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"ASSESSMENT OF ISCHEMIA MODIFIED ALBUMIN AS A MARKER OF GLYCEMIA STATUS IN TYPE2 DIABETES MELLITUS PATIENTS"

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Abstract:
Background: The novel biomarker of ischemia and oxidative stress is called ischemia modified albumin (IMA). IMA has been linked to an increase in diabetes mellitus, according to numerous research. The metabolic disease known as diabetes mellitus (DM) is characterized by hyperglycemia, hypertension, and hyperlipidemia. Therefore, estimating the IMA levels in type 2 DM individuals was our goal. additionally to assess the correlation between IMA and every lipid profile measure (TC, LDL, HDL, TG) in individuals with type 2 diabetes.

Subjects and Methods: 200 subjects were selected from the medicine OPD of INDEX Medical College and Hospital for the study. Out of which 100 were diagnosed with T2DM and remaining 100 were age and sex matched healthy controls.

Results: Patients with type 2 diabetes had significantly higher levels of fasting and postprandial plasma glucose, HbA1c, serum TG, TC, LDL, HDL, and IMA compared to control participants ($p < 0.05$). A noteworthy association was discovered between the IMA and the lipid profile.

Conclusion: According to the current study, IMA measurement in diabetic individuals with dyslipidemia can be an early indicator of ischemia and its severity. This might support improved DM management and prognosis.

Keywords: Type 2 diabetes mellitus, hyperglycemia, hyperlipidemia, MDA and IMA.

Introduction:

One of the more recent biomarkers of oxidative stress and ischemia is ischemia modified albumin (IMA).[1] Ischemia induces structural changes in the N-terminal end of albumin, leading to ischemia modified albumin, through its pathophysiological processes such as hypoxia and free oxygen radical.[2] A variety of clinical disorders, including ovarian torsion, chronic renal failure,

hypothyroidism, myocardial ischemia, thalassemia, and cancer, are associated with elevated IMA levels. Numerous studies have reported that diabetes mellitus increases IMA. In individuals with type 2 diabetes, Kaefer et al. discovered a relationship between glycated albumin, hyperglycemia, and C-reactive protein.[3] Hyperglycemia, hypertension, and hyperlipidemia are the independent acceleration factors of hyperglycemia and tissue damage, and diabetes mellitus (DM) is a collection of metabolic disorders characterized by hyperglycemia. Recurring exposure to this will result in both macro and microvascular problems.[4]

Within minutes of artery occlusion, free radical formation, a weakened antioxidant defense system, and the ischemia that goes along with diabetes cause alterations in the tertiary structure of human serum albumin, which is why it's called ischemia-modified albumin (IMA). Increased production of reactive oxygen species (ROS) may lead to structural alterations in the albumin molecule. These days, myocardial ischemia is recognized as a sign of oxidative stress and can be detected using IMA, a sensitive biomarker.[5] Hyperglycemia causes pathological alterations such as thickening of the capillary basement membrane, lipid accumulation and oxidation, and cellular proliferation that narrows the arterial arteries.[6] Atherosclerosis is triggered by low-grade systemic inflammation and endothelial dysfunction. Overt diabetes is typically diagnosed when macrovascular problems such as peripheral artery disorders, myocardial infarction, and stroke occur.[7] Our goal is to find out the levels of IMA in type 2 diabetes patients and assess its correlation with all of the lipid profile parameters (Total Cholesterol, Low Density Lipoprotein, High Density Lipoprotein, and Triglycerides) in T2DM participants in light of the aforementioned conclusion. If a correlation is discovered, IMA may be employed as a measure to detect cardiovascular complications in T2DM patients early on.

Subjects and Methods:

The present study was conducted in the Department of Biochemistry, INDEX Medical College and Hospital with the collaboration with Department of Medicine during the period from July, 2021 to August, 2022. 200 subjects were selected from the medicine OPD of INDEX Medical College and Hospital for the study. Out of which 100 were diagnosed with T2DM as per the American Diabetes Association (ADA) 2016 guidelines [8] and remaining 100 were age and sex matched healthy controls. All the subjects provided written informed consent, a thorough medical history, and ethical clearance. Exclusions from the trial were infection, corticosteroid medication, liver and kidney impairment, h/o ischemia episodes, and pregnancy.

Biochemical Parameters:

Each individual had a five milliliter aseptic venous blood sample drawn from the antecubital vein after an overnight fast. The leftover 1.5 ml was collected into a plain vacuum container, 1.5 ml into an EDTA tube, and 1.5 ml into a fluoride tube. For the purpose of estimating 2-hour postprandial glucose, 2.0 ml of blood was then drawn into a fluorine tube. Every tube underwent five minutes of centrifugation at 2500 rpm. The determination of glucose was done using plasma in a fluoride tube. The sample from the EDTA tube was utilized to estimate the HbA1c. A small eppendorf tube containing around 0.5 ml of the serum that had been isolated from the blood in a plain vacuum container was placed inside and kept at -20^0C until it was analyzed for IMA estimate. High density lipoprotein (HDL), triglycerides (TG), and total cholesterol (TC) were estimated using the remaining serum. Every estimate was carried out using an Erba EM-200 autoanalyzer. Serum IMA was determined manually by the albumin cobalt binding assay, the method described by Bar-Or et al.[9], Malondialdehyde (MDA) by thiobarbituric acid method.[10] and GSH by the method of Beutler et al. [11].The absorbance units (ABSU) for the results were displayed.

Statistical Analysis:

IBM SPSS Statistics 22 (SPSS Inc., Chicago, Ill., USA) was used to analyze the data. The mean ± SD was used to express all the data. Students t-test was used to compare two independent mean

groups for parametric data. Karl Pearson Correlation was employed in correlation investigations. A value of p less than 0.05 was deemed statistically significant.

Observation and Results:

The present study included 200 subjects, out of which 100 were type 2 diabetic and 100 were healthy controls. The mean age of the type 2 diabetic subjects was having higher 44.42 ± 10.26 years and in 41.0 ± 9.24 years for healthy controls. Similarly, the mean BMI of type 2 diabetic subjects was higher 25.54 ± 6.92 as compared to 23.93 ± 6.12 healthy controls [Table 1]. The mean duration of T2DM was 4.91 ± 1.64. The duration of diabetes was almost same between the male and female diabetic subjects. No statistical difference was noted.

Variables	Controls	Type 2 DM	P value
Age in years	41.0 ± 9.24	44.42 ± 10.26	0.03*
Height in cm	161.36 ± 24.56	159.52 ± 20.58	0.82**
Weight in Kg	62.4 ± 11.2	64.54 ± 11.68	0.02*
BMI kg/m2	23.93 ±6.12	25.54 ± 6.92	0.01*
Duration of diabetes	0.0	4.91 ±1.64	
Table 1: Anthropometric parameter of type 2 diabetic and healthy subjects			

***Statistically significant at P<0.05 and **Statistically significant not at P>0.05. BMI: Body mass index**

Table 2 shows the laboratory findings of all the subjects included in the study. The Fasting and postprandial plasma glucose, HbA1c, serum TC, TG, HDL, LDL, and IMA were significantly increased in T2DM patients than in control subjects with the p value <0.05. Similarly, the level of MDA was significantly increased whereas the level of GSH was significantly decreased in type 2 diabetic patients than in healthy subjects.

Variables	Controls	Type 2 DM	P value
FBS (mg/dl)	83.16 ± 22.32	138.12 ± 24.12	0.001
PPBS (mg/dl)	115.9 ± 26.54	223.2 ± 28.54	0.001
HbA1c (%)	4.91 ± 1.24	7.44 ± 2.31	0.03
TC (mg/dl)	177.0 ± 28.21	215.76 ± 26.5	0.001
TG (mg/dl)	138.06 ± 24.64	184.52 ± 26.54	0.001
HDL-c (mg/dl)	51.48 ± 10.46	38.54 ± 8.32	0.02
LDL-c (mg/dl)	96.64 ± 21.23	140.32 ± 21.3	0.001
MDA (nmol/ml)	1.65 ± 0.64	2.93 ± 0.21	0.04
GSH (mg/g ml)	19.69 ± 5.23	14.39 ± 6.2	0.02
IMA U/ml	45.15 ± 15.2	83.16 ± 21.89	0.001
Table 2: Shows the level of blood glucose, glycated haemoglobin, lipid profile, IMA, malondialdehyde and glutathione in type 2 diabetic and healthy subjects			

*Statistically significant at P<0.05. HbA1c: Glycated haemoglobin, TC: Total cholesterol, TG: Triglyceride, HDL-c: High density lipoprotein cholesterol, LDL-c: Low density lipoprotein cholesterol, VLDL-c: Very LDL-c, FBS: Fasting blood sugar.

Lipid profile parameters	**Serum IMA**	
	r-value	**p-value**
FBS	**0.26**	**0.01**
PPBS	**0.21**	**0.03**
HbA1c	**0.26**	**0.01**
Total cholesterol	**0.24**	**0.01**
Triglycerides	**0.32**	**0.02**
High density lipoproteins cholesterol	**0.086**	**0.39**
Low density lipoproteins cholesterol	**0.20**	**0.04**
Table 3: Shows the correlation of IMA with parameters of FBS, PPBS, HbA1c & lipid profile.		

[Table-3] IMA shows strongly positive correlated with fasting blood sugar (FBS), PPBS, HbA1c, total cholesterol, LDL, triglycerides ($P<0.05$) and IMA shows negative correlation with HDL ($P=0.39$).

Discussion:

It has been noted that type 2 diabetes occurring at a significantly younger age is on the rise[12]. For this reason, it's critical to diagnose it early and prevent problems in younger patients, such as myocardial infarction and stroke. Oxidative stress is elevated in hyperglycemia through multiple routes. One significant one is the electron transport chain's ability to produce superoxide radicals. [13] These free radicals not only affect the structure of circulating albumin but also harm the endothelium lining of the veins, resulting in macrovascular and microvascular problems. thus leads to an increase in IMA production when oxidative stress is present. In this investigation, we assessed the IMA and lipid profile levels in both type 2 DM patients and control participants. The results of the investigation demonstrated that type 2 DM patients had considerably higher IMA and lipid profiles. The IMA and the lipid profile were found to significantly positively correlate. Our results corroborated those of a study by Ukrinc et al. [14], which discovered that individuals with T2DM, whether or not they had cardiovascular problems, had noticeably higher levels of IMA than controls. Triglycerides and IMA were found to be higher in type 2 DM patients compared to healthy controls by Kaefer et al. [3]. Additionally, Rajendra et al. discovered that diabetic individuals with peripheral neuropathy had higher levels of IMA than those without peripheral neuropathy.[15] The involvement of IMA in diabetic nephropathy was explained by Turk et al. [16] Thus, IMA may function as a precursor to glycaemic management, the gravity of complications, and the advancement of the disease. Triglycerides, TC, LDL, and IMA were shown to be greater in type 2 diabetes patients with peripheral artery disorders than in those without such conditions, according to another study. [17]

Conclusion:

According to the current research, IMA measurement in diabetic individuals who are dyslipidemic may offer an early indicator of ischemia and its severity. This will contribute to improved diabetes mellitus management and prognosis.

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