكيمياء والكيمياء الحياتية

قياس مستويات الألبومين المعدل الإقفاري كعلامة مبكرة لتشخيص متلازمة الشريان التاجي الحاد

رسالة ماجستير

إلى مجلس كلية الطب/ فرع **الكيمياء والكيمياء الحياتية** / جامعة كربلاء كجزء من متطلبات نيل درجة الماجستير

من قبل

انعام كاظم محمد

بكالوريوس تقنية تحليلات مرضية

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