Diagnostic Value of "Ischemia Modified Albumin" in Early Detection of Myocardial Injury in Acute Coronary Syndromes

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

((* قالَ رَبِّ اشْرَحْ لِي صَدْرِي * وَيَسِّرْ لِي أَمْرِي *
وَاحْلُلْ عُقْدَةً مِنْ لِسَانِي *يَفْقَهُوا قَوْلِي))

سورة طه

صدَق اللّه العَظِيم

You can only go as far as you push

Dedication

Dedicate this simple effort, to my country (Iraq) , which is still bleeding so far.....,and still beats in my heart and soul.....

And dedicate this work to Arab Republic of Egypt, which was my second homeland, and did not feel alienated……...

Dedicate this work to my father who taught me everything ... and to my mother who bore all the odds of me.... and to my brothers and sisters for their support .... and to the Minister of Higher Education and Scientific Research Mr. Ali Aladeeb ,and to the Deputy Minister of Health Dr. Khames Al-Dulaimy and to the Director of Health Karkh dr.Jalil Al-shammary, and Professor dr.Salh Aljumaily for all help and support to finish my study..... and to the College of Medicine in University of Sulaymaniyah and to all my friends who gave me all the Walt……

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ABSTRACT

- ***BACKROUND:*** Acute Coronary Syndromes(ACS) represent a continuum of disease ranging from unstable angina, associated with reversible myocardial cell injury, to ST-segment elevation of myocardial infarction, associated with irreversible myocardial necrosis. Ischemia-Modified Albumin (IMA) as a sensitive biomarker of cardiac ischemia. IMA is a relatively new biomarker in the identification of myocardial ischemia in advance or in the absence of myocardial necrosis.

- ***Objective:*** This study was designed to assess sensitivity & specifity of "Ischemia Modified Albumin", a new biochemical marker of early detection of myocardial injury in acute coronary syndromes.

- ***METHODS:*** This study included 76 patients , who presented to the emergency department (ED) with acute chest pain within 3h of pain onset, between March and September 2013 , and 10 people(matched for age, gender and risk factors) as control group. The blood samples obtained from patients on admission ,and repeated 4-6 hours after admission to the coronary care unit(CCU) for those subsequently diagnosed with ACS by history, clinical examination , electro-cardiogram (ECG) and cardiac markers. IMA level was detected by Albumin-Cobalt Binding (ACB) test, and characteristic (ROC) curve was performed to detect the cut off value of IMA with best sensitivity, and the specificity in diagnosis of ACS.

RESULTS: There was a higher IMA level in paients with ACS (5.27 ±4) compared to control group (1.7 ± 0.8). The ROC curve showed that IMA level could be used to detect cases of myocardial injury in acute coronary syndromes at a level of 3.25u/ml, with 89.5% sensitivity and 100% specificity and 82% accuracy. On admission, there was a highly significant difference between IMA and troponin -I(Tn I) test regarding sensitivity in ST-elevation of myocardial infarction (STEMI=88.5 % vs.30.7%, p=0.001) and non ST-elevation of myocardial infarction (NSTEMI=94.4% vs. 16.7%,p=0.001) patients ,and also shown there was no significant difference between IMA on admision and cTnI at 4-6 hours after admission in STEMI (88.5% vs. 100%, p=0.633) and NSTEMI (94.4% vs. 100%, p= 0.829) patients ,and when comparing these changes in cTn I at 4-6 hours of admission to IMA results on admission revealed highly significant difference in favour of IMA in detecting myocardial ischemia in patients with unstable angina (UA=87.5% vs. 0%, p 0,001),but both (IMA and TnI)had 100% specificity.

- ***CONCLUSION:*** The IMA is highly sensitive for the early diagnosis of ACS in patients presenting to ED within 3 hours of pain onset, compared to other cardiac markers as Troponin I. IMA may be a useful biomarker for the identification of UA patients presenting with typical acute chest pain and/or abnormal electrocardiograms with negative Tn I.

- ***KEY WORDS:*** **Acute coronary syndromes** , **Cardiac biomarkers**, **Ischemia-Modified Albumin** .

CONTENTS

List of Abbreviations

ACC	: American College of Cardiology
ACS	: Acute coronary syndrome
AHA	: American Heart Association
AST	: Aspartate transaminase
BCS	: British Cardiac Society
BNP	: B-type natriuretic peptide
CABG	: Coronary artery bypass grafting
CAD	: Coronary artery disease
Ck	: Creatine Kinase
CHD	: Coronary heart disease
CMR	: Cardiac magnetic resonance
CRP	: C-reactive protein
CVD	: Cardiovascular disease
DM	: Diabetes mellitus
ECG	: Electrocardiogram
ED	: Emergency department
EMS	: Emergency medical service
ESC	: European Society of Cardiology
EU	: European Union
HTN	: Hypertension
IMA	: Ischemia-modified albumin
LBB	: Left bundle branch block
LDL	: Low density lipoproteins
LDH	: Lactate dehydrogenase
Mb	: Myoglobin
MI	: Myocardial infarction
MPO	: Myeloperoxidase
NPV	: Negative predictive value
NSTEMI	: Non ST segment elevation of myocardial infarction
PAD	: Peripheral arterial disease
PAPP-A	: Pregnancy-associated plasma protein
PCI	: Percutaneous coronary intervention

PIGF	: Placental growth factor
PPV	: Positive predictive value
STEMI	: ST segment elevation myocardial infarction.
RV	: Right ventricular.
TnI	: Troponin I.
TnT	: Troponin T.
UA	: Unstable Anginae.
URL	: Upper reference limit.
WHF	: World Health Federation.
WHO	: World health Organization.

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INTRODUCTION

Acute coronary syndromes (ACS) are due to the rupture or erosion of atheromatous plaques[1]. ACS represent a continuum of disease ranging from unstable angina, associated with reversible myocardial cell injury, to ST-segment elevation myocardial infarction, associated with irreversible myocardial necrosis[2][3]. Early identification and confirmation of ACS in patients presenting with acute chest pain in the emergency department (ED) are essential for correct medical management of the patients [4] [5].

Ischemia-Modified Albumin (IMA) is a novel marker of cardiac ischemia when measured by the Albumin Cobalt Binding (ACB) test[6]. IMA is a sensitive biomarker for the identification of myocardial ischemia ,and can be used to detect cardiac ischemia in patients with chest pain [7]. In non-ischemic physiological conditions, plasma cobalt are bounded to albumin, with minimal circulating free cobalt. In cases of Ischemia - Albumin undergoes a conformational change and loses its ability to bind transitional metals (copper or cobalt). IMA can be used to assess the proportion of modified albumin in ischemia; it is valuable for the diagnosis of myocardial ischemia in patients presenting with chest pain at the ED [6][7].

The usefulness of the conventional biomarkers of myocardial necrosis for the confident exclusion of the diagnosis of myocardial ischemia at the time of admission remains limited. Markers able to identify patients with myocardial ischemia without infarction might play an important role in the clinical setting since among those patients with a

definite ACS, early treatment may reduce the extent of myocardial injury, and thus rapid diagnosis and initiation of therapy is a central tenet of management [8]. In addition, given the increasing array of treatments for the heterogeneous population of patients admitted with ACS, effective risk stratification and targeting of therapy have become a focus of contemporary management of clinically evident myocardial ischemia[9][10].

AIM OF THE WORK

- The aim of this study is to asses the diagnostic value of Ischemia Modified Albumin as a new marker of myocardial injury.
- To compare IMA sensitivity & specifity to cardiac Troponin-I for early detection of myocardial ischemia.

CHAPTER I

Acute Coronary Syndrome

❖ Definition of Acute Coronary Syndrome (ACS):

Group of clinical syndromes compatible with acute myocardial ischemia" ,and refers to any group of symptoms attributed to obstruction of the coronary arteries [11] or ACS is the clinical manifestation of the critical phase of coronary artery disease [12]. Acute coronary syndrome usually occurs as a result of one of three problems includes: [13]

- NSTEMI (non ST elevation, abnormal biomarkers),
- STEMI (ST elevation, abnormal biomarkers),
- Unstable angina (no ST elevation, normal biomarkers), unstable angina includes: angina at rest, new angina, increasing angina, see figure (1.1)[12].

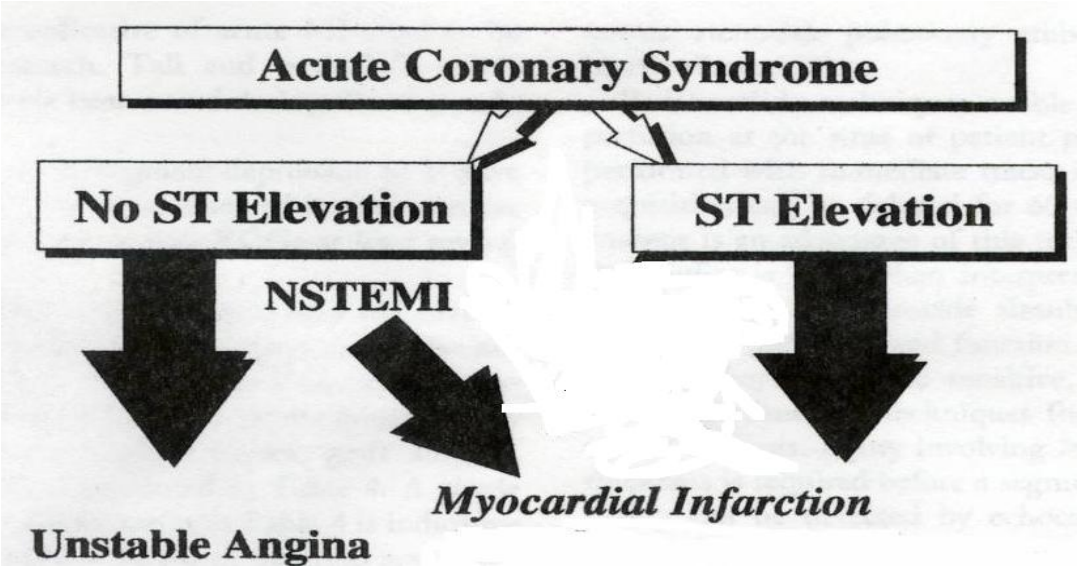

Figure 1.1: Acute Coronary Syndrome.[13]

• **Physiologic definition:** Plaque ruptures leading to thrombus formation, leading to partial or complete blockage of a coronary artery with or without myocyte death. The definition of acute coronary syndrome