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Original Research Article

EVALUATION OF SERUM LEVEL OF ISCHEMIA MODIFIED ALBUMIN IN A ACUTE CORONARY SYNDROME

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ABSTRACT

Background: The leading cause of death and reduction in years of life with a handicap globally is ischemic heart disease. The mortality rate is greatly decreased when patients with acute myocardial infarction are identified and treated promptly. Cardiovascular biomarkers do play a significant role in the early diagnosis and treatment of patients with ACS, in addition to ECG and other clinical characteristics. Serum Ischemia Modified Albumin (IMA) should be measured within 6 hours of the onset of chest pain, and its results should be correlated with LDH, CK-MB, TGL, T-CHOL, HDL, LDL, and VLDL.

Materials and Methods: The INDEX Medical College and Hospital Department of Biochemistry has undertaken this study. One hundred patients with acute coronary syndrome symptoms were included as subjects in the causality study. Their ECG results were correlated and were presented within six hours of the onset of discomfort. One hundred controls, matched for age and sex, served as the control group. Lipid profile, CKMB, LDH, SGOT, and IMA (ACB test) estimation were performed on blood samples.

Results: The control and study groups' respective mean IMA values were 36.98±15.7 and 114.87±16.63. Ischemia altered albumin's substantial association with CK-MB, lipid profile, and LDH was demonstrated by Pearson's correlation.

Conclusion: The current study's results support earlier research that found the Albumin Cobalt colorimetric assay can discriminate myocardial ischemia patients from non-ischemic patients ($p<0.001$). The IMA assay offers a quantitative, precise laboratory method for determining the occurrence of an ischemic myocardial event, which includes different kinds of angina. Acute Coronary Syndrome is diagnosed in individuals with continuous myocardial ischemia in the emergency department by measuring modified albumin levels. The diagnostic sensitivity of the procedure is increased by measuring IMA in addition to ECG and other indicators.

Keywords: Acute coronary syndrome, IMA, LDH, CPKMB & SGOT.

INTRODUCTION

The term "acute coronary syndrome" (ACS) refers to a broad range of clinical manifestations that may indicate myocardial ischemia.[1] A reduction in the oxygen and nutrition supplied to the heart myocytes as a result of insufficient blood perfusion is known as myocardial ischemia. Cell death brought on by extended ischemia is referred to as myocardial infarction.[2]

The leading cause of death and reduction in years of life with a handicap globally is ischemic heart disease.[3] Furthermore, low- and middle-income nations bear a sizable share of this load. The elements listed below highlight how crucial it is to create fresh approaches to diagnosis and treatment for this illness: a) Epidemiology of the disease b) Economical, social

and legal liabilities for clinicians & c) Lethal consequences of the disease. Nevertheless, when individuals with acute myocardial infarction are rapidly diagnosed and treated, the death rate is significantly reduced. Extensive physical examinations, detailed histories, and ECG findings are helpful in categorizing individuals, but they don't always appear to be enough for obtaining an early, definitive diagnosis.[4,5] Along with ECG and other clinical features, cardiovascular biomarkers are important in the early diagnosis and management of individuals with ACS. The term "biomarker," short for "biological marker," describes a characteristic material that can be measured objectively in serum or any other bodily fluid and recognized as a pharmacological response to therapeutic interventions, an important component of normal biological processes, or a sign of pathogenic processes.[6] While a single biomarker may serve this purpose in certain disorders, such coronary artery disease (CAD), the hunt for biomarkers is an ongoing effort in complex diseases like CAD.[7] When the coronary artery becomes blocked due to the onset of atherosclerotic plaque breakdown, myocardial perfusion is inhibited and platelet aggregation and thrombus formation are encouraged. Data from recent studies highlight that the reason of poor perfusion is the rupture of an unstable, fragile plaque and the ensuing inflammatory changes, rather than decreased blood flow as a result of the arteries narrowing due to the thickness of the manufactured plaque.[8] The electrical stability and contractility of the cardiac cells depend on oxygen and adenosine 5β-triphophate (ATP). As the myocardial perfusion gradually decreases, the following phases or changes take place. a) Ischemic phase: Both aerobic and anerobic metabolism occur in the cells during this period. b) Injury phase: Anaerobic metabolism also greatly decreases when aerobic metabolism fails due to a persistent reduction in perfusion. And c) Necrosis of the myocardial cells: As soon as perfusion is not restored in roughly 20 minutes, myocardial necrosis with irreparable damage continues.[9] Nowadays, many heart biomarkers are employed in clinical practice, including myoglobin, troponins, natriuretic peptides, creatine kinase (CK) and its component CK-MB, and others. These biomarkers point to cardiac necrosis, which happens after the pathogenesis of ACS. Recently, there has been an effort to provide an early assessment and risk stratification by indexing components of processes upstream from necrosis under the term "biomarkers." These components include those released during ischemia, elements of plaque destabilization and rupture, factors of thrombosis, molecules of inflammation, and acute phase reactants. In addition to being sensitive, the ideal biomarker of myocardial injury should be accurately measurable, cardiac-specific, and precise. These traits will influence treatment and improve patient outcomes. Ischemia modified albumin (IMA) has been approved by the US Food and Drug Administration as a biomarker for acute ischemia. Because albumin's N terminus is damaged when exposed to ischemic conditions, it cannot bind metals and can therefore be assessed using the albumin cobalt binding test. IMA levels increase 10 minutes after ischemia starts, indicating that IMA may be utilized to identify acute ischemia in its early stages, before necrosis appears. The goal of this research is to measure the serum levels of Ischemia Modified Albumin in paitents with ACS presenting within 6 hours of onset of chest pain.

MATERIAL AND METHODS

The study was conduct in the INDEX Medical College and Hospital. 100 patients with symptoms of acute coronary syndrome presented within 6 hours of onset of pain in the causality with ECG findings correlate and will take as subjects. 100 age and sex matched healthy persons were taken as control group.

Inclusion Criteria

- Patients admitted with complaint of chest pain within 6 hours of onset.
- Electro cardio graphic findings showing abnormal ST-T wave changes (ST segment elevation or depression or deep symmetrical T wave inversion).

Exclusion Criteria

- Presence of renal diseases.
- Presence of cirrhosis.
- Presence of stroke, skeletal muscle injury, malignancy, trauma.
- Critically ill patients.
- Any infectious diseases.
- Serum albumin <2gms/dl,
- Serum creatinine >3mgs/dl.

Blood Collection

Prior to the proceedings, informed consent were sought from each patient and control group. As soon as the participants meet the inclusion criteria and are admitted, a vein puncture will be used to obtain five milliliters of blood under strict aseptic precaution. The samples were separated into serum using a centrifuge. After taking a portion of the sample, the levels of albumin, creatinine, LDH, and CK-MB will be promptly analyzed. The remaining portion of the sample will be kept at -20o C for Ischemia Modified Albumin analysis. During their hospital stay, all individuals will have samples taken after a 12- to 14-hour fast. The samples will be analyzed for total cholesterol, triacylglycerol, and high density lipoprotein.

RESULTS

The current research work was carried out in the Department of Biochemistry, INDEX Medical College and Hospital, Indore, MP with the collaboration with Department of cardiology.

This study covered 200 patients in total. Two sets of study participants were used: group A (Control) consisted of healthy persons, group B (Acute

coronary syndrome) of ACS patients. In both groups, the distribution of participants by age is shown in Table 1.

The mean age of the study group was having higher 52.26±5.23 years and in 52.15±9.721 years for healthy controls whereas the mean BMI of study group was having higher 26.84±4.02 kg/m2 and in 25.38±2.59 kg/m2 for healthy controls. Similarly, the mean SBP of the T study group was significantly higher 147.92±14.2 as compared to 127.9 ± 8.49 healthy controls. Similarly, mean DBP of the study group was significantly higher 93.92±7.64 as compared to 79.16±4.37 healthy controls. [Table 2]

The mean serum random blood glucose was significantly higher (139.38±30.41) in study group as compared to controls (110.35±8.49) (P<0.01) in table-3.

All serum lipid and lipoproteins were significantly higher in study group as compared to healthy controls except HDL-c which is significantly lower in study group ad compared to healthy controls. Mean level of cholesterol value in study group was significantly higher than the mean serum of healthy controls (P<0.01). The mean level of triglycerides in study group was significantly (P<0.01) increased compared to healthy controls. The mean level of LDL-c & VLDL-c in study group was statistically significant (P<0.001) higher than the mean value of healthy controls. Mean level of serum HDL cholesterol was significantly (P<0.02) lower in study group as compared to the mean value of healthy controls. [Table 4] Also shows the kidney markers like urea & creatinine were significantly higher in study group as compared to healthy controls P<0.05). Mean level of serum urea in study group was significantly higher than the mean serum of healthy controls (P<0.01). Similarly, the mean level of creatinine in study group was significantly (P<0.002) increased compared to healthy controls.

[Table 5] Shows the cardiac markers like CPKMB, LDH & SGOT were significantly higher in study group as compared to healthy controls P<0.05). Mean level of serum CPK-MB value in Study group was significantly higher than the mean serum of healthy controls (P<0.01). The mean level of LDH in study group was significantly (P<0.001) increased compared to healthy controls. Similarly, the mean level of SGOT was significantly higher than the mean serum of healthy controls (P<0.01).

[Table 6] Shows the mean level of serum serum albumin and IMA value in study group were significantly higher than the mean serum of healthy controls (P<0.05).

[Table 7] Shows the Ischemis-modified albumin (IMA) shows significantly (P<0.05) strongly positive correlation with duration of ACS, RBS, TC, TG, LDL-c, CPK-MB, LDH and SGOT with study group. Ischemis-modified albumin (IMA) shows insignificantly negative correlation with HDL-c (P>0.05).

[Table 8] Shows the comparison of time duration and rise of IMA and CKMB.

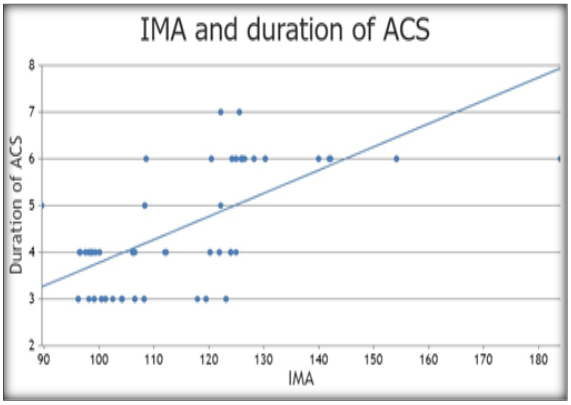

Figure 1: Shows the scatter diagram represents the significantly positive correlation between serum ischemia modified albumin and duration in study group

Table 1: Shows the distribution of participants a/c to age group

Age group (Yrs.)	Control (n=100)	Study group (n=100)	Total (n=200)
39-49	30	35	65
50-59	66	55	121
>60	4	10	14
Total	100	100	200

Table 2: Shows the mean level of anthropometric measurements of control and study group

Variable	Control (Mean±SD)	Study group (Mean±SD)	P- value
Age in years	52.15±9.21	52.26±5.23	0.43
Height in metres	1.61±0.07	1.62±0.08	0.87
Weight in kg	70.39±	70.61±	0.87
BMI kg/m2	25.38±2.59	26.84±4.02	0.002
SBP mmHg	127.88±8.49	147.92±14.2	0.01
DBP mmHg	79.16±4.37	93.92±7.64	0.01
Duration of ACS	-	4.512±1.28	-

Table 3: Mean and SD of the random blood glucose of the control and study groups

Variable	Control (Mean±SD)	Study group (Mean±SD)	P- value
RBS (mg/dl)	110.35±8.49	139.38±30.41	0.01

Table 4: Mean and SD of the RBS, Lipid profile, urea& creatinine of the control and study groups

Variable	Control (Mean±SD)	Study group (Mean±SD)	P- value
RBS (mg/dl)	110.35±8.49	139.38±30.41	0.01
Total cholesterol (mg/dl)	138.52±11.7	222.9±35.7	0.01
Triglycerides (mg/dl)	112.9±14.5	184.6±31.7	0.01
HDL-c (mg/dl)	51.4±5.2	35.7±5.82	0.02
LDL-c (mg/dl)	64.38±3.12.2	150.5±39.0	0.001
VLDL-c (mg/dl)	22.64±3.15	36.88±6.33	0.001
Urea (mg/dl)	25.36±3.58	29.9±4.87	0.01
Creatinine (mg/dl)	0.78±0.12	0.84±0.14	0.002

Table 5: Mean and SD of the cardiac markers of the control and study groups

Variable	Control (Mean±SD)	Study group (Mean±SD)	P- value
CPKMB (U/L)	12.03±2.35	68.99±30.79	0.01
LDH (U/L)	107.58±32.3	138.87±13.45	0.001
SGOT (U/L)	25.43±5.26	63.4±23.04	0.01

Table 6: Mean and SD of the sr. albumin and IMA of the control and study groups

Variable	Control (Mean±SD)	Study group (Mean±SD)	P- value
Serum albumin (gm/dl)	3.81±0.24	4.26±0.28	0.02
IMA(U/ml)	36.98±15.7	114.87±16.63	0.001

Table 7: Correlation between IMA and other parameters in both cases and study group

Biochemical Parameters	Study group	
	r-value	P-value
Duration in yrs.	0.64	0.001
Sr. albumin (gm/dl)	0.25	0.01
RBS (mg/dl)	0.40	0.000
TC (mg/dl)	0.23	0.02
TG (mg/dl)	0.25	0.01
HDL-c (mg/dl)	-0.04	0.69
LDL-c (mg/dl)	0.31	0.001
CPKMB U/L)	0.55	0.001
LDH (U/L)	0.21	0.03
SGOT (U/L)	0.37	0.001

Table 8: Shows the frequency for duration after onset of ACS and Serum levels of IMA and CPK-MB

Variables		Hrs.				Total	
		2 to 4 hrs.		4 to 8 hrs.		Count	%
		Count	%	Count	%		
IMA (U/ml)	Below 86	02	3.2	01	2.6	3	3.0
	Above 86	60	96.8	37	97.4	97	97.0
CPK-MB (U/L)	Below 24	11	17.7	01	2.6	12	12.0
	Above 24	51	82.3	37	97.4	88	88.0

DISCUSSION

All over the world, coronary heart disease is the cause of rising death and morbidity rates. Approximately 20–23% of patients who arrive at the emergency room have Acute Coronary Syndrome. In 1986, the World Health Organization created diagnostic markers for AMI, which identified biomarkers as an essential component of the illness and required that at least two of the following criteria be met: A) Chest pain in the past. B) ECG evolutionary alterations.C) Increases in serial cardiac indicators to twice the baseline level. But as time went on, it became less common to diagnose an AMI in the absence of myocardial damage. The role of markers was codified in a 2000 European Society of Cardiology/American College of Cardiology (ESC/ACC),[10] consensus conference that was updated in 2007 (Global Task Force). It stated that, in the appropriate clinical setting, the diagnosis should be considered evidence of myocardial injury based on cardiac markers.[11] Thus, the guidelines acknowledged the fact that the ECG findings' clinical presentation lacked sufficient sensitivity and specificity. Numerous research have suggested combining the use of multiple cardiac biomarkers with ECG and clinical results. In order to diagnose and treat Acute Coronary Syndrome (ACS) and avoid related consequences while lowering mortality, biomarkers for early detection of myocardial injuries—both ischemia and necrosis—are essential. More focus has been placed on the differential diagnosis of reversible vs irreversible myocardial ischemia and acute chest pain in clinical practice, as well as the measurement of serum levels of cardiac markers for the diagnosis of acute myocardial ischemia and stratification of the ACS risk. The

existence of myonecrosis determines the value of biomarkers in ACS. Many patients with ACS, however, may have myocardial ischemia without developing myonecrosis.[12] While readily available biomarkers such as CK-MB, CK-MB mass trop-I, LDH, and others are helpful in the diagnosis of ACS, they appear to be time-dependent and do not rise prior to myocyte necrosis. Furthermore, it takes longer for these markers to rise in the blood since they depend on cell death and protein leakage from the myocytes. The Albumin Cobalt Binding Assay can be used to measure the changes in serum albumin's N-terminus structure caused by myocardial ischemia, which prevents the protein from binding metals. Blood levels were observed to rise shortly after myocardial ischemia begins, to stay raised for six to twelve hours, and to recover to normal in twenty-four hours. A multicenter study on the predictive power of ACB for positive and negative cTrop I results within 6 to 24 hours after presentation was conducted in 2001 with 224 patients who had presented at the emergency room within 3 hours of the onset of symptoms suggestive of Acute Coronary Syndrome. The ACB test has a negative predictive value of 96% and sensitivity and specificity of 70% and 80%, respectively, at its ideal cutoff. In comparison to the combination of CKMB, myoglobin, and cTnT (86%), IMA showed a greater Negative Predictive value of 92% in a study of patients with suspected ACS. 76% and 74%, respectively, have been reported as the sensitivity and specificity of increased IMA for future mortality. According to Shaoguing Juand et al., the IMA concentration in the UA patients had considerably increased. Furthermore, an abnormal Left Ventricular Ejection Fraction (LVEF), which has been shown to be clinically significant in the early diagnosis and risk stratification of patients with Acute Coronary Syndromes, was adversely linked with IMA. In accordance with the above studies, in the study Ischemia Modified Albumin was increased earlier than CK-MB. The mean CK-MB level in the study group was (68.99±30.79) which is significantly higher than in the control group (12.03±2.35) and found to be increased after 4 hours of onset of chest pain. But didnot show significant increase as IMA in the early hours of ischemia. The mean value of IMA of the study group (114.87±16.63) was signicicantly higher than the control group (36.98±15.7). Patients who arrived after hours showed a favorable correlation between an increase in IMA value and CK-MB. Together with additional indicators including elevated CKMB and ECG abnormalities, ischemia modified albumin was relevant in this study for the identification of acute ischemic chest pain. More than 50% of patients who report to the emergency room with chest pain were admitted in order to rule out or confirm the presence of ischemic heart disease. This is because IMA is a biomarker of ischemia that can help with early diagnosis and rule out people who do not have ACS. Thus the serum levels of IMA can be used to both for diagnosis and rule in or rule out ischemic changes in the early hours. The mean total cholesterol level in the study group (222.9±35.7) was higher than the control group (138.52±11.7) which was statistically significantly. This coincides with studies done by Mari Luomala et al and Lucie Locaste et al which suggested that total cholesterol more than 150mg/dl as risk factor for cardiovascular events. The mean serum HDL –C which is lower in the study group compared to the control group (51.4±5.2 verses 35.7±5.82) which was statistically significantly ($p < 0.05$) and as per the recommendation of NCEP ATP III risk classification for HDL-C levels the serum HDL –C < 4omg/dl considered as high risk for IHD. The mean values of LDL-C, VLDL, and TGL are also significantly increased in the study group than the control group which contributes to increased risk for CHD. Pearson correlation analysis showed significant correlation between IMA with CK-MB, LDH, SGOT and the duration within which it increases. The strength of this study includes the homogenecity of the study group with respect to exclusion of possible confounding clinical conditions and proper timing of blood sampling. In this study mean value of IMA of study group was significantly higher than the control group and elevated within 2-3 hours. The mean value of CK-MB also significantly elevated but only after 4-6 hours and elevation of CKMB was well correlated with rise in IMA. Furthermore all the predisposing factors like smoking hypertension dyslipidemia, diabetes etc are present and significant number of patients are associated with these risk factors. The measurement of IMA was done by simple cost effective chemical method (Albumin Cobalt Binding Test) and was approved by FDA. Elevation in IMA identifies the early ischemic changes which will be reversible before irreversible necrosis occurs and are well correlated with CKMB levels also. Additionally, the IMA levels were much greater than those of the healthy group, and these findings are consistent with a large body of research. Ischemia Modified Albumin serum levels can therefore be utilized to detect ACS early on, assisting with diagnosis and treatment planning in the emergency room.

CONCLUSION

Myoglobin, Cardiac Troponin-I, and CK-MB are examples of biochemical markers that are solely appropriate for evaluating myocardial infarction. The current study's results support earlier research showing that the Albumin Cobalt colorimetric assay reliably separates myocardial ischemia patients from non-ischemic patients ($p<0.001$). The IMA assay offers a quantitative, precise laboratory method for determining the occurrence of an ischemic myocardial event, which includes different kinds of angina. Acute Coronary Syndrome is diagnosed in emergency department patients who are experiencing persistent myocardial ischemia by measuring their Ischemia Modified Albumin levels. The diagnostic

sensitivity of the procedure is increased by evaluating IMA in addition to ECG and other indicators.

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