

Adenosine Deaminase and Malondialdehyde Levels in Type-2 Diabetes Mellitus -a Short Study

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Received: 14 December 2013 Accepted: 5 January 2014 Published: 15 January 2014

Abstract

Diabetes mellitus is a group of metabolic disease characterized by a state of chronic hyperglycemia resulting from defect in insulin secretion, insulin action or both. Diabetes mellitus is a cluster of abnormal metabolic paradigm having common features of hyperglycaemia Type2 Diabetes mellitus has been shown to be a state of increased free radical activity³. Chronic hyperglycemic status favours auto-oxidation and the formation of advance glycation and products. There is a positive correlation between Adenosine deaminase and control of Type2 Diabetes Mellitus. Malondialdehyde (MDA) is the measure of lipid peroxidation of membrane lipids which is directly proportional to the oxidative stress on the membrane. The correlation of Malondialdehyde (MDA) and Adenosine deaminase(ADA) levels in relation to control of Type2 Diabetes mellitus based on HbA1C level indicate that there is an auto-oxidation of glucose which results in persistent production of Malondialdehyde (MDA) and ROS which can release advance glycation end product(AGE) and advanced lipoxidation end products (ALE).

Index terms— adenosine deaminase, malondialdehyde, glycosylated hemoglobin.

1 Adenosine Deaminase and Malondialdehyde Levels in Type-2 Diabetes Mellitus -a Short Study

Meenakshi Thakur ? & Dinesh Javarappa ? Abstract -Diabetes mellitus is a group of metabolic disease characterized by a state of chronic hyperglycemia resulting from defect in insulin secretion, insulin action or both. Diabetes mellitus is a cluster of abnormal metabolic paradigm having common features of hyperglycaemia Type2 Diabetes mellitus has been shown to be a state of increased free radical activity³. Chronic hyperglycemic status favours auto-oxidation and the formation of advance glycation and products. There is a positive correlation between Adenosine deaminase and control of Type2 Diabetes Mellitus. Malondialdehyde (MDA) is the measure of lipid peroxidation of membrane lipids which is directly proportional to the oxidative stress on the membrane. The correlation of Malondialdehyde (MDA) and Adenosine deaminase(ADA) levels in relation to control of Type2 Diabetes mellitus based on HbA1C level indicate that there is an auto-oxidation of glucose which results in persistent production of Malondialdehyde (MDA) and ROS which can release advance glycation end product(AGE) and advanced lipoxidation end products (ALE).

A case control comparative study was done with Type2 Diabetes mellitus and normal controls at BMCH&RC, Chitradurga. According to the criteria, blood sample were collected under aseptic precautions and evaluation of Fasting Blood Sugar, HbA1C, Adenosine deaminase(ADA), along with RBC membrane ghost preparation and estimation of Malondialdehyde (MDA) were done. In this study, It was found that there was significant increase of Adenosine deaminase(ADA) in serum of Type2 Diabetes mellitus cases (40.06 ± 9.16) in comparison to control groups (21.21 ± 5.72) with a statistical significance of ($P < 0.001$) along with Malondialdehyde (MDA) of RBC membrane which was also significantly increased (4).

2 Introduction

Diabetes mellitus is the major health problem affecting people all over the world. It is one of the most extensively investigated human diseases. Diabetes mellitus is a group of metabolic disease characterized by a state of chronic hyperglycemia resulting from defect in insulin secretion, insulin action or both.

During diabetes mellitus, persistent hyperglycemia produces free radicals specially ROS, for all tissues, glucose auto oxidation and protein glycosylation 1 . Diabetes mellitus is a cluster of abnormal metabolic paradigm having common features of hyperglycaemia 2 Type2 Diabetes mellitus has been shown to be a state of increased free radical activity 3 . Chronic hyperglycemic status favours auto-oxidation and the formation of advance glycation and products. The generation of free radicals in the diabetic patients can be due to the following mechanism.

Hyperglycaemia leads to activation of NADPH oxidase, which is a multi-subunit enzyme, that catalyses o 2 formation by one electron reduction of o 2 using NADPH or NADH as electron donor.

Hyperglycaemia causes formation of advanced glycation End products (AGEs) as result of noenzymatic reactions between intra-cellular glucosederived dicarbonyl precursors with the amino group of both intracellular and extracellular proteins 4 . The AGEs stimulate receptors for advance glycation end products (RAGE). Their interaction is believed to initiate and aggravate the diabetic complications.

Furthermore, in the presence of superoxide dismutase, superoxide anion leads to formation of H_2O_2 which is responsible for the activating the signaling molecules leading to inflammation, cell growth, apoptosis and fibrosis 5 .

Malondialdehyde(MDA) is an end product of lipid peroxidation. Reactive oxygen species degrade polyunsaturated fatty acid, forming Malondialdehyde (MDA). This compound is a reactive aldehydes and is one of the many reactive electrophilic species that causes toxic stress in cells and form covalent protein adducts which are referred to as advanced lipoxidation end products (ALE) 6 .

Persistent hyperglycaemia in diabetes mellitus leads to increased formation of free radicals through various mechanisms. In the study Ayaz K. Mallick et al showed significant levels in increased erythrocyte membrane lipid peroxidation as increased Malondialdehyde (MDA). levels. The study also showed a significant positive correlation between the erythrocyte Malondialdehyde (MDA) levels and glycated haemoglobin. This is due to auto oxidation of glucose which causes persistent generation of ROS or Malondialdehyde (MDA) pointing towards the fact that prolonged hyperglycaemia appears to be a cause for increased oxidative stress which in turn leads to life threatening complications 7 .

Adenosine deaminase, an enzyme, which is present in red cells and the vessel wall catalyses the irreversible hydrolytic deamination of adenosine to inosine and 2-deoxyadenosine to 2-deoxyinosine. Inosine and 2-deoxyinosine are converted to hypoxanthine, xanthine and finally to uric acid. Adenosine deaminase (ADA) is considered as a good marker of cell mediated immunity. High lymphocyte Adenosine deaminase (ADA) activities were found to be elevated in diseases in which there is cell mediated immune response 8,9 . In a study, Hoshino T et al reported elevated Adenosine deaminase (ADA) activity in the serum of Type 2 Diabetes mellitus patients 8 .

Adenosine deaminase (ADA) plays a crucial role in lymphocyte proliferation and differentiation and shows its highest activity in T-lymphocytes 10 .

3 II.

4 Material and Methods

5 a) Inclusion criteria i.

Patients with clinically proven Type2 Diabetes Mellitus who are on oral anti diabetic treatment with a known history of Diabetes Mellitus for a minimum period of 3 months and between 30-50 years were taken. The criteria of uncontrolled Diabetes mellitus was ascertained on the basis of HbA1C (>7%). ii.

Controls are healthy individuals with age and sex matched without any major illness or on any medications.

6 b) Exclusion criteria

The Patients of the following criteria were excluded from the study: i.

Patients with Type 1 Diabetes Mellitus. ii.

Patients with history of smoking. iii.

Patients with history of Hypertension.

III.

7 Methods

10ml of fasting blood sample were collected.

? Serum Adenosine deaminase (ADA) activity was estimated by enzymatic (Giusti.G.Galanti.B) method.

? RBC Membrane Malondialdehyde (MDA). was estimated by (Okhawa et al) after RBC ghost preparation by (Dodge et al) method. ? Glycosylated hemoglobin was estimated by Ion exchange chromatography. The results were statistically analyzed with student 'T' test.

A case control comparative study was performed with Type2 Diabetes mellitus and normal subject according to criteria.
IV.

8 Results

The present study included a total number of 50 subjects including 25 Type2 Diabetes mellitus cases and 25 normal controls.

Table 1 narrates Malondialdehyde (MDA) levels in RBC membrane and serum levels of Adenosine deaminase (ADA) in Type2 Diabetes mellitus cases and normal controls.

Table ?? narrates HbA1C levels in Type2 Diabetes mellitus cases and normal controls.
V.

9 Discussion

Table 1 show the MDA content of RBC membrane of Type2 DM is significantly increased ($P<0.001$) (4.23 ± 0.21) as compared to normal control groups (3.28 ± 0.19) which clearly exhibits free radical injury due to increased production of Malondialdehyde (MDA) resulting from persistent hyperglycaemia and lipidperoxidation and oxidative stress of the membrane. This is in accordance to the study of Rama Srivastan, Hattice Passagula and SA Mousa 12 .

Table 1, also shows the Adenosine deaminase(ADA) level in the serum of Type2 DM is increased significantly (40.09 ± 9.72) as compared to normal control subjects (21.21 ± 5.72) in our study, which is in accordance with the study of Shivprakash M et al9, Misha sushant et al 11 , and Hoshino T et al8 who observed in their study that Adenosine exerts potent metabolic effects acting through its receptors on various tissues. Adenosine stimulates glycogenolysis, gluconeogenesis and also been observed that hyperglycaemia is associated with increased level of Adenosine deaminase (ADA), which is one of the factor which leads to increased production of oxidative stress by generation of reactive oxygen species(ROS).

Adenosine deaminase(ADA) activity is suppressed, insulin sensitivity may be improved and cellular proliferation, inflammation and T-cell activity all of which are associated with the pathophysiology of insulin resistance can also be affected.

Therefore insulin resistance may have an important relationship with Adenosine deaminase(ADA) activity.

Table ?? shows the HbA1C levels in Type 2 Diabetes mellitus cases are more pronounced. (7.73 ± 0.67) in the control group of HbA1c between 7-8% which is average control of Type2 Diabetes mellitus cases and there by 74% increase of cases with the above Diabetes Mellitus control parameters with mean HbA1c being significant with $P<0.001$ with an average blood glucose level of 168.5 mg/dl.

1

		Malondialdehyde (MDA)	Adenosine	Fasting blood
		nmol/mg protein	deaminase(ADA) IU/L	sugar
				mg/dl
Normal	control	3.28 ± 0.19	21.21 ± 5.72	70
n=25				
Type 2 DM	n=25	$4.23^{***} \pm 0.21$	$40.06^{***} \pm 9.16$	170
Note : 1. Table 2				
HbA1C	Cases no.	Percentage %	Control no.	Percentage %
< 7.0	0	0	25	100
7 -8	17	74	0	0
8 -9	05	20	0	0
9 -10	03	6.0	0	0
Total	25	100	25	100
		7.73 ± 0.67		5.34 ± 0.59

Figure 1: Table 1 PARAMETERS

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