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Research Article

The Level of Ischemic Modified Albumin (IMA) as Risk Marker for Cardio Vascular Disease (CVD) among some diabetic patients (type II) in Khartoum State-Sudan

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Abstract

Background: Recent literature reports show large interest in ischemic modified albumin (IMA) biochemical marker for detection of myocardial injury. Special attention is focused in estimation of IMA test for the diagnosis and evaluation of myocardial ischemia as well as others acute coronary syndrome in emergency patients. **Objective**: evaluation of ischemia-modified albumin (IMA) in well controlled and uncontrolled patients with type 2 diabetes mellitus and estimation of its connection with cardiovascular disease.Measurement the levelof IMA as risk marker for cardio vascular disease (CVD) in diabetic patients that arrived to emergency department with signs and symptoms of CVD. **Methodology**: 140 subjects enrolled in this study ,70 diabetes mellitus patients with signs and symptoms of CVD, and other 70 apparently non diabetic healthy subjects' as controls, , the levels of biomarker IMA was measured as the risk marker of CVDin controlled and uncontrolled diabeticpatients with type2,the Diagnostic potential was evaluated by receiver operating characteristic analysis and their relationships were analyzed. This study was done in Shab Hospital, Khartoum. Period from 1st of February 2015 to October 2015. **Results**: The results showed that CVD were predominant among diabetic female 57 % and peaked at age 75.5 years among 40-75 year old. The IMA was significantly increase in diabetic patients when compare with normal healthy group with cut off value (0.97 IU/L), and there is also significantly increase in IMA level in uncontrolled diabetic patients (Mean ± SD; 14.70 + 10.66) that presented with acute chest pain and havea signs and symptoms of cardiac ischemia when compared with the well-controlled diabetic patients(Mean ± SD; 3.74 ± 3.68). controlled and uncontrolled diabetic patients were determined by the level of their HBA1c and comparison with the means of IMA level in their serum. **Conclusions**: increase IMA level in poor control and long stand diabetic patients could help to identify the higher risk for develop to CVD, and The most common complication such as suffering from local or systemic hypoxic conditions, as acute ischemic stroke, peripheral vascular disease.

Keywords: Ischemia, Type 2 diabetes mellitus, cardiovascular disease, Ischemic Modified Albumin

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1. Introduction

Recent literature reports show large interest in new biochemical marker- ischemic modified albumin (IMA) for detection of myocardial injury. Special attention is focused in estimation of IMA test for the diagnosis and evaluation of myocardial ischemia as well as others acute coronary syndrome in emergency patients [1]. Because ischemia, and the resulting biochemical changes, can occur in any vessel, the specificity of IMA for cardiac ischemia is unclear [1]. Myocardial ischemia and accompanying hypoxia induced the structural modification of human serum albumin (HAS)[2]. HAS performs many essential functions in organism, among the others direct protective oxidative stress. This molecule represents one of the circulating antioxidant in plasma and plays a vital role in the efficient antioxidant defense of the organism [2, 3].

There are several data on IMA in patients with different states with ischemia of non-cardiac origin such as systemic sclerosis [4, 5] peripheral vascular disease, skeletal muscle ischemia during arthroscopic knee surgery and exercise induce, but no one concerns diabetes [6]. Hyperglycemia and oxidative stress can induce chronic ischemia in diabetic patients. It could lead to necrosis of different tissues [7, 8]. Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion and insulin action or both. The chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of normal functioning of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels [9]. The prevalence of diabetes mellitus is rising all over the world and have been increasing rapidly recently in Sudan reach 1.4 million cases in 2015 [10]. Uncontrolled state of hyperglycemia leads to a variety of complications including peripheral vascular diseases, nephropathy, neuropathy, retinopathy, morbidity, and/or mortality. Type 2 diabetes and their related complications of hypertension, hyperlipidemia and atherosclerotic vascular disease and also demonstrated an association of metabolic syndrome with the development of cardiovascular disease (CVD), and more confirmation related to mortality rate increment was given by Type 2 diabetes and their related complications cardiovascular disease remains the leading cause of death, and myocardial infraction (MI) tend to be more extensive and have poorly survival rate than in age, weight and sex matched in individuals without diabetes [11].

2. Material and Methods

Study design

This quantitively exploratory descriptive research study was done Al shab's Hospital for Cardiology and Chest in Khartoum during 1st of February 2015 to October 2015.

Inclusion criteria:

Test group: Standardized clinical data were collected for each patient, which included time of presentation at the emergency department, approximate duration of symptoms of the acute chest pain.

Exclusion criteria:

Patients with liver disorders, autoimmune disorders, pregnant women, patients with symptoms and signs suggestive of acute mesenteric ischemia, acute renal failure, peripheral vascular disease, or brain ischemia were not enrolled in the study.

Study population

Patient Selection

Seventy patients with type 2 diabetes mellitus, arriving to Emergency unit in hospital. suffering from acute chest pain with manifestations suggestive of acute myocardial ischemia, including those such as chest pain, shortness of breath, lower jaw pain, left arm pain, epigastric pain, new or increasing lower extremity edema, palpitations, and other symptoms suggestive of an anginal equivalent. The ECG measured in the ED as part of the standard of care at the AL Shab Hospital. '

Control group selection

Seventy healthy volunteers' individuals' age and sex matched whom didn't have any evidence of diabetes and coronary artery disease were taken as the control group.

Samples processing

Demographic dates(sex, age), an ECG and Biochemical dates were collected .Blood for IMA and HbA1C levels were collected within two hours of arrival, IMA riskmarker testing were performed before any heparin/thrombolytic treatment was started. Blood samples collected in tubes containing lithium heparin at the time of the patient's presentation to the emergency department, centrifuge for 5 minutes and preserve at -70 C.

Technique of use:

Ischemic Modified Albumin (IMA): that assayed in intervals at 2 - 4 hours and 6 - 8 hours. The microtiter plate provided in this kit has been pre-coated with an antibody specific to IMA. Standards or samples are then added to the appropriate microtiter

plate wells with a biotin-conjugated antibody preparation specific for IMA and Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated.Then a TMB (3,3',5,5' tetramethyl-benzidine) substrate solution is added to each well. Only those wells that contain IMA, biotin-conjugated antibody and enzyme-conjugated Avidin will exhibit a change in color. The enzyme-substrate reaction is terminated by the addition of a sulphuric acid solution and the color change is measured spectrophotometrically at a wavelength of 450 nm ± 2 nm. The 3 concentration of IMA in the samples is then determined by comparing the O.D. of the samples to the standard: reference values reported by the manufacturer (0.21+ 0.65)by EISA themicro titer plate provided kit has been pre-coated with an antibody specific to IMA.

HbA1c assay: was done by method based on boronate affinity chromatography using NYCOCARD READER II.

Ethical consideration

The study protocol was approved by ethical committee for medical and health research at Omdurman Islamic University and local ethics committee of Medical Director of AL Shab Hospital- Khartoum. Data analysis was done using statistical package SPSS version Parametric values were analyzed using one-way analysis of variance (ANOVA), followed by T. test and Pearson's correlation analysis, used for statistical analysis of the data; $p < 0.05$ was considered to be statistically significant'

3. RESULTS

This study was conducted on 70 Known diabetic patients (type 2) arrived to the emergency department of AlShab Hospital, Khartoum state, with acute chest pain, as case group, and 70 apparently non diabetic healthy subjects' volunteers whom didn't have any evidence of coronary artery disease. Age and sex for both groups were matched.

Table 1 shows that demographics dates 30 male (43%) and 40 female (57%) and the 70 healthy control group 30 male (43%) and 40 female (43%). And age means in 2 groups

was (57.5 ±17.6) versus (59.4±18.5) years (p =0.992). There was no significant difference Table:2 shows that means level of IMA in both diabetic patients (case group) and in the normal healthy non diabetic control group. means ± SD (10.78±10.25), (3.21±10.73) respectively , (P.Value 0.003), There was significant difference

Figure 1 shows that The diagnostic performance of IMA obtained from Receiver operating characteristic, area under curve (ROC , AUC=0.84.) have a sensitivity (81.4%)and specificity (80%) at cut off value =0.97

Group		Frequency	Percent	Meanof Age ±SD	P.value
case	Female	40	57.0%	57.5 ±17.6	0.992
	Male	30	43.0%		
	Total	70	100.0%		
control	Female	40	57.0%	59.4±18.5	
	Male	30	43.0%		
	Total	70	100.0%		

Table 1: Baseline demographic (Sex & age) characterizations in case and the control group.

Group		Number	Mean	Std. Deviation	P.value
AMI	case	70	10.78	10.25	0.03
	control	70	3.21	10.73	

Table 2: Comparison means of plasma (IMA) in case group and control group.

HBA1c % level in DM		N	Mean	Std. Deviation	P.value
AMI IU\mL	≤ 7% HBA1c	25	3.74	3.68	0.0001
	>7% HBA1c	45	14.70	8.66	

Table 3: IMA means level within Diabetic Groups (Controlled Group = ≤ 7% HBA1c with HBA1c level, Uncontrolled > 7% HBA1c)

Table 3. shows that Serum levels of IMA were high significant different when compare the poor controlled diabetic group (45 patients , HbA1c > 7%) with signs and symptoms of ischemic heart disease ,and good controlled diabetic group (25 patients HbA1c < 7%) , Mean± SD; (14.70±8.66), (3.74± 3.68), respectively P. Value 0.0001.

Figure 2 shows that Uncontrolled diabetic patients (HbA1c > 7 %) with long during have high frequency level of IMA ,whereas controlled patients(HbA1c < 7 %) have a lower frequency , Figure 2 shows that the female have high frequency to D.M than male.

4. Discussion

The IMA measurement as a marker of myocardial ischemia without myocardial necrosis and/or preceding myocardial necrosis has introduced the hope for improved diagnosis in patients with IHD without or with non-specific ECG changes [12]. IMA has been proven to be an early biochemical marker to detect ischemia in patients of myocardial

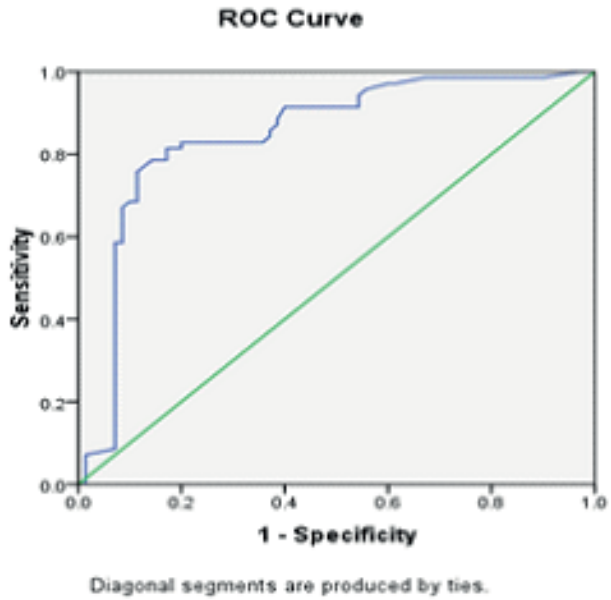

Figure 1: Diagnostic performance of IMA as risk marker in diabetic patients, AUC=0.84. Sensitivity=81.4% and specificity=80% at cut off value =0.97.

infarction. The lack of oxygen modifies albumin at N-terminus residues, thus decreasing its affinity to Co (II) [13].

Increased IMA levels have been found in a number of conditions with an ischemic element in their pathophysiology. Only one preliminary study has been reported so far in diabetes mellitus with vascular complications, which showed increased levels of IMA and its positive correlation with glycated haemoglobin (HbA1C), therefore this study was planned to analyze IMA levels in type 2 diabetes mellitus patients devoid of renal and cardiovascular complications [14, 15].

The levels of IMA were expressed as IU/ml units, in study population use it as risk marker for cardiovascular disease. We found that the Serum levels of IMA were significantly higher in diabetic patients when compared with normal healthy non diabetic (p value = 0.003)this agree with previous study show that the IMA is a novel marker of tissue ischemia and accepted as a marker of oxidative stress in type 2 diabetes patients [15] and others study report that definite and precise mechanisms for IMA production in vivo, it appears to be related to the generation of reactive oxygen species (ROS) due to ischemia-reperfusion that modifies metal binding domains of albumin molecule [16]. Diabetic complications are due to various micro and macroangio-pathic events producing increased oxidative stress and decreased levels of antioxidants, which can lead to modification of albumin molecule of IMA than patients with less than 5 years

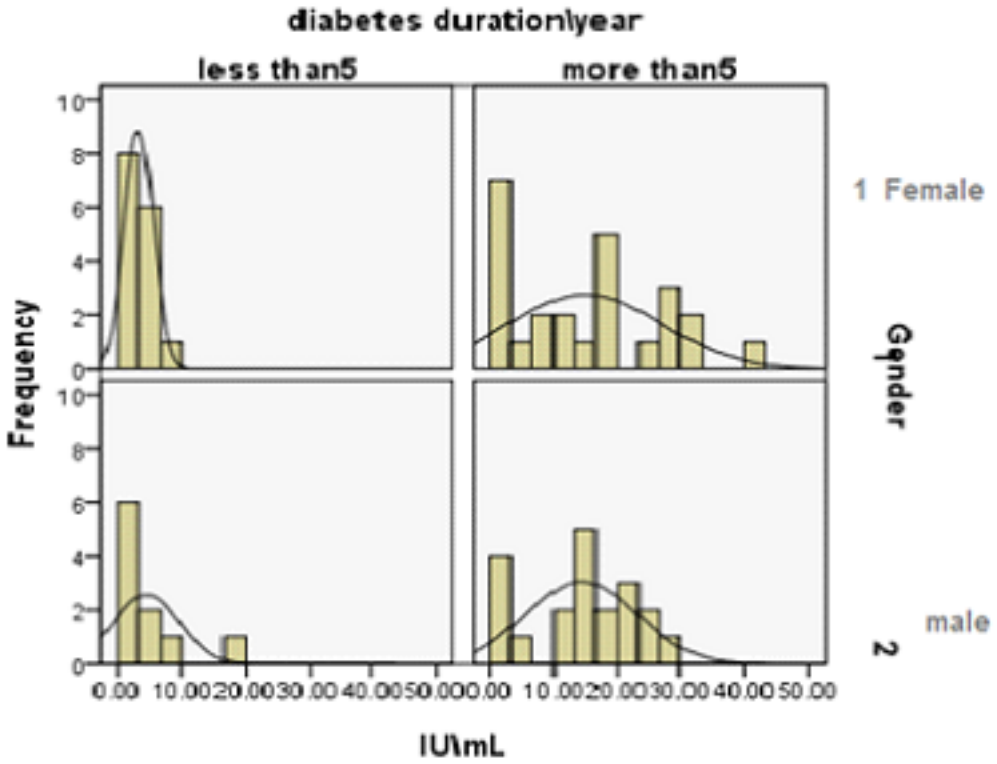

Figure 2: Histogram shows long–stand diabetes patients AMI levels frequency accordance to gender. (1 represent female, 2 represent males).

duration of diabetes(long-stand diabetes) have a lower than the other one [18, 17]. In this current study there was significantly difference increase in IMA level among poor controlled (HBA1c > 7%) diabetic patients (mean; 14.70 ± 8.66)when compared with the good controlled(HBA1c < 7%), diabetic (mean; 3.74 ± 3.68), the patients(long-stand diabetes) duration more than 5 years have high frequency level of IMA than patients with less than 5 years duration .By referring to the gender (Figure 2) show that the female have high frequency of IMA Ul/ml level rather than male.

5. Conclusion

Ischemic Modified Albumin level was elevated significantly within long duration and uncontrolled diabetic patient whom have sign of early myocardial ischemia, As cardiac biomarkers IMA show as highly sensitive for early diagnostic of acute chest pain.

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