ORIGINAL ARTICLE

Correlation Of HbA_{1c} With Vitamin C And Oxidative Stress In Type 2 Diabetes Mellitus

Shilpashree YD[1], Devaki RN[2]

ABSTRACT

Introduction: Diabetes mellitus results from body's inability to produce insulin or use insulin to its full potential, and is characterized by high circulating glucose. The present study was undertaken to evaluate the oxidative stress and antioxidant status and to correlate these with glycaemic control.

Methods: This cross sectional study was carried out in the Department of Biochemistry, JSS Medical College, Mysore. Thirty patients with type 2 diabetes mellitus and 30 unrelated age and sex matched controls were included in the study. Glycated haemoglobin was estimated in whole blood. Serum malondialdehyde and Vitamin C levels were estimated by thiobarbituric acid method and dinitrophenylhydrazine method respectively.

Results: Mean serum malondialdehyde levels were significantly greater in type 2 diabetics. There was a statistically significant negative correlation between serum malondialdehyde and Vitamin C in type 2 diabetics (r = -0.176). Highly significant negative correlation was found between Vitamin C and HbA_{1c} in diabetic controls. (r=-0.168).

Conclusion: There exists an inverse relationship between oxidative stress and antioxidants in type 2 diabetics and is a result of poor glycaemic control.

Keywords: Antioxidant vitamins, diabetes, glycaemic control, lipid peroxidation, oxidative stress.

How to cite this article: Shilpashree YD, Devaki RN. Correlation of HbA_{1c} with Vitamin C and oxidative stress in type 2 diabetes mellitus. International Journal of Contemporary Medical Research. 2015;2(2):382-385

[1]Assistant Professor, Department of Biochemistry, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Karnataka, India. [2]Professor and HOD, Department of Biochemistry, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, Karnataka, India

Corresponding author: Dr. Shilpashree YD, Department of Biochemistry, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Karnataka, India

Source of Support: JSS University, Mysore

Conflict of Interest: None

INTRODUCTION

Diabetes Mellitus (DM) is a result of body's inability to produce insulin or use insulin to its full potential and is characterized by increased glucose in circulation. It affects more than 230 million people worldwide and is the fourth leading cause of mortality globally. Diabetes is a chronic disease and sustained hyperglycaemia affects both microvessels and macrovessels throughout the body. It is the leading cause of blindness and visual impairment, non-injury amputation, and end stage renal disease in adults in developed countries.[1]

One of the commonly suggested pathogenesis in complications of diabetes is oxidative stress, an imbalance between the free radical generation and scavenging system. This imbalance may be due to exaggerated free radical production or decline in antioxidant defense mechanism or both.[2] Hyperglycaemia can induce oxidative stress via glucose oxidation and subsequent formation of advanced glycation end products, altered eicosanoid metabolism and decreased antioxidant defences.[3]

Malondialdehyde (MDA) is a highly toxic product formed by lipid peroxidation by free radicals. Studies have shown that its concentration is considerably increased in DM, correlating with poor glycaemic control.[4]

Vitamin C is a water soluble vitamin and an aqueous phase antioxidant. As an antioxidant it directly reacts with superoxide and hydroxyl radical and other various hydroperoxides. Both ascorbate and ascorbyl radical have redox potential and react with most other biologically relevant radicals. Vitamin C offers the most effective protection against plasma lipid peroxidation.[2] HbA_{1c} is the standard measure of

long-term control of blood glucose level. Glycation is the non-enzymatic addition of a sugar residue to amino group of proteins. Glycated proteins are formed post-translationally from the slow, non-enzymatic reaction between glucose and amino groups of proteins. HbA_{1c} level is not affected by food intake and any recent change in the blood sugar level. Hence, estimation of HbA_{1c} can be very useful in diagnosing diabetes in patients admitted to hospital with random hyperglycemia because it can be done even in random blood samples. One percent reduction in HbA_{1c} is said to decrease chronic complications of diabetes to an extent of 30%.[5]

Very few studies were available among the population of Mysore regarding status of oxidative stress and antioxidant status in type 2 DM. The present study was undertaken to evaluate the serum levels of oxidative stress marker MDA and antioxidant Vitamin C and their correlation with glycaemic control.

MATERIALS AND METHOD

This cross sectional study was done during the period between February 2012 to January 2013, in the Department of Biochemistry, JSS Medical College, Mysore. The study was conducted after obtaining the approval of institutional ethical committee. After explaining the details of the study a written informed consent was taken from all the participants. Thirty participants in the age group 40-80 years were randomly selected from type 2 diabetics who visited the outpatient Department of Medicine of JSS Hospital, Mysore. Participants with acute or chronic infections, fever, anaemia, malignancy, acute and chronic nephritis, cirrhosis, congestive heart failure were excluded from the study. None of the participants were on antioxidant supplementation. Thirty unrelated age and sex matched apparently healthy individuals were included as control participants.

Collection of sample

Fasting, un-haemolysed venous blood (5ml) was drawn from all the participants using universal precautions. 2ml of blood sample collected in EDTA vacutainers was used for estimation of HbA_{1c} in whole blood. 3ml of the blood sample was collected in plain vacutainers, serum was carefully separated and stored at -20^0 C until biochemical analysis and was used to estimate blood glucose, MDA and Vitamin C.

Biochemical analysis

Fasting blood glucose was estimated by GOD-PAP method using RANDOX KIT-GL 3815 in the Randox Imola auto analyser.[6] Assessment of oxidative stress was done by quanitifying the thiobarbituric acid reactivity as MDA in spectrophotometer. [7,8] Vitamin C was measured by 2,4 dinitrophenylhydrazine method.[9] HbA_{1c} was estimated by using RX SERIES HA 3830 KIT in the Randox Imola auto analyzer.[10]

STATISTICAL ANALYSIS

SPSS for windows version-16 (2007) was employed for statistical analysis. Comparison between cases and controls was done using analysis of variance (ANOVA), independent sample's t test and Pearson correlation coefficient test.

RESULTS

The mean values of FBS, MDA, Vitamin C and HbA_{1c} in cases and healthy controls are shown in table-1. The serum MDA level was significantly elevated ($p<0.001$) and the Vitamin C level was significantly ($p<0.001$) decreased in type 2 diabetics compared to controls. Increase in HbA_{1c} level was also significant ($p<0.001$) in type 2 diabetics compared to healthy controls.

Figure 1 shows the correlation between MDA and Vitamin C in cases. There was a significant negative correlation between plasma MDA and Vitamin C in cases ($r=-0.366$). There was a positive correlation (Figure 2) between plasma MDA and HbA_{1c} ($r=0.276$) indicating that as HbA_{1c} increases, MDA also increases. Correlation study revealed inverse relationship (Figure 3) between Vitamin C and HbA_{1c} ($r=-0.314$).

DISCUSSION

In the present study, the serum level of MDA,

Vitamin C was evaluated and its relationship with HbA_{1c} was studied. The values were compared between type 2 diabetics and healthy controls or non-diabetics.

Parameters	Type 2 Diabetics	Healthy Controls
FBS (mg/dl)	124.86±22.09	93.26±8.90
HbA_{1c} (%)	7.7±1.02	5.13±0.54
Vitamin C (mg/l)	9.46±2.84	12.29±3.80
MDA(nmol/ml)	5.05±2.64	1.81±0.61

Table-1: Biochemical parameters in the study participants

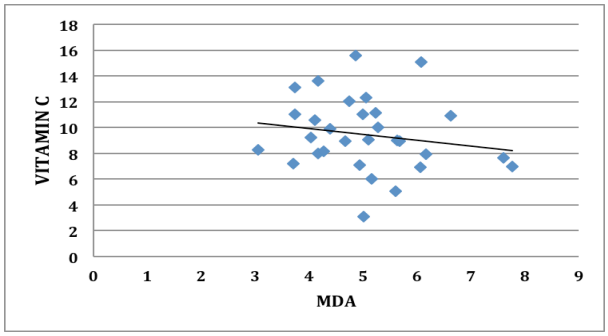

Figure-1: Correlation between MDA and Vitamin C

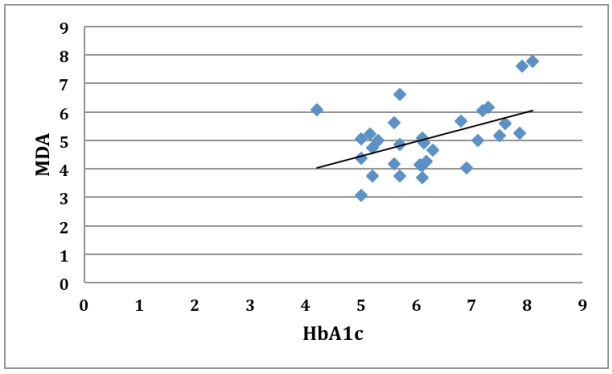

Figure-2: Correlation between HbA_{1c} and MDA

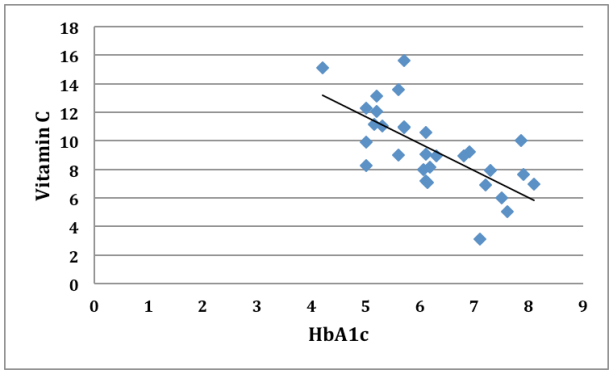

Figure-3: Correlation between HbA_{1c} and Vitamin C

We observed an increase in the level of MDA and significant decrease in antioxidant Vitamin C in type 2 diabetics, suggesting an imbalance of oxidative stress and antioxidant status in diabetes. We also observed a positive correlation between MDA and HbA_{1c} in type 2 diabetics. Findings of the present study are in agreement to previous studies done by peers in the same field of research.[10-12] This elevation of MDA levels may result from hyperglycaemic state that induces overproduction of oxygen free radicals in diabetes.[13]

Pathogenic mechanisms which can cause increased lipid peroxide formation in diabetics include, hyperglycaemia induced glucose auto oxidation, formation of prostaglandin H2 by cyclooxygenase pathway, increased sorbitol pathway activity and formation of non-enzymatic glycation of proteins and lipids.[14] Increased levels of oxidative damage products in serum of diabetic patients' correlates with the development of vascular complications.[15]

Decrease in Vitamin C levels could be due to its increased consumption in the antioxidant defence against elevated lipid peroxidation due to oxidative stress. Other likely mechanism for low Vitamin C is inhibition of ascorbic acid carrier that also transports glucose by the hyperglycaemia of diabetes.[16-18]

The correlation of MDA and Vitamin C with HbA_{1c} shows a positive and negative correlation respectively suggesting that good glycaemic control is essential for proper balance of oxidative and antioxidant status in diabetes.

CONCLUSION

To conclude, increase in oxidative stress measured as high MDA levels and decrease in antioxidant status measured as low Vitamin C levels along with their association with glycaemic control and decreased antioxidant status could lead to the of complications associated with diabetes. Therefore, it appears reasonable to suggest supplementation of Vitamin C to treat elevated oxidative stress and lipid peroxidation that may predispose diabetic patients to complications associated with diabetes. Future research centering on the therapeutic role of antioxidant supplementation may prove worthwhile in diabetes.

REFERENCES

1. Renu AK, Chan P. Oxidative Stress and Diabetic Retinopathy. Exp Diabetes Res 2007;2007:43603.
2. Moussa SA. Oxidative stress in diabetes mellitus. Romanian J Biophys 2008;18: 225-36
3. Mehta SR, Kashyap AS, Das S. Diabetes Mellitus in India: The Modern Scourge. Med J Armed Forces India 2009;65:50-4.
4. Jakus V. The role of free radicals, oxidative stress and antioxidant system in diabetic vascular diseases. Bratesl Lek Listy 2000;101:541-51.
5. Bunn HF. Nonenzymatic glycosylation of protein: relevance to diabetes. Am J Med 1981;70:325-30.
6. Sacks DB. Carbohydrates. 4th ed. In: Teitz Textbook of Clinical Biochemistry, Burtis CA, Ashwood ER, Burns DE, eds. Philadelphia: WB Saunders; 2006. pp. 837-901
7. Kurnet D, Tappe KJ. Effect of vitamin E, Ascorbic acid and mannitol on alloxan induced lipid peroxidation in rats. Arch. Biochemistry and Biophysics 1982;216: 204-12.
8. Erum SK. Lipid peroxide in cerebrovascular disorder determined by a new colorimetric method. Clin Chem Acta 1978;90:37-43.
9. Mustafa K, Yavuz S, Selim K. The vitamin A, retinol binding protein, β carotene and zinc Concentration in children with insulin dependent diabetes mellitus. Gazi Med. J 1995;6:71-4.
10. Bansal V, Kalita J, Misra UK. Diabetic neuropathy. Postgrad Med J 2006; 82:95-100.
11. Pasupathi P, Chandrasekar V, Kumar US. Evaluation of OS, antioxidant and thyroid hormone status in patients with diabetes mellitus. J Medicine 2009; 10:60- 66.
12. Rani HS, Madhavi G, Rao VR, Sahay BK, Jyothy A. Risk factors for coronary heart disease in type ii diabetes mellitus. IJCB 2005; 20:75-80.
13. Srivatsan R, Das S, Gadde R, Kumar KM, Taduri S, Rao N et.al. Antioxidants and Lipid Peroxidation Status in Diabetic Patients with and without Complications. Arch Iranian Med 2009;12:121 – 127.
14. Maritim AC, Sanders RA, Watkins JB. Diabetes, OS, and antioxidants: a review. J Biochem Mol Toxicol 2003; 17: 24–38.
15. Kesavulu MM, Rao R, Giri R, Vijaya J, Subramanyam G, Apparao C. Lipid peroxidation and antioxidant enzyme status in type 2 diabetics with coronary heart disease. Diab Res Clin Pract 2001;53: 33-39.
16. Ramakrishna V, Jailkhani R. Evaluation of OS in Insulin Dependent Diabetes Mellitus (IDDM) patients. Diagn Pathol. 2007;2:22.
17. Kapeghain JC, Verlangieri AJ. The effects of glucose on ascorbic acid uptake in heart endothelial cells: possible pathogenesis of diabetic angiopathies. Life Sci 1984; 34:577-84.
18. Jain A, Manjunath RGS, Saxena P, Mishra N. Diabetes and its association with periodontal tissues. International Journal of Contemporary Medical Research 2015;2(1):79-85.