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ISCHEMIA MODIFIED ALBUMIN A POTENT BIOCHEMICAL MARKERS AS HIGH SENSITIVE TROPONIN IN ACUTE MYOCARDIAL INFARCTION

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ALI MOHAMMED ABDULJABBAR NOORI

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ISCHEMIA MODIFIED ALBUMIN A POTENT BIOCHEMICAL MARKERS AS HIGH SENSITIVE TROPONIN IN ACUTE MYOCARDIAL INFARCTION

By Ali Mohammed Abduljabbar NOORI

May 2022

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

Advisor **:** Prof. Dr. Volkan EYÜPOĞLU
Co-Advisor **:** Dr. Riadh Abdual Al- Rassol HENWA

Examining Committee Members:

Chairman **:** Assoc. Prof. Dr. Şevki ADEM
Chemistry
Çankırı Karatekin University

Member **:** Prof. Dr. Volkan EYÜPOĞLU
Chemistry
Çankırı Karatekin University

Member **:** Assoc. Prof. Dr. Ebru AKKEMİK
Food Enginering
Siirt University

Approved for the Graduate School of Natural and Applied Sciences

Prof. Dr. İbrahim ÇİFTÇİ
Director of Graduate School

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Ali mohammed Abduljabbar NOORI

ABSTRACT

ISCHEMIA MODIFIED ALBUMIN A POTENT BIOCHEMICAL MARKERS AS HIGH SENSITIVE TROPONIN IN ACUTE MYOCARDIAL INFARCTION

Ali Mohammed Abduljabbar NOORI

Master of Science in Chemistry

Advisor: Prof. Dr. Volkan EYÜPOĞLU

Co-Advisor: Dr. Riadh Abdual Al- Rassol HENWA

May 2022

Acute myocardial infarction (AMI) is a common sign of coronary heart disease. AMI is a form of myocardial ischemia necrosis caused by coronary artery blockage. AMI can cause chronic post-sternal discomfort, shock, arrhythmia, and death. Cardiac troponin (cTn) is the preferred AMI biomarker. This is a case-control included 80 patients (52 men and 28 women) with AMI at the Cardiac Care Unit (CCU) in Al-hussein Medical City, 20 healthy volunteers (12 men and 8 women) without CHD. Data of IMA test value from AMI and control group was used to calculate the ROC curve with an Area Under the Curve:0.767 (95% of CI, 0.673--0.860). There was a big difference in the median serum concentration of Ischemic modified albumin Troponin high-sensitive among the control and patient groups. Accordingly, the selected diagnostic cut-off was > 60 ng/ml analyzed for their clinical sensitivity (76.45%), specificity (81.88%), positive predictive value (88.33 ng\ml), and negative predictive value (33.33 ng\ml), as well as there was a positive correlation between serum concentration of IMA and hs-cTn. In conclusion: IMA is considered a potent marker for early diagnosis of AMI and a distinguishable test between ischemic and non-ischemic chest pain, as well as having high sensitivity and specific cut-off value, making it able to compare with hs-cTn in the identification of AMI.

2022, 40 pages

Keywords: Acute myocardial infarction, Ischemia modified albumin, Troponin

ÖZET

İSKEMI MODİFİYE ALBÜMİN, AKUT MİYOKARD ENFARKTÜSÜ TANISINDA YÜKSEK DUYARLI TROPONİN GİBİ GÜÇLÜ BİR BİYOKİMYASAL BELİRTEÇ

Ali Mohammed Abduljabbar NOORI
Kimya, Yüksek Lisans
Tez Danışmanı: Prof. Dr. Volkan EYÜPOĞLU
Eş Danışman: Dr. Riadh Abdual Al- Rassol HENWA
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Akut miyokard enfarktüsü , koroner kalp hastalığının yaygın bir belirtisidir. AMI, koroner arter tıkanıklığının neden olduğu bir miyokardiyal iskemi nekrozu şeklidir. Kardiyak troponin (cTn), tercih edilen AMI biyobelirteçtir. Bu çalışmada Al-hussein Medical City'deki Kardiyak Bakım Ünitesinde (CCU) AMI'li 80 hastayı (52 erkek ve 28 kadın), KKH'si olmayan 20 sağlıklı gönüllüyü (12 erkek ve 8 kadın) içeren bir vaka kontrolü temelinde dizayn edilmiştir. AMI ve kontrol grubundan alınan IMA test değerinin verileri, Eğri Altındaki Alan:0,767 (%95 CI, 0,673—0,860) ile ROC eğrisini hesaplamak için kullanılmıştır. Kontrol ve hasta grupları arasında yüksek duyarlıklı iskemik modifiye albümin Troponin'in medyan serum konsantrasyonunda büyük bir fark tespit edilmiştir. Buna göre, klinik duyarlılıkları (%76,45), özgüllükleri (%81,88), pozitif öngörü değerleri (88,33 ng\ml) ve negatif öngörü değerleri (33,33 ng\ml) için analiz edilen seçilen tanısal eşik > 60 ng/ml idi. , ayrıca serum IMA konsantrasyonu ile hs-cTn arasında pozitif bir korelasyon olduğu tespit edilmiştir. Sonuç olarak: IMA, AMI'nin erken teşhisi için güçlü bir belirteç ve iskemik ve iskemik olmayan göğüs ağrısı arasında ayırt edilebilir bir test olarak kabul edilebilir, ayrıca yüksek duyarlılık ve spesifik cut-off değerine sahip olduğu görülmüştür. Bu bağlamda elde edilen sonuçların hs-cTn ile AMI'nin karşılaştırılmasını mümkün kılacağı sonucunu çıkarabiliriz.

2022, 40 sayfa

Anahtar Kelimeler: Akut miyokard enfarktüsü, İskemi modifiye albümin, Troponin

PREFACE AND ACKNOWLEDGEMENTS

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Ali Mohammed Abduljabbar NOORI

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CONTENTS

LIST OF SYMBOLS

-	Minus
%	Percent
**	Significant
/	Divide
+	Plus
<	Greater than
=	Equel
>	Less than
±	Plus-minus
≤	Greater or equal to
≥	Less or equal to
dL	Deciliter
g	Gram
gm	Gram
kg	Kilogram
kDa	Kilo Daltons
L	Liter
m^2	Square meter
mcg	Microgram
mg	Microgram
min	Minute
hr	Hour
mL	Milliliter
mmol	Milli mole
mol	Mole
ng	Nanogram
nm	Nanometer
NS	Non-significant
Pg	Pico gram
rpm	Revolutions per minute
µL	Microliter

LIST OF ABBREVIATIONS

ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
AST	Aspartate aminotransferase
CCU	Cardiac Care Unit
CHD	Coronary Heart Disease
CK	Creatin Kinase
cTn	Cardiac Troponin
DM	Diabetes Mellitus
ECG	Electrocardiogram
ELISA	Enzyme linked immunosorbent assay
ETC	Electrochemiluminescence
FDA	Food and Drug Administration
H2O2	Hydrogen peroxidase
HRP	Horseradish peroxidase
HSA	Human serum albumin
Hs-cTn	High sensitive - Cardiac Troponin
IDH	Ischemic Heart Disease
LDH	Lactate Dehydrogenase
NSTMI	Non-ST-elevation Myocardial Infarction
NTS	N-terminal sequence
OD	Optical Density
PCI	Percutaneous Coronary Intervention
RFs	Risk Factors
ROC	Receiver operating curve
ROS	Reactive oxygen species
STMI	ST-elevation Myocardial Infarction

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1. INTRODUCTION

Acute myocardial infarction (AMI) is among the greatest frequent illnesses in poor nations, accounting for around a quarter of all cases (Meenakshisundaram et al., 2020). In the medical community, it is known as a heart attack, and it happens when there is a sudden blockage in blood flow in one or more of the coronary vessels, cutting off blood supply to a section of the heart muscle, resulting in necrosis (massive cell death, a permanent damage). If the blockage is severe, the heart may be unable to beat (cardiac arrest). A susceptible atherosclerotic sign, which is an unsteady accumulation of fats, white blood cells (particularly macrophages & monocytes) within a blood vessel walls, is the most common cause of coronary artery occlusion or blockage in the majority of cases. Myocardial infarction is a condition that generally originates inside the endocardium and progresses to the epicardium (Rathore et al., 2017). However, chest discomfort is the most prevalent sign of acute myocardial infarction, which may radiate into the shoulder, arm, back and neck as well as the jaw. Whenever this sort of discomfort occurs, tt always starts in the middle as well as the left side of a chest and seems to last in a few minutes before moving to another location. Although symptoms of acute myocardial infarction normally appear gradually over several minutes rather than instantly, this is not always the case (Bhagwat & Padmini, 2014). The prevalence of myocardial infarction varies substantially from country to country. An acute myocardial infarction (STEMI) or maybe a non-ST elevated myocardial infarction (NSTEMI) is a kind of heart attack occurs in roughly 650.000 and 180.000 individuals each year, respectively, in the United States and the United Kingdom; internationally, more than 3 million persons suffer STEMIs while 4 million suffer NSTEMIs (Anwar et al., 2016). Indians are 4 times more susceptible to AMI than those in other countries, owing to a combination of hereditary and lifestyle variables that contribute to metabolic dysfunction. The occurrence of myocardial infarction throughout India is 64.37 per 1000 persons, four times higher than the global average (Author, 2015). A year after a myocardial infarction, one in every 25 patients dies. Myocardial infarction is the leading cause of death in India, accounting for 31.7% of all deaths. In 1970, around 7% of Indians had cardiovascular disease; by 2011, that number had risen to 32% (Lim et al., 2012). The most recent clinical implications of ACS

might range from innocuous to potentially deadly in their severity. History, physical examination, and electrocardiogram (ECG) are routinely used clinical methods for risk classification, although they may be insufficient in many patients (Chacko et al., 2018). IHD can be detected early using biochemical indicators such as creatine kinase in muscle and brain, myoglobin, and troponin, all of which are desirable and feasible (Pan et al., 2014). Troponin is more specific than C-reactive protein in the identification of myocardial infarction linked with CK-MB. It takes 12 hours after cardiac damage for the test to attain maximal sensitivity, decreasing its sensitivity in the early identification of IHD (Biswas et al., 2014). When a patient has severe chest pain, especially when the baseline ECG is non-interpretable, it is difficult to make a diagnosis of myocardial ischemia. There is no rapid and definite test that can be referred to as a gold standard for ruling off myocardial ischemia (Vijaya & Gayathri, 2014). When reactive oxygen species (ROS) are reduced under oxygen stress conditions, IMA is produced, resulting in hypoxia and acidosis. Although the exact mechanism of IMA formation is unknown, it appears to be linked to the production of ROS, which alter the metallic binding affinity of molecules (Bhakthavatsala Reddy et al., 2014). Myocardial ischemia should be identified as soon as possible when it occurs in order to prevent myocardial cell damage (Vijaya & Gayathri, 2014). The IMA has indeed been proven to be a novel blood biomarker indicating myocardial ischemia and oxidative stress, according to the research (Patil et al., 2013). The IMA has evolved into a cardiac biomarker test that is readily available and approved for regular medical implementation in Europe, as well as accepted by FDA in the USA market (MYTHILI & MALATHI, 2015). The index of myocardial ischemia (IMA) rises within minutes of the onset of ischemia and returns to baseline within six hours of perfusion. To avoid exceeding the clinical decision limit for the cardiac troponin test, a robust myocardial ischemia biomarker is becoming more useful (Pan et al., 2014).

1.1 The Study Objectives

The current study's objectives are to analyze the possible role of ischemic modified albumin as a cardiac biomarker in the diagnosis of patients suffering from acute myocardial infarction, in addition to the diagnostic value of ischemic modified albumin in comparison to high sensitive cardiac troponin.

2. LITERATURE REVIEW

2.1 Myocardial Infraction

Approximately 50 per cent of the all the mortality occur as a result of cardiovascular disorders, which account for some more over four million deaths annually Europe only (Townsend et al., 2015). Coronary artery disease is the most common reason for death among these conditions, particularly acute myocardial infarction (AMI) determined aimed at nearly totally of the death caused by disease of the coronary artery (Mendis et al., 2011). Changing human routine as well as activities, especially those in countries under developing, has resulted in a constant and significant rise in the commonness of the acute myocardial infarction during past several decades, with yearly increases exceeding 3.5 percent (Benjamin et al., 2017). Patients that reach toward emergency rooms suffer from chest discomfort each time are recognized have AMI at a rate of around 10 percent (Haasenritter et al., 2012). Acute myocardial infarction remains to be a prominent reason of morbidity besides death around the world, it arises as a result of myocardial ischemia (Rathore, 2018). Acute myocardial infarction (AMI) is among the most frequent illnesses in poor nations, accounting for around a quarter of all cases (Meenakshisundaram et al., 2020). A heart attack follows as soon as single or additional coronary arteries abruptly get blocked, preventing blood supply from reaching a piece of the muscle heart, triggering necrosis. This is what is commonly referred to as a heart attack. If indeed the blockage remains significant, heart may be unable to beat (cardiac arrest). A susceptible atherosclerotic plaque, it is an unsteady accumulation of lipids, white blood cells (particularly macrophages & monocytes) inside the wall of a blood vessel, is the most common cause of coronary artery occlusion or blockage in the majority of cases. Myocardial infarction is a condition that generally originates inside the endocardium and progresses to the epicardium (Rathore et al., 2017). However, chest discomfort is the most prevalent sign of acute myocardial infarction, which may radiate into the shoulder, arm, back and neck as well as the jaw. Whenever this sort of discomfort occurs, it always begins with in middle or left side of the chest as well as lasts for a few minutes. Although symptoms of acute myocardial infarction normally appear gradually over many minutes rather than instantly, this is not always the case (Anwar et al., 2016). Acute myocardial

infarction is characterized according to whether or not there is ST-segment elevation on the electrocardiogram (ECG), and it is additionally subdivided into the following six different kinds: coronary artery atherothrombosis (type 1), supply-demand mismatch (type 2), infarction starting to cause untimely death even without possible chance for biomarker or ECG verification (type 3), infarction associated with grafting of coronary artery bypass (type 4a), coronary artery bypass grafting (type 4b), and surgery of coronary artery bypass (type 5) are the types of coronary artery atherothrombosis that can occur (Thygesen, Alpert, et al., 2012). Recognizing that acute coronary syndrome (ACS) is most usually caused by intracoronary clotting and will immediate conquering the obstructed inside coronary artery considerably improves patient consequences in this highest category has been changed the way AMI diagnosis has been approached throughout the years. Developing solutions that would permit for together primary detection in addition elimination of AMI has piqued the interest of many researchers. The former would allow for immediate, frequently life-saving actions, while those would allow for fast and comfortable patient release, resulting in a significant reduction in overall healthcare expenditures. The presence of acute chest pain throughout the context of characteristic ECG alterations remains to be the most important factor in determining the diagnosis of AMI. it, on the other hand, is present in around 90 percent of patients who arrive with chest pain; furthermore, the detection accuracy of ECG abnormalities in AMI are also quite poor (J. J. Wang et al., 2018).

2.1.1 Epidemiology

It has been three to four decades since the attuned commonness of hospitalization aimed at acute myocardial infarction or deadly coronary artery disease occurrence within United States has decreased via four to five percent every year, epidemiological features of acute myocardial infarction consume changed substantially (Mozaffarian et al., 2016). There are an estimated 550,000 new cases involving acute myocardial infarction and 200,000 recurrences every year (Mozaffarian et al., 2016). According to the International Classification of Diseases and Related Health Problems, ischemic heart disease has surpassed all other diseases in terms of disorder life years (Murray et al., 2015). Meanwhile, the worldwide incidence of cardiovascular disease and acute myocardial

infarction has migrated from high-income nations to low- also middle-income countries, where further than eighty percent of entirely fatalities from cardiovascular disease currently happen (Murray et al., 2015). In a study of 156,424 people from 17 countries who have been tracked for a mean of 4.1 years, the researchers found (Yusuf et al., 2014). Since wealth is a direct predictor of risk factor load, the largest risk factors encumbrance was found in in height-income nations in addition the lowest encumbrance found in low-income countries, the researchers concluded that. On the other hand, incidence of acute myocardial infarction was shown to have an inverse association with income (1.92, 2.21, and 4.13 instances per thousand individuals within high, middle, and low-income nations, respectively; P0.001 for the overall trend) and to be inversely related to income. The increased adoption of prevention methods and revascularization treatments in higher-income nations has been related to the reduction of the heavy incidence of risk factors in these countries (Libby, 2013).

2.1.2 Pathophysiology

STEMI (ST elevation myocardial infarction) and NSTEMI (non-ST elevation myocardial infarction) are two types of acute myocardial infarction. The condition known as unstable angina is often referred to as acute coronary syndrome (ACS), for the reason that is a prelude for myocardial infarction and can be fatal. Unstable angina has a pathogenesis with NSTEMI, and the two conditions are denoted to as non-ST-segment elevation-acute coronary syndrome (ACS) (NSTE-ACS). For the most part, they have typically been grouped together when making managerial choices. Type 1 myocardial infarction occurs when a susceptible atherosclerotic plaque ruptures or when the endothelium of the coronary artery is eroded, which is the most common cause (Libby, 2013). The presence of severe stenosis (defined as a diameter of less than 70%) is required to cause angina; however, such stenosis is fewer probable to result in myocardial infarction type 1 since they appear to contain dense fibrotic caps that are fewer probable to snagging then because indemnity flow forms throughout period. Susceptible plaques, conversely, tend to have thirty–fifty percent constriction, thin fibrous caps, in addition include greater cells response to inflammatory, for instance lipid-laden macrophages, than healthy plaques (Thygesen et al., 2012). When a plaque ruptures, the thrombogenic components of the

plaque are released, resulting in platelet activation, the commencement of the coagulation cascade, a mural thrombus is formed, and atherosclerotic material is embolized downstream as a result of this process. If the hypercoagulable condition causes the rupture of further susceptible fibroatheromas, it is probable that the more than one culprit lesion will be identified. An increase in cardiac biomarkers in peripheral blood will be found as a result of myocyte necrosis as a result of this process. If the channel was partially or totally blocked, how long it was obstructed, how much myocardium was fed, how many collaterals were present, and how well the vessel was re-perfused after treatment, all have a role in determining the degree of ischemia (Libby, 2013).

2.1.3 Risk factors

Coronary Heart Disease (CHD) is a foremost reason of morbidity and death, and development of the illness is influenced significantly by the existence of risk factors (RFs) in the population (Kayani & Ballantyne, 2018). Hypertension, dyslipidemia, smoking, obesity, & diabetes mellitus (DM) are all key risk factors aimed at the development the acute myocardial infarction, which occurs when the heart fails suddenly (Leifheit-Limson et al., 2015). The frequency of these risk factors during a first or any occurrence of AMI has been investigated in a number of studies, with the majority revealing high incidence of at least one risk factor (about 85 percent to 90 percent) (Shah et al., 2014). An additional contributor to the development and diagnosis of AMI has been identified as substance abuse (DeFilippis et al., 2018). In the aftermath of an AMI, differences in consequences have been seen throughout ethnic and gender lines. These differences are thought to be caused by differences in basic risk factor patterns (T. Gupta et al., 2018). Despite the fact that AMI rates in the United States have been declining in recent years, the incidence of these modifiable RFs throughout an AMI is actually growing (A. Gupta et al., 2014).

2.1.4 Diagnostic biomarkers of Acute Myocardial Infarction

Through recent years, occurrence of acute myocardial infarction (AMI) has increased dramatically, posing a major threat to health of human. Cardiac biomarkers are crucial

for diagnosis and prognosis of acute myocardial infarction (Shevtsova et al., 2021). There is a tiny, but not insignificant, fraction of patients who do not have evident symptoms and/or ECG alterations, and this proportion is increasing. In this context, the necessity for new diagnostic criteria has been underlined, and cardiac biomarkers have appeared as the most apparent method of achieving this goal. Traditionally, repeated, daily monitoring of cardiac biomarkers was used mainly as a tool to validate the identification of acute myocardial infarction. Ever since their importance has grown steadily, and cardiac biomarker alterations are present considered key of criteria to acute myocardial infarction (AMI) diagnosis (Ibanez et al., 2018).

2.1.4.1 Classical biomarkers intended for Acute Myocardial Infarction diagnosis

As a consequence of myocardial ischemia and subsequent myocardial necrosis, a large number of cardiac enzymes are released and circulate in the body's bloodstream. Aspartate aminotransferase (AST) and creatine kinase (CK) were the first enzymes to be identified as indicators of acute myocardial infarction (AMI). The concept of delta change, which was presented as an early symptom of the illness, was also used to identify patients with AMI. Previously, the cardiac enzymes AST and LDH were the first to be used in the identification of acute myocardial infarction (Parsanathan & Jain, 2020).

2.1.4.2 Cardiac Troponins current cardiac biomarker for identification of AMI

Troponin play a crucial role in the relationship between actin and myosin as well as the control of contractile activity in rejoinder to calcium also protein phosphorylation throughout cytosol. In addition to tropomyosin, the troponin complex is found on the actin filament. For AMI diagnostic purposes, cardiac-specific isoforms of cardiac troponin I and troponin T be present within myocardial tissue while troponin C into both the heart and the skeletal muscle will have expressed (Morrow et al., 2007). Serum cTn concentration must be deliberate by means of a coefficient of difference of ten percentages, Third Universal Definition of Myocardial Infarction requires at least one cTn to be over the ninety-nine percentile of the maximum acceptable limit (Apple et al., 2012). When high-sensitivity troponin (hs-cTn) investigation was developed, it allowed

for earlier detection of myocardial damage, with aberrant cTn discovered inside twenty-four hours of the beginning of symptoms (Body, 2018). Although higher blood cTn levels are indicative of myocardial injury, the underlying mechanisms behind this result remain a mystery at this time. Furthermore, in addition to coronary embolism and coronary artery spasm, AMI can be induced by an increase in challenge for or reduction in supply oxygen, or it can be caused by a combination of these factors. Furthermore, to spontaneous AMI pursue acute coronary blockage beside plaque rupture, AMI also develop as a result of arrhythmia and hypertension. Patients suffer from coronary heart disease & those with non-cardiac conditions may have increased levels of cTn (Manikkan, 2018). Furthermore, the level of cTn is elevated in individuals with renal failure who do not have symptoms of acute coronary syndrome (ACS), despite the fact that are at a greater hazard for abnormalities of cardiac in the first place. A further research found that fifty percentage of individuals suffering from renal failure and an elevated cTn concentration make sure coronary arteries that were free of flow-limiting stenosis when they had an angiographic examination (Mueller et al., 2013). cTn is persistently increased in these patients, signaling that they have a thyroid condition. As demonstrated in multiple clinical studies, meta-analysis has shown that in some malignancies, high cTn levels are advantageous for diagnostic purposes and correspondingly act as an autonomous prognostic signal (Das & Mishra, 2017). Because abnormalities can be used to distinguish subgroups of patients who will gain so much from initial invasive therapy after ACS, the cTn level can be used to aid in clinical decision-making regarding if a further aggressive otherwise more traditional management sequence must be taken later ACS diagnosis (Tan et al., 2016).

2.1.4.3 Ischemia Modified Albumin generation and itis role as a cardiac biomarker in AMI diagnosis

A few alterations in albumin characteristics are observed following ischemic strokes, which are connected thru oxidative stress, the generation of reactive oxygen species, besides the acidosis increased (Lee & Wu, 2015). When exposed to oxidative stress, the amino acid sequence Asp1-Ala2-His3-Lys4 of N-terminal sequence of Human serum albumin remains highly sensitive for biochemical changes and destruction. As a result, the NTS affinity for conversion metals, particularly cobalt, will diminished. Ischemia-

modified albumin (IMA) was the name given to this particular type of albumin (Watanabe et al., 2017). The genesis of the IMA was the subject of several theories. In Figure 2.1, we see an auto-degradation of NTS as one possible option. The cleavage of the peptide link between Ala2 and His3 is caused by the nucleophilic assault of the Asp1- amine nitrogen present over carbonyl of peptide that link among Ala2 & His3. This results in the cyclic dipeptide discharge. By way of a consequence, shortened albumin does not have the ability to bind transition metal ions (Leblanc et al., 2018).

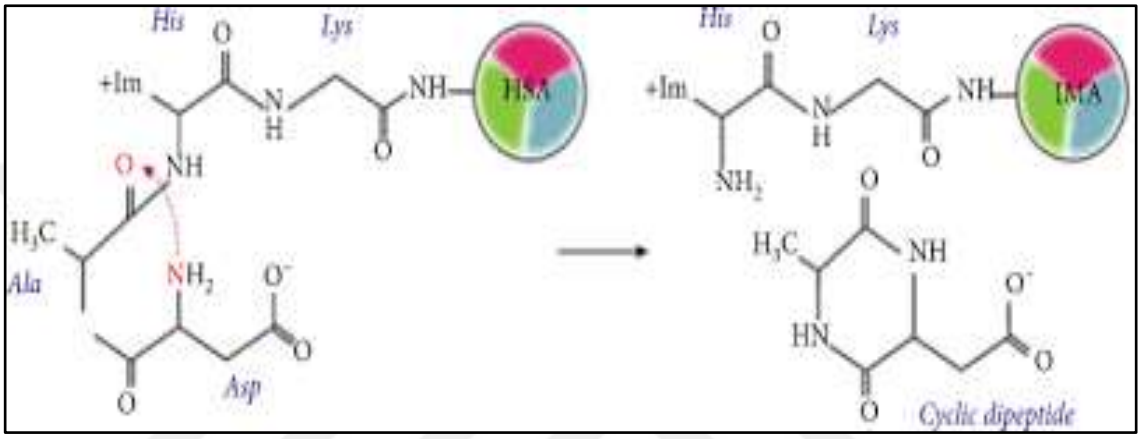

Figure 2.1 IMA establishment as a result of dipeptide cleavage

Another concept of a production is established on the synthesis of the reactive oxygen species as a result of the Fenton reaction, which is described in more detail below. Acute ischemia, according to this hypothesis, is accompanied by acidosis and the release of Cu2+ from weakly bound Cu2+ sites on the surface of circulating proteins and peptides. It is possible that free Cu2+ will be transformed to Cu+ in the manifestation of the reducing substances (such as, ascorbic acid), which will then combine with O2 and create superoxide radicals. Cu+ is oxidized to Cu2+ during this process, and the albumin N-terminus scavenges the ions produced by this reaction. As a result of the activity of superoxide dismutase, after being turned into hydrogen peroxide (H2O2), the superoxide radicals undergo the Fenton reaction, where they are either eliminated by catalase or transformed into hydroxyl free radicals. Because of the damage caused by free radicals to HSA, up to 3 N-terminal amino acids are lost, and Cu^{2} is released into environment as a result of the damage. The phases of the previously stated procedure are performed again and again in a chain reaction (C., 2013). Furthermore, following an ischemic episode,

IMA quickly increases. Figure 2.2 depicts the steps of IMA creation that occur as a result of this process. This suggested process, while theoretically appealing, has not been demonstrated to be effective in practice. In humans, the Human Serum Albumin half-life is around three weeks. Assuming that Human Serum Albumin contains an intact NH2-terminus, it's in vivo half-life qualities would be identical. After an ischemic cardiac episode, clinical and experimental evidence shows, however, that IMA quickly recovers to baseline levels (Arıcan et al., 2020).

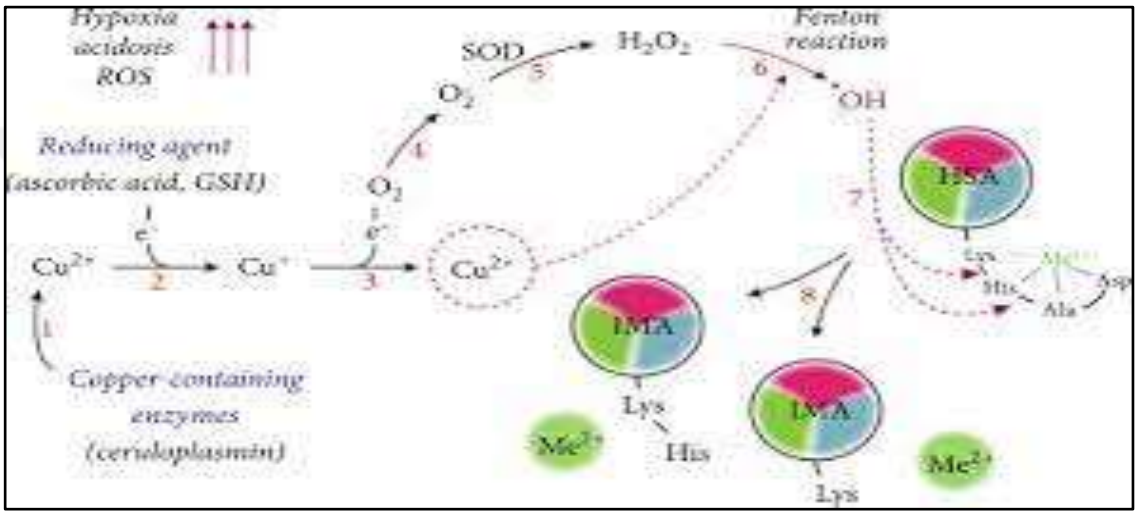

Figure 2.2 The process of IMA production that is triggered by oxidative stress

As a result, IMA is a temporary and reversible change to albumin rather than a permanent one. It seems doubtful that truncated albumin can be rapidly regenerated. Each person with a high IMA concentration contained two amino acid residues from of the pure albumin NTS that were not present in the other. however this was not the case in six of seven ischemia people and one non-ischemic individual who had non-truncated NTS, as shown by Bhagavan et al (Bhagavan et al., 2003). According to Bar-Or and colleagues, was revealed that IMA can be created by both truncation and the acetylation of NTS, which was identified by employing synthetic peptides having modified the primary two-twelve amino acids of HSA sequence (Cho et al., 2022).

This change, on the other hand, has not been proven in vivo. When three distinct receptors for Co2+-ions in human serum albumin were examined using spectroscopic and thermodynamic methods, the A and B sites were shown to have more avidity from the N

terminal binding site, resulting in a different conclusion from the N terminal binding site (Sokołowska et al., 2009). In exchange for single of the other cobalt-binding sites on albumin, fatty acids connected to the protein, leading to a negative allosteric interaction between two proteins. Some researchers believe the production fatty acids during myocardial ischemia consequences in the attachment of these fatty acids to albumin, which lowers albumin's capability to actually start cobalt by a ratio of two (Lu et al., 2012). The reduction in albumin affinity for transition metal ions is a common indication to all suggested methods, which takes all of the foregoing into consideration. There is no currently approved mechanism for the IMA creation. As this population is considered to be a clinical perfect to reperfusion of myocardial ischemia, kinetics of myocardial infarction development in patients have chronic stable angina who had percutaneous coronary intervention (PCI) were studied. According to the findings of these trials, patients with such a test for positive exercise stress and coronary artery disease saw a rise in blood IMA through six-ten minutes of having PCI, the elevation continued for approximately six-twelve hrs. until reverting to typical within twelve-twenty-four hrs (Bar-Or et al., 2001). It can take up to 12 hours on average for athletes who participate in short-term physical activity to restore their IMA concentrations to their pre-exercise levels (Dahiya et al., 2018). These findings demonstrate that IMA rapidly recovers to its reference line concentration following ischemia. Albumin will have a half-life of 19-20 days, which means that the albumin modification may just be transitory otherwise IMA may be swiftly eliminated from the body The quantity of IMA present changes depending on the period of ischemic proceedings, concentration of IMA available following long ischemia (25-60 minutes) are substantially higher than any of those existing after short ischemia (15-21 minutes) (C., 2013). Even before myocardial necrosis occurs, positive IMA levels appear within minutes of ischemia and persist for several hours, making this biomarker superior to cTn. As a result, an initial assessment of the patient's condition that shows no positive IMA results indicates a low risk of adverse events, which saves money (Blindauer et al., 2016). After IMA stayed utilized in concurrence with cTnT data in addition electrocardiography in patients by doubted acute coronary syndrome, diagnostic precision at admission rose. Truthfully, IMA conjunction to cTnT outcomes consider a much further sensitive marker for detecting unfavorable cardiac problems than cTnT alone (Mehta et al., 2015).

3. MATERIALS AND METHODS

3.1 Materials

3.1.1 Chemicals and reagent

Analytical reagents include Human Ischemic Modified Albumin, Cardiac High Sensitive Troponin and various substrates and all others materials were purchased from (BIOASSAY TECHNOLOGY LABORATORY, ROSHE companies) respectively.

3.1.2 Patients groups

This is a case-control study accompanied during period between November 2021 to March 2022, whole blood sample was obtained from 80 patients (52 males and 28 females) suffering from acute myocardial infarction, at the Cardiac Care Unit (CCU) in Al-hussein Medical City. This study also included a total of 20 apparently healthy volunteers (12 males and 8 females) without chronic heart disease, the patients groups are illustrated in Figure 3.1. Ethical approval was taken, verbal consent was taken for inclusion in the study, the information obtains from all patients by direct interview.

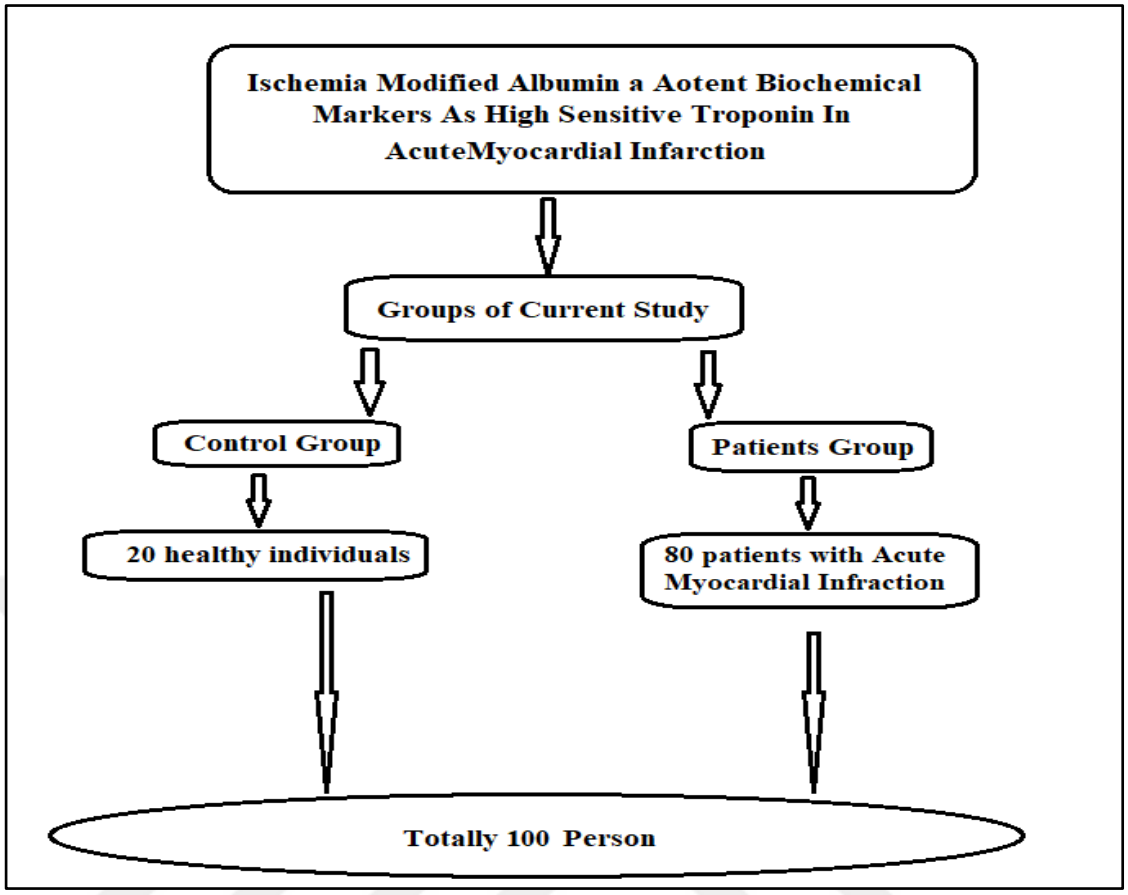

Figure 3.1 Groups of the current study

3.1.3 Instruments

Instruments & equipment utilized throughout current study were shown in the table 3.1.

Table 3.1 The instruments and equipment which used in the current study

Instruments and equipment	Company- country
Centrifuge EBA 20	Hettich (Germany)
ELISA reader	BioTek (UK)
ELISA washer	BioTek (UK)
Eppendorf Centrifuge	Labogene (Denmark)
Incubator	Memmert (Germany)
Multichannel pipette	cleaver (USA)
Pipette	Cleaver (USA)
Refrigerator	Beko (Turkey)
Roche cobas E411	(Germany)
Tips (different sizes)	China

3.1.4 Blood sample collection

Three milliliters (3 ml) of venous blood from each participating subject were obtained and was dispensed into a gel tube containing clot activator and left in the room temperature to clot for about (10) minutes, and then, centrifuged for about (ten min for 4000 rpm). Separated serum was distributed into 3 Eppendorf tubes which were frozen at -20 until the valuation of the Ischemia Modified Albumin and Cardiac high sensitive troponin.

3.2 Methods

3.2.1 Measurement of Ischemia Modified Albumin (IMA) by means ELISA technique: Lot No. (20211216)

3.2.1.1 Principle

These kits were constructed on the ELISA technology. Anti- Human IMA antibodies were pre-coated over plates. Sample contain IMA will bounded with anti-Human IMA which present in plate, antibody labeled with biotin were loaded into wells later, and douched by means of wash buffer. Then HRP-Streptavidin are supplementary then boundless conjugates are detached through buffer used to wash.

The substrate solution is utilized to presentation reaction of HRP, yield blue color product due to stimulated the substrate via HRP enzyme will change to yellow color next are added stop solution. The quantity of the Human IMA of sample apprehended in plate is comparative with yellow color density, optical density read by microplate reader. Absorbance at 450nm, then the Human IMA concentration can be accounted.

3.2.1.2 Procedure

Concerning the method of work, it is summarized in eight steps, which are explained in the diagram below in Figure (3.2)

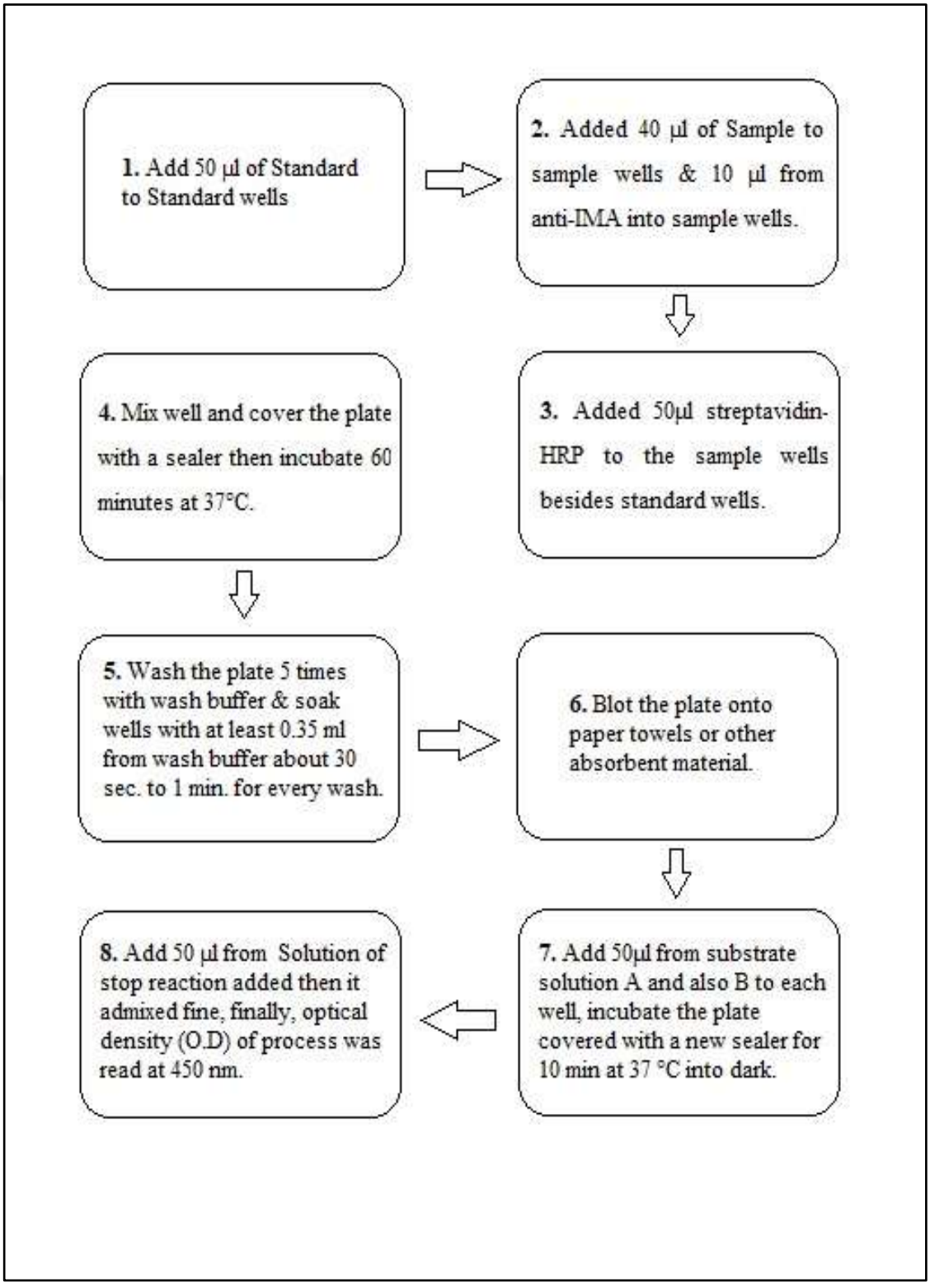

Figure 3.2 Experimental method diagram of IMA measurement

3.2.1.3 Interpretation of results:

Figure (3.3) showed standard curve of Human Ischemic Modified Albumin.

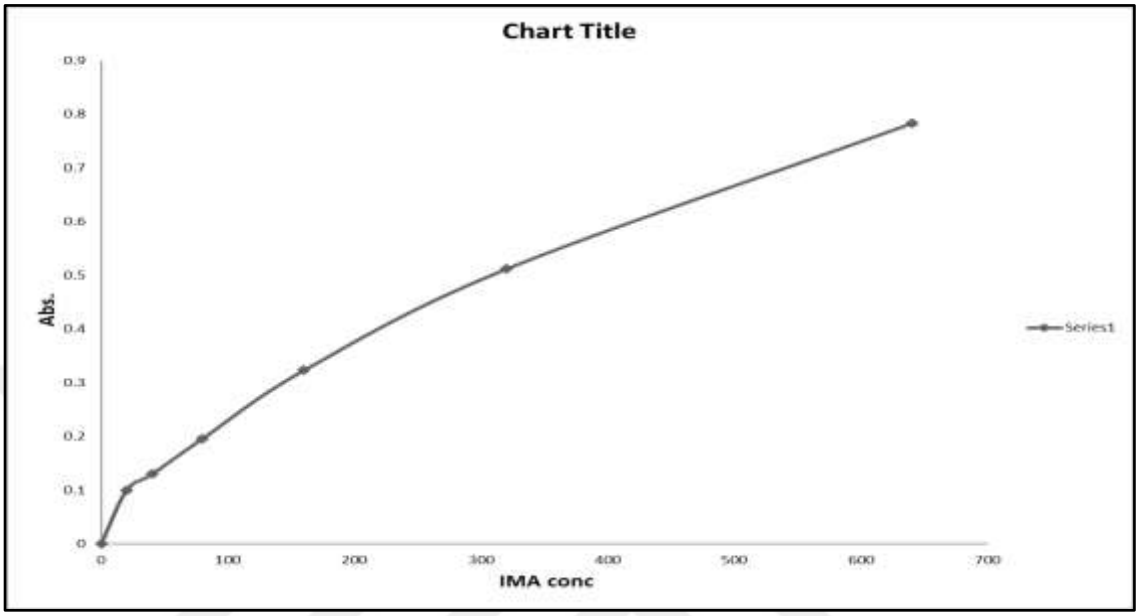

Figure 3.3 Standard curve of IMA

3.2.2 Assessment of cardiac high sensitive troponin by means COBAS E400 technique: (Lot No: 52366901)

3.2.2.1 Principle of assay

The Roche Diagnostic Cobas E 411 Immunoassay System is a completely automated, haphazard entry, controlled by software system for immunoassay investigation. This system contains three principles: the first is competitive principle used for very minor analytes, second is sandwich principle (single or double steps) used for very big analytes and third principle is a bridging principle used for reveal antibodies in the specimen.

The Cobas E411 automates the immunoassay reactions using electrochemiluminescence (ECL). ECL is an operation wherein extremely reactive species are produced on the surface of an electrode from the steady forerunners. These extremely reactive species react together, generating light. In addition to tripropylamine, a ruthenium (II)-tris

(bipyridyl) [Ru (bpy)] complex has been used to enhance ECL immunoassays (TPA). The illuminating step is where the final chemiluminescent product is created. Electrochemically induced chemiluminescent reactions that result in the emission of light after the ruthenium complex have been initiated by introducing voltage into immunological complexes which are coupled to the streptavidin-coated microparticles.

3.2.2.2 Procedure

The procedure of assay was done according the routine test powered by Cobas E411 as in figure 3.4

Figure 3.4 Cobas E411

3.2.3 Statistical issue analysis

The statistical issue of analysis results is expressed as median and 5-95 confidence intervals. For comparison between groups for abnormally distributed specific Mann Whitney test are used. So, Pearson correlation made to estimate the connection between each pair of variables. P value less than 0.05 was reflected statistically significant. All analyses were approved by SPSS 20.0 software (SPSS Inc, Chicago, Illinois, USA). Receiver operating curve (ROC) was used to estimate the cutoff for IMA plasma value. Diagnosis and performance of analyzes according to their sensitivity, specificity, positive predictive value and negative predictive value.

4. RESULTS

4.1 Demographic characteristics of study groups

4.1.1 Sex distribution among study groups

The sex distribution during this current study according to patients group there were 28 (35.4%) females and 51(64.6%) males who suffering from myocardial infraction, in contrast the sex distribution among healthy control group included 8 (40%) females and 12 (60%) males, also there were no significant difference between the study groups throughout the study (p-value=0.705). As exposed in the table: (4.1).

Table 4.1 The sex distribution among study groups

Sex	Study groups			
	AMI		Control	
	Count	Column N %	Count	Column N %
Female	28	35.4%	8	40.0%
Male	51	64.6%	12	60.0%
P value	0.705^{NS}			

NS: Non-significant, AMI: Acute Myocardial Infarction

4.1.2 Age distribution among study groups

During this current study age of the all participants fluctuated from 36 near 69 years in respect of patients cluster, while from 35 to 69 years in respect to control group. Also there were moderate difference in the median of age among study groups (56 and 43 years, patients and control groups) respectively. As exemplified in the table: (4.2).

Table 4.2 The age distribution among study groups

Age (years)	Study groups					
	AMI			Control		
	Median	Percentie 05	Percentile 95	Median	Percentile 05	Percentile 95
	56.00	40.00	69.00	43.00	35.50	67.00

4.2 Serum concentration of high sensitive Troponin I among study groups

During this current study there were strong difference in the median of the serum concentration of Troponin T high sensitive among control group and patient's groups (1.50, 418.00 pg/ml) respectively. As revealed in the following table & figure (4.3, 4.1) respectively.

Table 4.3 The serum concentration of Troponin high -sensitive among study groups

Troponin I -high sensitive (pg/ml)	Study groups					
	MI			Control		
	Median	Percentile 05	Percentile 95	Median	Percentile 05	Percentile 95
	418.00	31.00	44000.00	1.50	1.00	2.00

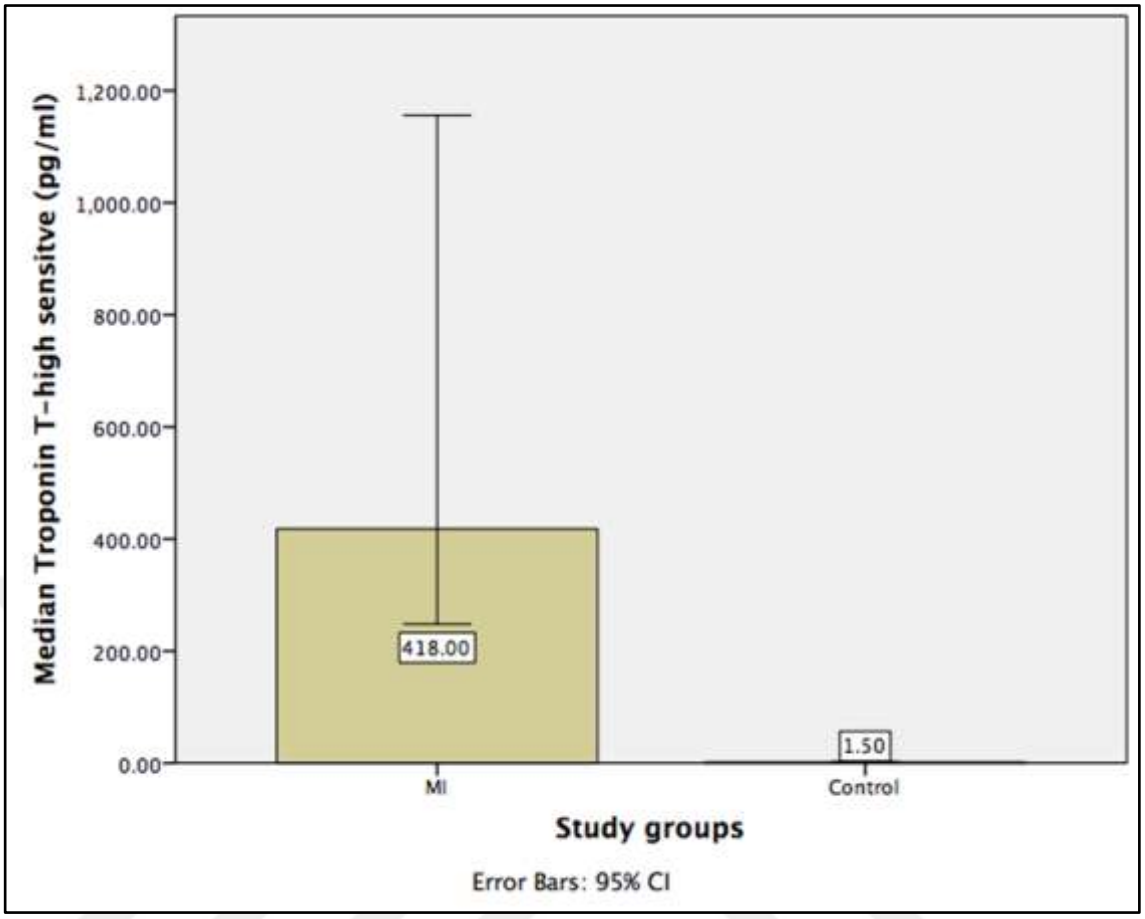

Figure 4.1 Illustrate the serum concentration of Troponin high- sensitive among study groups

4.3 Serum concentration of Ischemic Modified Albumin among study groups

During this current study there were strong difference in the median of the serum concentration of Ischemic Modified Albumin among control group and patient's groups (52, 98.9 ng/ml) respectively. As demonstrated in the following table & figure (4.4, 4.2) respectively.

Table 4.4 The serum concentration of Ischemic Modified Albumin among study groups

Ischemia Modified Albumin (ng/ml)	Study groups					
	MI			Control		
	Median	Percentile 05	Percentile 95	Median	Percentile 05	Percentile 95
	98.90	32.90	237.30	52.00	30.55	73.30

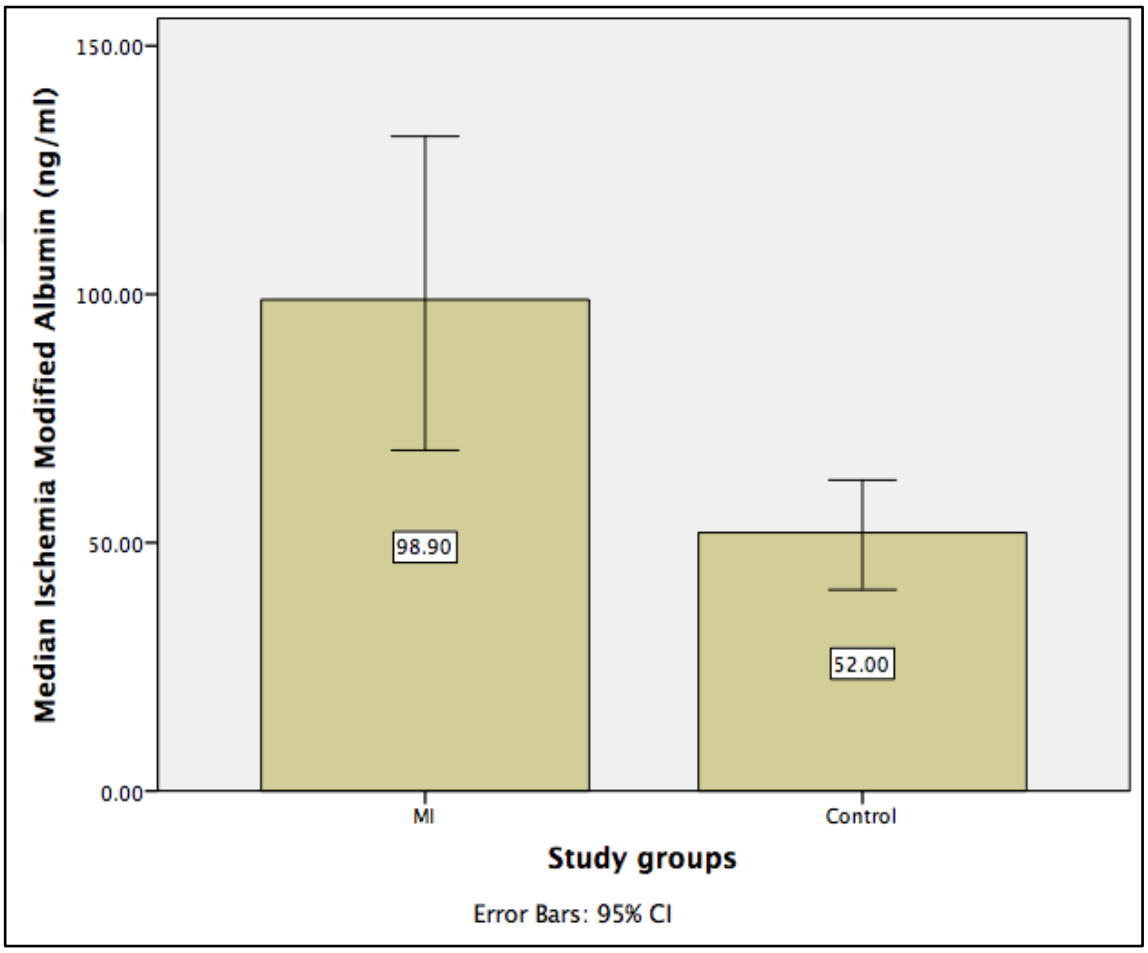

Figure 4.2 Illustrate the serum concentration of Ischemic Modified Albumin among study groups

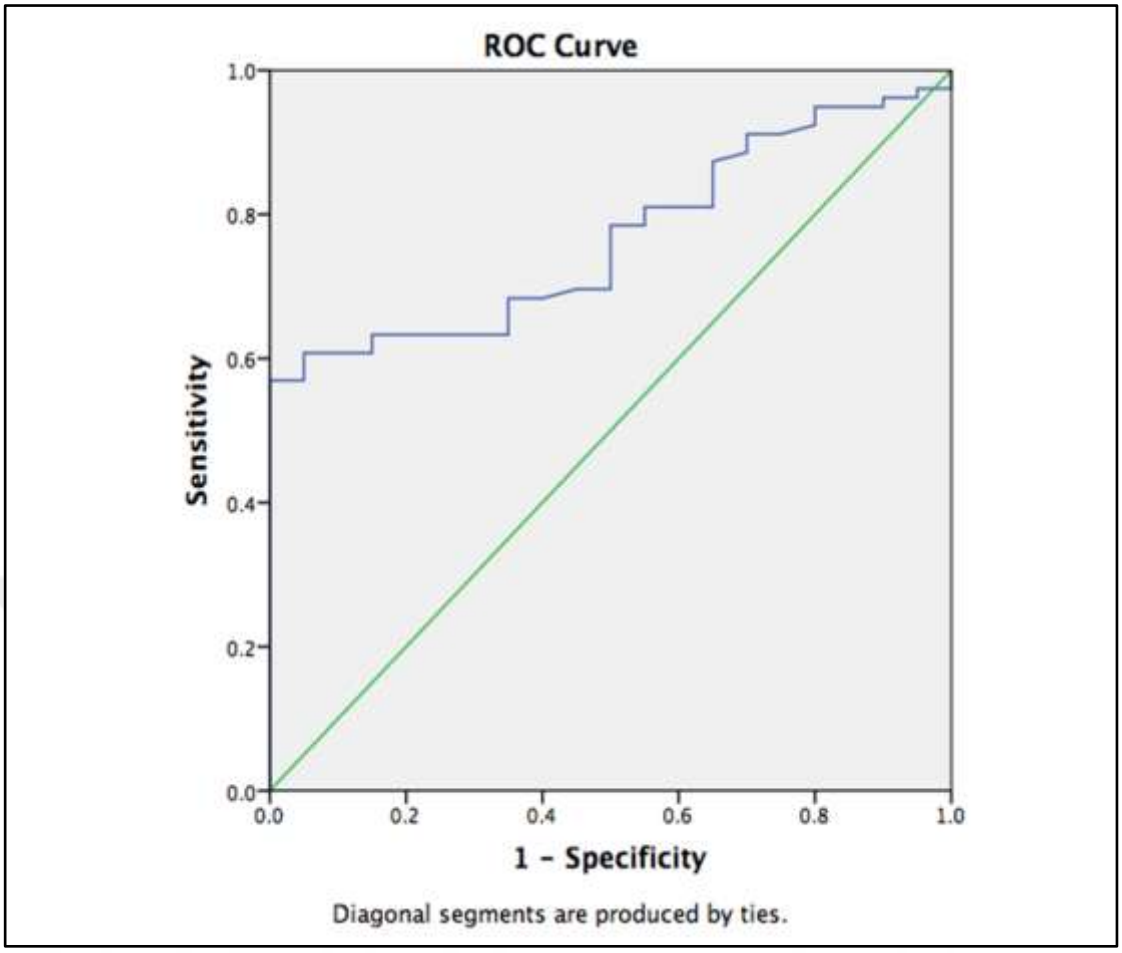

Figure 4.3 ROC curve for AMI patients in the IMA values

Area under curve and cut-off value and it is sensitivity, specificity as well as positive – negative predictive values of IMA in patients with MI are shown in Table (4.5) & (4.6).

Table 4.5 The Area Under the Curve (AUC)

Area	**Std. Error**	**Asymptotic Sig**	**Asymptotic 95% Confidence Interval**	
			Lower Bound	Upper Bound
0.767	0.048	<0.001	0.673	0.860

Table 4.6 The cut-off value and it is sensitivity, specificity as well as positive –negative predictive values of IMA in patients with AMI

		Study groups	
		MI	**Control**
IMA	>60 (ng/ml)	53	7
	%	67.1%	35.0%
	< 60 (ng/ml)	26	13
	%	32.9%	65.0%
Total	Count	79	20
	%	100.0%	100.0%
P value		0.011	
Sensitivity		67.09 (56.15-76.45)	
Specificity		65 (43.29-81.88)	
Positive Predictive Value		88.33 (77.82-94.23)	
Negative Predictive Value		33.33 (20.63-49.02)	

4.4 The correlation between IMA and troponin high- sensitive

During this current study there was positive correlation between serum concentration of Ischemic Modified Albumin and high sensitive cardiac Troponin (rs =0.265* and p value 0.018). As demonstrated in following table & figure (4.5, 4.3), respectively.

Table 4.7 The correlation between serum concentration of IMA and cTpI h-sensitive in AMI

		Troponin T-high sensitive (pg/ml)
Ischemia Modified Albumin (ng/ml)	Correlation	0.265*
	P value	0.018

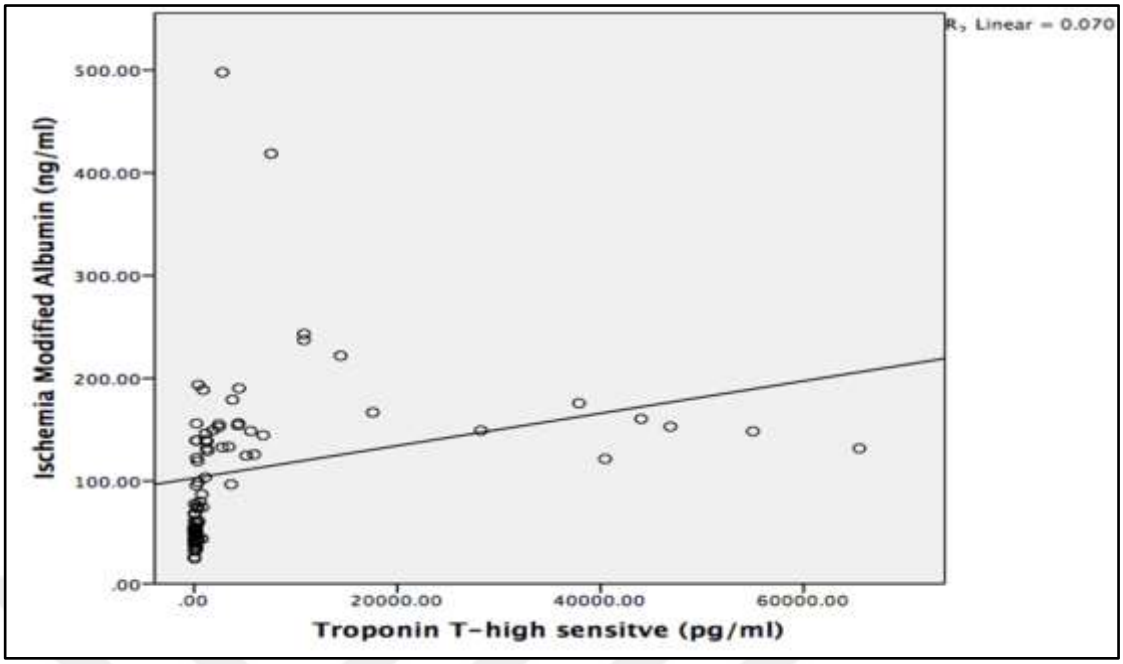

Figure 4.4 Illustrate the correlation between serum concentration of IMA and cTpI h-sensitive

5. DISCUSSION

5.1 Demographic characteristics of study groups

5.1.1 Sex distribution among study groups

This results showed no significant difference according to age between groups of study with (p-value =0.705). in another hand other study that evaluated the serum concentration of Ischemic Modified Albumin which included fifty ischemic patients and fifty heathy control individuals the sex distribution throughout it according to patients group 24 (48%) were females and 26 (52%) were males, in contrast the sex distribution in respect to the control group 22 (44 percentage) were females and male's percentage were 28 (56 percentage) also demonstrated no significant difference among study groups p-value (0.688) (Jena et al., 2017).

In addition, study the same biomarker in same disease that involved 50 patients with acute ischemic within one hour, one, two, three and six day of time and compared first-hour for assessment value of IMA with age- and sex-matched control group, the sex distribution in respect to patients group 39 were males and 11were females, while according to control group 30 were males and 20 were females, this study also indicated no significant difference among study groups (Menon et al., 2018).

5.1.2 Age distribution among study groups

This current study concordance with another study performed by Mishra, Bijaya, et al.in 2018 which enrolled 50 patients and 50 sex-age matched healthy control group, the age ranged from 21 to 96 years, this study revealed there were highly difference in mean between patients and control group (62.32±16.63, 41.98±5.40 years) respectively. Also and there was significant statistically difference with p value (p-0.001), in respect to age among study groups (Mishra et al., 2018).

Additional study was accompanied on 102 patients who offered to the Emergency Section through six hrs. suffer from acute chest pain & 110 healthy individuals with age and sex matched offers who designed the group of control during this study patient divided into two groups one group with unstable angina and other with myocardial infarction the age distribution among study groups results showed mild difference in mean (40.1±12.34, 43.1±13.01, 48.8±14.56 years) respectively (Patil et al., 2013).

5.2 Serum concentration of high sensitive Troponin I among study groups

This study showed higher difference in median of serum concentration of troponin high-sensitive between patients with MI in compare to healthy control enrolled throughout this study,the findings of this study agree with outcomes of other study that demonstrated higher significant ($p < 0.01$) in the mean concentration of the troponin in patients with MI in contrast with group of healthy controls. In the related approach, the mean concentration of troponin was significantly higher ($p < 0.01$) elevated in the MI patients unresisted survival when compatible with survival MI patients (Patil et al., 2017).

Also compatible with other study which investigated the concentration of cardiac troponin I in both serum and saliva (stimulated & unstimulated), these results of serum concentration of the cTnI in the patients suffering from AMI, in during both twelve & twenty-four hours subsequently admission showed highly difference in median [6.41 (2.69---11.58) & 4.07 (2.14---8.98) mg/l], respectively were high significantly from the group of control healthy subjects 0.14 (0.08---0.23) mg/l ($P<0.0001$). In other hand in same study the remain concentration of cTnI in salivary demonstrated to be significantly greater in median in the AMI patients througho ut the first twelve & twenty-four hours [0.40 (0.17---0.62) and 0.71 (0.52---1.07) ng/l], respectively subsequent the beginning of MI related to the healthy control group 0.19 (0.08---0.27) ng/l. in respect to motivator saliva the concentration of the cTnI indicated no found significant difference were noticed among at all study groups (Mirzaii-Dizgah & Riahi, 2013).

Furthermore, this current study finding similarly with other study accompanied on Pakistani population that during it the participants were clustered in respect to the

choosing criteria as group of patients & group of control. patients group was additional classified as (A, B &C groups. Subjects who diagnosed with Ischemic Heart Disease (IHD) represent group A, while subject's identification with PCI and MI represent B and C groups), respectively. In normal, healthy subjects represent the control group, with identical age as matched to case groups were selected for comparison, this study showed significant statistically difference in serum troponin concentration among patient's groups in compare to control group (p-value=0.001) (Panjwani et al., 2019).

5.3 Serum concentration of Ischemic Modified Albumin among study groups

This study showed higher difference in median of serum concentration of Ischemic Modified Albumin between patients with MI in compare to healthy control enrolled throughout this study.This study concoredance with other study that demonstrated that the IMA serum concentration of acute coronary syndrome patients were highly significant incompatible with those of healthy control group (p=<0.001). while in same study in respect to categorized patients group those of patients with STEMI were significantly higher difference in mean of IMA serum concentration than those of the NSTEMI group ($2.4 \pm 0.1, 1.8 \pm 0.3$), respectively with ($p<0.001$) (Aladağ et al., 2021).

Additional study also compatible with this current study that indicated that the production of IMA in AMI patients was significantly higher in contrast to the normal group ($P<0.001$), regarding to evaluation the serum concentration of IMA among patient's subgroups after treatment where patients divided into poor prognosis as well as good prognosis when finding the IMA serum concentration in poor prognosis patients were significantly higher in mean of IMA than those in good prognosis patients (77.61 ± 20.15, 62.21 ± 21.47), respectively ($P < 0.05$) (Ding et al., 2021).

Furthermore, our study agrees with previous research that investigate the role of IMA as an early acute coronary syndrome diagnostic marker also revealed that serum IMA level identification was conducted in both groups, where it was found mean of IMA equal 0.410 along with 0.081 SD in group of normal control, while mean of IMA in respect to ACS

group 0.823 along with 0.191 SD, the variance among the both groups existence statistically significant ($p<0.0001$) (Mishra et al., 2018).

Information the test value of IMA in AMI and apparently healthy group was utilized in calculation the curve of ROC with an Area Under the Curve was 0.767 (95% CI, 0.673---0.860) as shown in Figure 4-3. Accordingly, the selected diagnostic cut-off was > 60 ng/ml examined for their medical sensitivity was (76.45%), specificity was (81.88%), positive predictive value was (88.33 ng\ml) and negative predictive value (33.33 ng\ml), which is considered as a good diagnostic marker for MI.

Other study was utilized the IMA for diagnosis the ischemic heart disease and it demonstrated the cut-off value to the diagnosis of acute myocardial ischemia that achieved by ROC investigation was 40.65 U/mL. Besides the both sensitivity & specificity for distinctive acute ischemia cardiac disease was 60.0 percentage & 80.5 percentage, correspondingly (P. Wang et al., 2017).

Furthermore, previous study also indicated the ideal indicative cut-off point for concentration IMA in serum through the study group was establish to be 104 U/ml the maximizing amount of specificity and sensitivity were 75.6% (95% CI 60.5–87.1), 72.1% (95% C.I. 56.3–84.7), respectively as well as the positive & negative predictive values were 73.9% (95% C.I. 58.9–85.7). 73.8% (95% C.I. 58.0–86.1), respectively. Areas under curve, its 95% confidence interval were Acute coronary syndrome: 0.766 (CI: 0.664-0.868), STEMI: 0.752 (CI: 0.629- 0.874), NSTEMI: 0.793(CI: 0.645- 0.940) (Sygitowicz et al., 2013).

5.4 The correlation between IMA and troponin high- sensitive

This study designated two common indicators of AMI: Ischemic Modified Albumin and Cardiac troponin (cTnT). CTnT is regarded to be the furthermost perfect primary diagnostic guide for AMI at current, in addition it is moreover an vital marker for patients' disease assessment, prognosis decision and healing consequence remark (CL et al.,

2008).The outcomes of current study exhibited that the serum concentration of IMA & cTnT in the AMI patients were significantly higher in in compared with control group, and there were positive correlation between IMA & cTnT, this results compatible with other study which found that Pearson correlation examination indicated that serum concentration of IMA were correlated positive along with CTnT serum concentration in patients with AMI (Ding et al., 2021). In other hand the outcomes of this current study disagree with previous study that demonstrated there was no significant correlation between these markers in patients with MI (Ertekin et al., 2013).

6. CONCLUSIONS AND RECOMMEDDATIONS

6.1 Conclusions

1- The elevation of serum Troponin high-sensitive concentration in patients more than healthy controls referee that cardiac Troponin high-sensitive considered the golden biomarker for diagnosis of acute myocardial infarction.
2- The increased the serum of Ischemic Modified Albumin in patients suffer from acute myocardial infarction more in compare to healthy controls indicate that IMA can be considered a potent biomarker in compare with troponin high-sensitive for diagnosis acute myocardial infarction and other cardiac ischemic cases.
3- Area Under the Curve:0.767 (95% of CI, 0.673--0.860), and the selected diagnostic cut-off of IMA was > 60 ng/ml analyzed for their clinical sensitivity (76.45%), specificity (81.88%) positive predictive value (88.33 ng\ml) and negative predictive value (33.33 ng\ml), which is considered as a good diagnostic marker for AMI.
4- The positive correlation between serum concentration for both Ischemic Modified Albumin and Troponin high-sensitive in patients with AMI indicate that utilize these biomarkers together lead to increase the sensitivity of prognosis and definitive diagnosis of acute myocardial infarction.

6.2 Recommendations

1- Investigate the serum level of Ischemic Modified Albumin with other markers that use in early diagnosis of AMI and compare it is serum concentration to evaluate the sensitivity and specificity of IMA cut-off value with these markers cut-off value in diagnosis and prognosis patients with AMI.
2- Investigate the concentration of IMA with Troponin before and after therapy of AMI and compare between these two measurements in order to use the IMA and Troponin as a predictive value to the regression of ischemia and chest pain in patients with AMI.
3- Further research need to investigate the IMA role in diagnosis others diseases such as placental histopathological change and early diagnosis of acute appendicitis as well as in tumors development.

REFERENCES

Aladağ, N., Asoğlu, R., Ozdemir, M., Asoğlu, E., Derin, A., Demir, C., & Demir, H. 2021. Oxidants and antioxidants in myocardial infarction (MI): Investigation of ischemia modified albumin, malondialdehyde, superoxide dismutase and catalase in individuals diagnosed with ST elevated myocardial infarction (STEMI) and non-STEMI (NSTEMI). Journal of Medical Biochemistry, 40(3), 286–294.

Anwar, A., Khan, H. A., Hafeez, S., & Firdous, K. 2016. A comparative study of creatine Kinase-MB and troponin levels among diabetic and non diabetic patients with acute MI. Pakistan Journal of Medical and Health Sciences, 10(1), 296–297.

Apple, F. S., Collinson, P. O., & IFCC Task Force on Clinical Applications of Cardiac Biomarkers. 2012. Analytical characteristics of high-sensitivity cardiac troponin assays. Clinical Chemistry, 58(1), 54–61.

Arıcan, S., Dertli, R., Baktik, S., Hacibeyoglu, G., Erol, A., Ulukaya, S. O., Goger, E., & Erel, Ö. 2020. The effect of low dose ionizing radiation exposure on dynamic thiol-disulfide homeostasis and ischemia modified albumin levels: an observational study. Brazilian Journal of Anesthesiology (English Edition), 70(3), 233–239.

Author, C. 2015. Study of Significance of Estimation of Lipid Profile in Patient.

Bar-Or, D., Winkler, J. V, Vanbenthuysen, K., Harris, L., Lau, E., & Hetzel, F. W. 2001. Reduced albumin-cobalt binding with transient myocardial ischemia after elective percutaneous transluminal coronary angioplasty: a preliminary comparison to creatine kinase-MB, myoglobin, and troponin I. American Heart Journal, 141(6), 985–991.

Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., de Ferranti, S. D., Floyd, J., Fornage, M., Gillespie, C., Isasi, C. R., Jiménez, M. C., Jordan, L. C., Judd, S. E., Lackland, D., Lichtman, J. H., Lisabeth, L., Liu, S., Longenecker, C. T., … American Heart Association Statistics Committee and Stroke Statistics Subcommittee. 2017. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation, 135(10), e146–e603.

Bhagavan, N. V, Lai, E. M., Rios, P. A., Yang, J., Ortega-Lopez, A. M., Shinoda, H., Honda, S. A. A., Rios, C. N., Sugiyama, C. E., & Ha, C.-E. 2003. Evaluation of

human serum albumin cobalt binding assay for the assessment of myocardial ischemia and myocardial infarction. Clinical Chemistry, 49(4), 581–585.

Bhagwat, K., & Padmini, H. 2014. Co-relation between lactate dehydrogenase and creatine kinase-MB in acute myocardial infarction. International Journal of Advanced Research in Pharmaceutical & Bio Sciences, 4, 1+. https://link.gale.com/apps/doc/A404494988/HRCA?u=anon~bf3bd5cb&sid=googleScholar&xid=292573b2

Bhakthavatsala Reddy, C., Cyriac, C., & Desle, H. B. 2014. Role of "Ischemia Modified Albumin" (IMA) in acute coronary syndromes. Indian Heart Journal, 66(6), 656–662.

Biswas, S., Bhattacharyya, S., Ghosh, C., Banerjee, S., Mukherjee, K., & Basu, A. 2014. ASSESSMENT OF OXIDATIVE STRESS AND ANTIOXIDANT STATUS AMONG NEWBORNS IN RELATION TO MODE OF DELIVERY. International Journal of Current Research and Review, 6, 65–73.

Blindauer, C. A., Khazaipoul, S., Yu, R., & Stewart, A. J. 2016. Fatty Acid-Mediated Inhibition of Metal Binding to the Multi-Metal Site on Serum Albumin: Implications for Cardiovascular Disease. Current Topics in Medicinal Chemistry, 16(27), 3021–3032.

Body, R. 2018. Acute coronary syndromes diagnosis, version 2.0: Tomorrow's approach to diagnosing acute coronary syndromes? Turkish Journal of Emergency Medicine, 18(3), 94–99.

C., D. 2013. Biomarkers of Cardiac Ischemia. In Ischemic Heart Disease. InTech.

Chacko, S., Haseeb, S., Glover, B. M., Wallbridge, D., & Harper, A. (2018). The role of biomarkers in the diagnosis and risk stratification of acute coronary syndrome. Future Science OA, 4(1), FSO251.

Cho, Y., Mirzapour-Kouhdasht, A., Yun, H., Park, J. H., Min, H. J., & Lee, C. W. 2022. Development of Cobalt-Binding Peptide Chelate from Human Serum Albumin: Cobalt-Binding Properties and Stability. International Journal of Molecular Sciences, 23(2).

CL, Z., YM, J., X, G., & X, W. 2008. Clinical value of h FABP, hs CRP, cTnT examination to diagnose acute myocar dial infarction. J Dalian Med Univ, 30, 170–172.

Dahiya, K., Kumar, R., Dhankhar, R., Verma, M., Kumari, A., Roy, P. S., Dalal, D., Singh Ghalaut, V., & Chugh, K. 2018. Status of Ischemia Modified Albumin in Athletes Before and After Moderate Exercise. The Open Biomarkers Journal, 8(1), 42–46.

Das, B., & Mishra, T. K. 2017. Cardiac troponins: Current status. Journal of Indian College of Cardiology, 7(1), 1–5.

DeFilippis, E. M., Singh, A., Divakaran, S., Gupta, A., Collins, B. L., Biery, D., Qamar, A., Fatima, A., Ramsis, M., Pipilas, D., Rajabi, R., Eng, M., Hainer, J., Klein, J., Januzzi, J. L., Nasir, K., Di Carli, M. F., Bhatt, D. L., & Blankstein, R. 2018. Cocaine and Marijuana Use Among Young Adults With Myocardial Infarction. Journal of the American College of Cardiology, 71(22), 2540–2551.

Ding, M., Li, M., & Yang, H. 2021. Clinical diagnostic value of combined detection of IMA, D-D and MCP-1 in acute myocardial infarction. Experimental and Therapeutic Medicine, 21(5), 457.

Ertekin, B., Koçak, S., Dündar, Z. D., Girişgin, S., Cander, B., Gül, M., Döşeyici, S., Mehmetoğlu, İ., & Şahin, T. K. 2013. Diagnostic value of ischemia-modified albumin in acute coronary syndrome and acute ischemic stroke. Pakistan Journal of Medical Sciences, 29(4).

Gupta, A., Wang, Y., Spertus, J. A., Geda, M., Lorenze, N., Nkonde-Price, C., D'Onofrio, G., Lichtman, J. H., & Krumholz, H. M. 2014. Trends in acute myocardial infarction in young patients and differences by sex and race, 2001 to 2010. Journal of the American College of Cardiology, 64(4), 337–345.

Gupta, T., Kolte, D., Khera, S., Agarwal, N., Villablanca, P. A., Goel, K., Patel, K., Aronow, W. S., Wiley, J., Bortnick, A. E., Aronow, H. D., Abbott, J. D., Pyo, R. T., Panza, J. A., Menegus, M. A., Rihal, C. S., Fonarow, G. C., Garcia, M. J., & Bhatt, D. L. 2018. Contemporary Sex-Based Differences by Age in Presenting Characteristics, Use of an Early Invasive Strategy, and Inhospital Mortality in Patients With Non-ST-Segment-Elevation Myocardial Infarction in the United States. Circulation. Cardiovascular Interventions, 11(1), e005735.

Haasenritter, J., Stanze, D., Widera, G., Wilimzig, C., Abu Hani, M., Sonnichsen, A. C., Bosner, S., Rochon, J., & Donner-Banzhoff, N. 2012. Does the patient with chest pain have a coronary heart disease? Diagnostic value of single symptoms and

signs--a meta-analysis. Croatian Medical Journal, 53(5), 432–441.

Ibanez, B., James, S., Agewall, S., Antunes, M. J., Bucciarelli-Ducci, C., Bueno, H., Caforio, A. L. P., Crea, F., Goudevenos, J. A., Halvorsen, S., Hindricks, G., Kastrati, A., Lenzen, M. J., Prescott, E., Roffi, M., Valgimigli, M., Varenhorst, C., Vranckx, P., Widimský, P., & ESC Scientific Document Group. 2018. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Socie. European Heart Journal, 39(2), 119–177.

Jena, I., Nayak, S., Behera, S., Singh, B., Ray, S., Jena, D., Singh, S., & Sahoo, S. 2017. Evaluation of ischemia-modified albumin, oxidative stress, and antioxidant status in acute ischemic stroke patients. Journal of Natural Science, Biology and Medicine, 8, 110. https://link.gale.com/apps/doc/A478132222/HRCA?u=anon~81e7793&sid=googleScholar&xid=cc608716

Kayani, W. T., & Ballantyne, C. M. 2018. Improving Outcomes After Myocardial Infarction in the US Population. Journal of the American Heart Association, 7(4).

Leblanc, Y., Bihoreau, N., & Chevreux, G. 2018. Characterization of Human Serum Albumin isoforms by ion exchange chromatography coupled on-line to native mass spectrometry. Journal of Chromatography. B, Analytical Technologies in the Biomedical and Life Sciences, 1095, 87–93.

Lee, P., & Wu, X. 2015. Review: modifications of human serum albumin and their binding effect. Current Pharmaceutical Design, 21(14), 1862–1865.

Leifheit-Limson, E. C., D'Onofrio, G., Daneshvar, M., Geda, M., Bueno, H., Spertus, J. A., Krumholz, H. M., & Lichtman, J. H. 2015. Sex Differences in Cardiac Risk Factors, Perceived Risk, and Health Care Provider Discussion of Risk and Risk Modification Among Young Patients With Acute Myocardial Infarction: The VIRGO Study. Journal of the American College of Cardiology, 66(18), 1949–1957.

Libby, P. 2013. Mechanisms of acute coronary syndromes and their implications for therapy. The New England Journal of Medicine, 368(21), 2004–2013.

Lim, S. S., Vos, T., Flaxman, A. D., Danaei, G., Shibuya, K., Adair-Rohani, H., Amann,

M., Anderson, H. R., Andrews, K. G., Aryee, M., Atkinson, C., Bacchus, L. J., Bahalim, A. N., Balakrishnan, K., Balmes, J., Barker-Collo, S., Baxter, A., Bell, M. L., Blore, J. D., … Memish, Z. A. 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet (London, England), 380(9859), 2224–2260.

Lu, J., Stewart, A. J., Sadler, P. J., Pinheiro, T. J. T., & Blindauer, C. A. 2012. Allosteric inhibition of cobalt binding to albumin by fatty acids: implications for the detection of myocardial ischemia. Journal of Medicinal Chemistry, 55(9), 4425–4430.

Manikkan, A. T. 2018. Elevated Troponin I Levels in Diabetic Ketoacidosis Without Obstructive Coronary Artery Disease. Journal of the Endocrine Society, 2(9), 1020–1023.

Meenakshisundaram, R., Senthilkumaran, S., Thirumalaikolundusubramanian, P., Joy, M., Jena, N. N., Vadivelu, R., Ayyasamy, S., & Chandrasekaran, V. P. 2020. Status of Acute Myocardial Infarction in Southern India During COVID-19 Lockdown: A Multicentric Study. Mayo Clinic Proceedings. Innovations, Quality & Outcomes, 4(5), 506–510.

Mehta, M. D., Marwah, S. A., Ghosh, S., Shah, H. N., Trivedi, A. P., & Haridas, N. 2015. A synergistic role of ischemia modified albumin and high-sensitivity troponin T in the early diagnosis of acute coronary syndrome. Journal of Family Medicine and Primary Care, 4(4), 570–575.

Mendis, S., Puska, P., Norrving, B., Organization, W. H., Federation, W. H., & Organization, W. S. 2011. Global atlas on cardiovascular disease prevention and control / edited by: Shanthi Mendis ... [et al.] (p. Published by the World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization). World Health Organization.

Menon, B., Ramalingam, K., & Krishna, V. 2018. Study of Ischemia Modified Albumin as a Biomarker in Acute Ischaemic Stroke. Annals of Neurosciences, 25(4), 187–190.

Mirzaii-Dizgah, I., & Riahi, E. 2013. Salivary troponin I as an indicator of myocardial infarction. The Indian Journal of Medical Research, 138(6), 861–865.

Mishra, B., Pandey, S., Niraula, S. R., Rai, B. K., Karki, P., Baral, N., & Lamsal, M. 2018. Utility of Ischemia Modified Albumin as an Early Marker for Diagnosis of Acute Coronary Syndrome. Journal of Nepal Health Research Council, 16(1), 16–21. http://www.ncbi.nlm.nih.gov/pubmed/29717283

Morrow, D. A., Cannon, C. P., Jesse, R. L., Newby, L. K., Ravkilde, J., Storrow, A. B., Wu, A. H. B., Christenson, R. H., Apple, F. S., Francis, G., Tang, W., & National Academy of Clinical Biochemistry. 2007. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. Clinical Chemistry, 53(4), 552–574.

Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., Das, S. R., de Ferranti, S., Després, J.-P., Fullerton, H. J., Howard, V. J., Huffman, M. D., Isasi, C. R., Jiménez, M. C., Judd, S. E., Kissela, B. M., Lichtman, J. H., Lisabeth, L. D., Liu, S., … Turner, M. B. 2016. Heart Disease and Stroke Statistics—2016 Update. Circulation, 133(4).

Mueller, M., Vafaie, M., Biener, M., Giannitsis, E., & Katus, H. A. 2013. Cardiac troponin T: from diagnosis of myocardial infarction to cardiovascular risk prediction. Circulation Journal : Official Journal of the Japanese Circulation Society, 77(7), 1653–1661. http://www.ncbi.nlm.nih.gov/pubmed/23803255

Murray, C. J. L., Barber, R. M., Foreman, K. J., Abbasoglu Ozgoren, A., Abd-Allah, F., Abera, S. F., Aboyans, V., Abraham, J. P., Abubakar, I., Abu-Raddad, L. J., Abu-Rmeileh, N. M., Achoki, T., Ackerman, I. N., Ademi, Z., Adou, A. K., Adsuar, J. C., Afshin, A., Agardh, E. E., Alam, S. S., … Vos, T. 2015. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. Lancet (London, England), 386(10009), 2145–2191.

MYTHILI, S., & MALATHI, N. 2015. Diagnostic markers of acute myocardial infarction. Biomedical Reports, 3(6), 743–748. https://doi.org/10.3892/br.2015.500

NS, T., SG, G., & WJ, C. 2016. Efficacy of early invasive management after fibrinolysis for ST-segment elevation myocardial infarction in relation to initial troponin status. Can J Cardiol, 32, 1221.e11–1221.e18.

Pan, Q., Qin, X., Ma, S., Wang, H., Cheng, K., Song, X., Gao, H., Wang, Q., Tao, R.,

Wang, Y., Li, X., Xiong, L., & Cao, F. 2014. Myocardial protective effect of extracellular superoxide dismutase gene modified bone marrow mesenchymal stromal cells on infarcted mice hearts. Theranostics, 4(5), 475–486.

Panjwani, J. P., Naqvi, F., Siddiqui, I. A., Fawwad, A., & Zakir, U. 2019. ROLE OF ISCHEMIA MODIFIED ALBUMIN AND TOTAL OXIDATIVE STRESS AS A BIOMARKER IN THE DIAGNOSIS OF MYOCARDIAL INFARCTION IN PAKISTANI POPULATION. 16(3), 667–671.

Parsanathan, R., & Jain, S. K. 2020. Novel Invasive and Noninvasive Cardiac-Specific Biomarkers in Obesity and Cardiovascular Diseases. Metabolic Syndrome and Related Disorders, 18(1), 10–30.

Patil, S. M., Bankar, M., Padalkar, R., & Phatak, A. 2017. Comparative Study of Potential Diagnostic Biomarkers in Myocardial Infarction with Survival and Myocardial Infarction without Survival. Indian Journal of Medical Biochemistry, 21(2), 106–111.

Patil, S. M., Banker, M. P., Padalkar, R. K., Pathak, A. P., Bhagat, S. S., Ghone, R. A., & Phatake, A. S. 2013. The clinical assessment of ischaemia modified albumin and troponin I in the early diagnosis of the acute coronary syndrome. Journal of Clinical and Diagnostic Research : JCDR, 7(5), 804–808.

Rathore, V. 2018. Risk Factors of Acute Myocardial Infarction: A Review. Eurasian Journal of Medical Investigation. https://doi.org/10.14744/ejmi.2018.76486

Rathore, V., Singh, N., Rastogi, P., Mahat, R. K., Mishra, M. K., & Shrivastava, R. 2017. Lipid profile and its correlation with C-reactive protein in patients of acute myocardial infarction. International Journal of Research in Medical Sciences, 5(5), 2182.

Shah, B., Bangalore, S., Gianos, E., Liang, L., Peacock, W. F., Fonarow, G. C., Laskey, W. K., Hernandez, A. F., & Bhatt, D. L. 2014. Temporal trends in clinical characteristics of patients without known cardiovascular disease with a first episode of myocardial infarction. American Heart Journal, 167(4), 480-488.e1.

Shevtsova, A., Gordiienko, I., Tkachenko, V., & Ushakova, G. 2021. Ischemia-Modified Albumin: Origins and Clinical Implications. Disease Markers, 2021, 1–18.

Sokołowska, M., Wszelaka-Rylik, M., Poznański, J., & Bal, W. 2009. Spectroscopic

and thermodynamic determination of three distinct binding sites for Co(II) ions in human serum albumin. Journal of Inorganic Biochemistry, 103(7), 1005–1013.

Sygitowicz, G., Janas, J., Białek, S., Pręgowski, J., Pera, Ł., & Sitkiewicz, D. 2013. Ischaemia modified albumin in patients with acute coronary syndrome and negative cardiac troponin I. Scandinavian Journal of Clinical and Laboratory Investigation, 73(2), 130–134.

Thygesen, K., Alpert, J. S., Jaffe, A. S., Simoons, M. L., Chaitman, B. R., White, H. D., Joint ESC/ACCF/AHA/WHF Task Force for Universal Definition of Myocardial Infarction, Authors/Task Force Members Chairpersons, Thygesen, K., Alpert, J. S., White, H. D., Biomarker Subcommittee, Jaffe, A. S., Katus, H. A., Apple, F. S., Lindahl, B., Morrow, D. A., ECG Subcommittee, Chaitman, B. R., … Wagner, D. R. 2012. Third universal definition of myocardial infarction. Journal of the American College of Cardiology, 60(16), 1581–1598.

Thygesen, Kristian, Alpert, J. S., Jaffe, A. S., Simoons, M. L., Chaitman, B. R., & White, H. D. 2012. Third Universal Definition of Myocardial Infarction. Circulation, 126(16), 2020–2035.

Townsend, N., Nichols, M., Scarborough, P., & Rayner, M. 2015. Cardiovascular disease in Europe--epidemiological update 2015. European Heart Journal, 36(40), 2696–2705.

Vijaya, D., & Gayathri, B. 2014. Role of Ischemia Modified Albumin in the Early Diagnosis of Acute Myocardial Infarction. 353–358.

Wang, J. J., Pahlm, O., Warren, J. W., Sapp, J. L., & Horáček, B. M. 2018. Criteria for ECG detection of acute myocardial ischemia: Sensitivity versus specificity. Journal of Electrocardiology, 51(6S), S12–S17.

Wang, P., Zhu, Z. L., Zhu, N., Yu, H., Yue, Q., Wang, X. L., Feng, C. M., Wang, C. L., & Zhang, G. H. 2017. [Application of Ischemia Modified Albumin for Acute Ischemic Heart Disease in Forensic Science]. Fa Yi Xue Za Zhi, 33(5), 493–496.

Watanabe, H., Imafuku, T., Otagiri, M., & Maruyama, T. 2017. Clinical Implications Associated With the Posttranslational Modification-Induced Functional Impairment of Albumin in Oxidative Stress-Related Diseases. Journal of Pharmaceutical Sciences, 106(9), 2195–2203.

Yusuf, S., Rangarajan, S., Teo, K., Islam, S., Li, W., Liu, L., Bo, J., Lou, Q., Lu, F.,

Liu, T., Yu, L., Zhang, S., Mony, P., Swaminathan, S., Mohan, V., Gupta, R., Kumar, R., Vijayakumar, K., Lear, S., … PURE Investigators. 2014. Cardiovascular risk and events in 17 low-, middle-, and high-income countries. The New England Journal of Medicine, 371(9), 818–827.

CURRICULUM VITAE

Personal Information

Name and Surname : Ali Mohammed Abduljabbar NOORI

Education

MSc	Çankırı Karatekin University Graduate School of Natural and Applied Sciences Department of Chemistry	2022 -Present
Undergraduate	University of karbala College of Science Department of Chemistry	2009-2010