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Study of Oxidative Stress and Its Relation to Glycemic Control in Type 2 Diabetes Mellitus.

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ABSTRACT

Diabetes Mellitus is a metabolic disorder primarily affecting the Carbohydrate metabolism where Glucose is underutilized, leading to hyperglycemia. If Diabetic patients follow rigorous measures to keep their Glucose levels in the normal range much of the complications associated with Type 2 Diabetes Mellitus can be prevented. This study was undertaken to underline the importance of strict glycemic control. Type 2 Diabetic subjects attending the Diabetic O.P of Sree Balaji Medical College and Hospital were recruited for the study. They were compared with age and sex matched Healthy volunteers. Malondialdehyde (MDA) was assayed as a marker of oxidative stress. The results show that whenever the Glycaemic control is low the Oxidative stress marker is high and Vice versa.

Keywords: Glycemic control, oxidative stress, Malondialdehyde, hyperglycemia

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INTRODUCTION

Diabetes Mellitus is a metabolic disorder primarily affecting the Carbohydrate metabolism where Glucose is underutilized, leading to hyperglycemia. Avoiding oral glcaemic drugs is quite common among the diabetics [1]. When there is hyperglycaemia, proteins in the body undergo non enzymatic glycation. Measurement of Glycated proteins; primarily Glycated haemoglobin is effective in monitoring long term glucose control in people with diabetes mellitus. Hyperglycaemia induces oxidative stress. Oxidative stress is defined in general as surplus formation and/or inadequate removal of highly reactive molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) [2].

Free Radicals cause tissue damage by reacting with polyunsaturated fatty acids in membranes and this leads to increase in lipid peroxidation [3]. The occurrence of free radical induced lipid peroxidation causes considerable changes in the structural organization and function of the membrane and makes it leaky [4].

Reactive oxygen species degrade polyunsaturated fatty acids leading to malondialdehyde (MDA) formation [5].

ROS like Hydroperoxides have toxic effects on cells both directly and through degradation to highly toxic hydroxyl radicals. They also react with transition metals like iron or copper to form stable aldehydes such as malondialdehyde that damage cell membranes. Peroxyl radicals can remove hydrogen from lipids, producing hydroperoxides that propagate the free radical pathway further [6]. MDA is a highly reactive aldehyde and is a reactive electrophile species that causes toxic stress in cells and forms advanced glycation end products (7). The plasma lipid peroxidation products increase depending upon the level of glycemic control. The production of this aldehyde is used as biomarker to measure the levels of oxidative stress [8,9]. Peroxidation of membrane lipids leads to formation of MDA resulting in increased membrane rigidity,decreased cellular deformability, reduced erythrocyte survival and lipid fluidity as seen in diabetes mellitus. The raised MDA levels indicate the increased oxidative stress [10].

MATERIALS

A total of ninety three -93 (male 48, female 45) patients with Type 2 diabetes in the age group of 30-50 yrs attending the Diabetic OP of Sri Balaji Medical College & Hospital were recruited for the study and were compared with eighty eight (88) age and sex matched healthy controls (male 33 and female 55).

Inclusion criteria for cases:

- Type 2 diabetic patients in the age group of 30- 50 years.
- Diabetic patients without any associated disorders like hypertension, Ischaemic heart disease as well as any chronic disease which can induce increased oxidative stress.
- Patients under medication for diabetes but not on any antioxidants.

Inclusion criteria for Healthy controls

- Healthy Subjects who were not on any antioxidant supplementation.

Exclusion Criteria for cases

- Patients with any other chronic illness
- Smokers and alcoholics.

Exclusion criteria for Healthy controls

- Smokers and alcoholics.

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Ethical Clearance

Ethical clearance was obtained from the Ethical Clearance Committee of SBMC&H.

METHODS

Fasting Blood sugar (FBS) & Post prandial blood sugar (PPBS) were assayed using the GOD POD method**.**

Glycohemoglobin: Estimated by Ion exchange resin method.

Malondialdehyde was assayed by a spectrophotometric assay of Thio barbituric acid reactive substances.

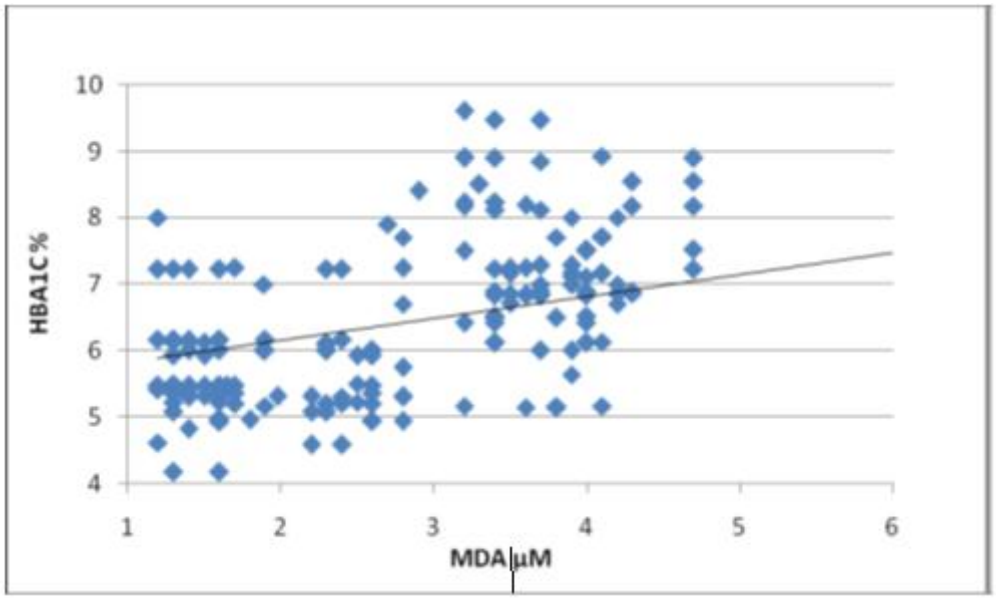
RESULTS

The statistical analysis was done using SPSS Package.The diabetic subjects FBS values are 169.63 +/- 69.43 mg/dl whereas the healthy controls had FBS as 88.22 +/- 13.25 mg/dl . The difference is strongly significant. The p value is <0.001. In our study diabetic subjects had elevated Post prandial blood sugar levels expressed as Mean ± S.D to be 244.46 ± 88.19mg/dl. The healthy controls had values as 112.33 ± 24.35mg/dl with strongly significant p value of < 0.001.The Normal Glycated Hemoglobin levels according to ADA criteria range from 4-5.6%. HbA1C of 6.5% or more is considered Diabetic levels. Glycated Hemoglobin levels expressed as Mean ± S.D in Diabetic patients of our study was 7.22 ± 1.03 whereas in healthy controls it was 5.61± 0.64. The levels show a significant difference between Cases and controls. The values are expressed as Mean+/-S.D.The values in diabetic subjects was 3.61 +/- 0.63 µM/L. In case of healthy controls the MDA levels were 1.93 +/- 1.51 µM/L. p value is < 0.001.

Pearson's correlation of Malondialdehyde vs Glycated Hemoglobin: MDA vs HbA1C

The r value was 0.59 showing a large positive correlation between the two parameters in our study results. Glycated hemoglobin levels reflect the extent of oxidative stress which is evidenced by the MDA levels.

Graph 1: Scatter plot showing the correlation of Malondialdehyde vs Glycated Hemoglobin



DISCUSSION

Significantly increased levels of FBS, PPBS and HbA1c indicate a poor glycaemic control in the diabetic patients. This increase would have been the forerunner of increased glycation of proteins and other

biomolecules. In uncontrolled or poorly controlled diabetes, there is an increased glycation of a number of proteins including hemoglobin. Several studies have reported that Glycated hemoglobin (HbA1c) was found to be increased in patients with diabetes mellitus and the amount of increase is directly proportional to the fasting glucose levels. The level of Glycated hemoglobin is also measured as one of the markers of degree of oxidative stress in Diabetes mellitus [11-16].

There is significant increase in MDA levels among Diabetic patients in comparison to the controls according to our study. The observed increase in malondialdehyde release might be attributed to the increase in peroxidative damage to lipids from oxidative stress in diabetes .There are several studies supporting the theory of increased oxidative stress in diabetes mellitus by way of estimating MDA by TBARS method.

Malondialdehyde rise hints the increased lipid peroxidation due to the increased production of Reactive oxygen species, secondary to chronic hyperglycaemia. Maritim et al have reported the increased oxidative damage manifested as increased MDA levels among patients with Type 2 Diabetes Mellitus [17]. Prabhakar Reddy et al have reported hyperglycemia induced oxidative stress evidenced by increased MDA levels among Diabetic patients [18]. Increased MDA levels among diabetics have also been evidenced in a study report from Pakistan [19], Rama Srivatsan et al have reported increased MDA levels in Diabetics with complication [20]. A study from Gwalior India also shows decreased TAS and Increased MDA levels in Type 2 Diabetes [21].

CONCLUSION

Tight Glycaemic control could prevent the development of Diabetic complications. This would increase the longevity and quality of life of patients with diabetes.

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