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RESEARCH ARTICLE

A COMPARATIVE ANALYSIS OF SERUM MALONDIALDEHYDE LEVELS AS A MARKER OF OXIDATIVE STRESS IN ACUTE MYOCARDIAL INFARCTION CASES WITH AND WITHOUT T2DM.

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Abstract

Oxidative stress is considered as one of the important mechanism in the causation of type 2 diabetes (T2DM) as well as cardiovascular diseases. Quantification of serum malondialdehyde (MDA) is generally employed as reliable marker of assessment of oxidative stress. The objective of the present study was to estimate serum MDA levels in acute myocardial infarction cases with and without T2DM. A total of 60 AMI patients were studied, including 30 cases of AMI with T_2DM and an equal number of cases of AMI without T2DM. Mean serum levels of MDA were 543.17± 56.97 and 423.50 ± 51.12 nmol/dL respectively in cases of AMI with T2DM and those without T2DM ($p<0.05$). Significantly elevated levels of serum MDA were observed in T2DM cases with AMI than those without T2DM. Significance of the results has been discussed in terms of age at onset as well as severity of AMI.

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Introduction:-

Enhanced oxidative stress resulting due to elevated levels of free radicals in plasma is considered as a mechanism responsible for cardiovascular manifestations in Type 2 diabetics' mellitus (T2DM)[1]. Various abnormalities in T2DM including hyperglycemia, hyperlipidemia, and insulin resistance are considered as responsible for excessive free radical generation.[1]These free radicals and their intermediate reactive species damage various components of the cells like proteins, lipids and DNA. The reactive oxygen free radicals interact with plasma proteins like LDL and the oxidized LDL thus formed is involved in foam cell formation resulting in the initiation of atherosclerosis which is commonly associated with the risk of myocardial infarction. [2, 3]

There are reports regarding detection of advanced glycation end products (AGES) and oxidative stress in non-diabetic patients with coronary artery disease.[4] In a study carried-out on non-diabetic patients with coronary artery disease kanauchi et al (2001) reported significantly increased levels of advanced glycation end products (AGES). AGE's formation may cause oxidative stress [5]. Increased oxidative stress, even in non-diabetic subjects may lead to insulin resistance[4].Hence the objective of the present study was to carry-out a comparative evaluation of serum MDA levels as a marker of oxidative stress in AMI patients with T2DM and those without T2DM. MDA is a stable end product of lipid peroxidation resulting from interaction of reactive oxygen species with lipid bilayer of cellular membranes. It is considered as a reliable marker of oxidative stress.

Materials and Methods:-

Institutional Ethics Committee (Deccan College of Medical Sciences, Hyderabad) approval was taken prior to initiation of the study. A total of 60 AMI cases admitted to the Intensive coronary care unit of Cardiology Department Princess Esra Hospital (DCMS, Hyderabad) were randomly selected. Of these 30 cases were of AMI

with T2DM and the remaining 30 were without T2DM. Demographic details of all the patients like gender, age and body mass index (BMI) were recorded. Values of HbA1C, fasting and post-lunch blood sugar levels as well as serum lipid levels were also noted. From each patient 5ml of blood was drawn and dispensed into vials without anti-coagulant for separation of serum. Estimation of MDA was done by the thiobarbituric acid reactive substance assay according to the method described by Mahfouz. [6]

Results:-

Demographic details of the AMI patients are shown in table 1. In each of the two groups of AMI patients the number of males to female cases was 19 and 11 respectively. The age range in the AMI group with T2DM was 36-70 years while it was 41-75 years in the AMI group without T2DM. The mean age at presentation for the group with AMI alone was 57 years while it was 47 years for the AMI group with T2DM So far as BMI is concerned 30.33% (10 out 30) AMI cases with diabeties had a BMI of less than 25 while 46.67% (14 out 30) AMI cases without T2DM had normal BMI (less than 25). Fifty percent of diabetic cases with AMI had a BMI in the range 25-29.99, while 46.47% (14 out 30) AMI cases without T2DM belonged to the over-weight group (BMI 25-29.99). In the category of BMI ≥ 30, 5 cases (16.67%) of AMI with T2DM were present while only 2 (6.67%) cases of AMI without T2DM belonged to this category. (Table 1)

Table 1:- Demographic details of the two groups of Acute myocardial Infarction (AMI) patients.

	DM Patients with AMI N=30	**Non-DM Patients with AMI N=30**
Age range	36-70 years	41-75 years
Gender: Males/Females	19/11	19/11
Body Mass Index (BMI)		
<25	10 (33.33%)	14 (46.47%)
25-29.99	15 (50%)	14(46.47%)
≥30	5 (16.67%)	2 (6.67%)

The mean total cholesterol was 254.70 ± 20.13 mg/dL in AMI + T2DM group and it was 238.40 ± 12.13 mg/dL in the group AMI without diabetes (Table 2). The mean fasting and post lunch blood sugar levels of the AMI cases with diabetes were in the hyper glycemic range (Table 2). Mean HbA1C value was significantly higher in the group with diabetes than the AMI group without T2DM. Statistically significant difference was observed between the mean fasting and post-lunch blood sugar levels between the two AMI groups. The mean serum MDA levels were significantly less (423.50 ± 51.12 nmol/dL) (P<0.01) in AMI cases without T_2 DM compared to their diabetic counter parts. (543.17±56.97nmol/dL) (Table 3).

Table 2:- Mean fasting and post prandial blood sugar levels and mean HbA1C in the two acute myocardial Infarction (AMI) groups.

	T_2 DM patients with MI (n=30)	**Non- Diabetic patients with MI (n=30)**	**P - Value**
Total serum Cholesterol	254.70 ± 20.13	238.40 ± 12.13	<0.05
HbA1C	8.67±0.76	5.81±0.26	<0.0001
FBS (mg/dL)	169.87±21.67	104.37±8.22	<0.001
PLBS (mg/dL)	268.27± 37	156.73±35.22	<0.002

Table 3:- Details of Serum MDA levels in AMI patients with T_2DM and without T_2DM.

Parameters	**T_2DM Patients with AMI (n=30)**	**Non-DM patients with AMI (n=30)**	**P- Value**
MDA $_{nmol/dL}$	543.17± 56.97	423.50± 51.12	<0.01

Discussion:-

The role of enhanced oxidative stress in the pathogenesis of T2DM has been well documented. It is known that high plasma levels of free fatty acids (FFA) and hyperglycemia which are characteristic features of T2DM, stimulate reactive oxygen species production through protein kinase-c dependent activation of NAD(P)H oxidase.[7]

Moreover elevated levels of FFA also decrease intracellular GSH and additionally impair the endogenous defense against free radical mediated injury.[8]

The observed significant increase in mean serum MDA levels (543.17± 56.97 nmol/dL) ($P<0.05$) in AMI cases with T2DM compared to the mean MDA levels in non-diabetic AMI cases may be explained on the basis of hyperglycemia and FFA mediated excessive ROS generation in AMI+ with T2DM cases. As for the non-diabetic AMI group is concerned various reasons that can be attributed to the generation of reactive oxygen species in these cases: these reasons are obesity and overweight and elevated levels of serum cholesterol and triglycerides. Moreover in obese individuals, anti-oxidant defenses are lower than their normal weight counter parts and their levels inversely correlate with central obesity.[9] This contention is supported by reports available in the literature claiming enhanced ROS generation in normal individuals who are overweight/obese and those who have significantly elevated levels of cholesterol, triglycerides than individuals whose BMI was within normal range. Important conclusions drawn from the present study are

1. The mean serum MDA levels in AMI group with T2DM was significantly higher than that in the non-diabetic AMI group ($P<0.05$) indicating that in AMI cases with T2DM the rate of oxidative stress induced cellular damage is significantly higher.
2. The elevated levels of MDA also explain early onset of AMI in T2DM cases than their non-diabetic counterparts. Further it is reported that in CAD cases with T2DM the frequency of cases with multiple vessel stenosis is higher than their non-diabetic counterparts.

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