Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

ORIGINAL RESEARCH

Comparison Of Oxidative Stress Level In Diabetes Mellitus As Compare To Normal Individual

[1]Mohd Nadeem, [2]Balwinder Kaur, [3]Sachin Agarwal

[1]Assistant Professor, [3]Associate Professor, Department of General Medicine, Rajshree Medical Research Institute, Bareilly, Uttar Pradesh, India
[2]Deputy CMO Ambala, Haryana, India

Correspondence:
Sachin Agarwal
Associate Professor, Department of General Medicine, Rajshree Medical Research Institute, Bareilly, Uttar Pradesh, India
Email: dksbly521999@gmail.com

Abstract

Introduction: Diabetes mellitus is one of the common metabolic disorders characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism due to absolute or relative deficiency of insulin secretion or its action. The present study has been undertaken to determine the oxidative stress by measuring the antioxidant levels in diabetes mellitus patients. The level HbA1C, Malondialdehyde (MDA) and uric acid concentration in serum of normal and diabetic subjects has been studied.

Material and method: A total of 100 participants were taken in this study. Venous blood was drawn from the antecubital vein from each patient. The blood samples were then transported to the central laboratory within an hour of collection for analysis. HbA1c was measured using Nycocard reader, MDA was measured by semi automated analyser and serum uric acid was analysed by using fully automated analyser and test value were recorded for further analysis.Statistical analysis of collected data has been determined by using SPSS (16.0). P value <0.05 was considered as statistically significant.

Results: Statistically significant differences were observed in the mean HbA1C level of diabetic patient (8.2± 2.7 %) and normal Individuals (4.17± 0.7 %). (p = 0.001) and other parameters such as MDA and Uric acid also indicate elevated level in diabetic patients.

Conclusion: From this study we can conclude knowing the inter-relation between hyperglycemia and parameters like HbA1C, MDA and Uric acid can provide useful information about the degree of oxidative stress and antioxidant level in human body. This can be beneficial during treating patients

Key words: Diabetes mellitus, MDA, HbA1c, Uric acid, Oxidative stress, ROS

Introduction

Diabetes mellitus is one of the common metabolic disorders characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism due to absolute or relative deficiency of insulin secretion or its action[(1)]. People with diabetes mellitus are at an increased risk of chronic complications which affect many organ systems. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome[(2)].It is a well-established fact that diabetes is a risk factor for cardiovascular disease[(3,4)]. While microvascular complications of diabetes include nephropathy and retinopathy, macrovascular complications resulting in atherosclerotic

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

cardiovascular disease such as coronary artery disease, cerebrovascular disease and peripheral vascular disease are the leading cause of death in the diabetic population [5,6]. The Diabetes Control and Complications trial (DCCT) demonstrated that tight control of blood glucose is effective in reducing clinical complications significantly,but even optimal control of blood glucose could not prevent complications suggesting that alternative treatment strategies are needed [6]. As per estimate of the International Diabetes Federation (IDF), the total number of people in India with diabetes which was around 50.8 million in 2010 would be 87.0 million by 2030[7]. Oxidative stress plays a major role in cellular injury from hyperglycemia. High glucose level can lead to free radical production. Weak defense system of the body becomes unable to counteract the enhanced ROS generation and as a result condition of imbalance between ROS and their protection occurs which leads to domination of the condition of oxidative stress[8].Oxidative stress is defined as a state in which oxidation exceeds the capacity of antioxidant systems in the body secondary to a loss of the balance between them. It not only causes hazardous events such as lipid peroxidation and oxidative DNA damage, but also physiologic adaptation phenomena and regulation of intracellular signal transduction[9]. Studies have demonstrated that hyperglycemia-induced oxidative stress led to the activation of mitogen-activated protein kinase (MAPK), which may have contributed to neuronal pathogenesis[10,11].Increased oxidative stress as well as reduction in antioxidant capacity could be related to the complications in patients with diabetes such as oxidative DNA damage and insulin resistance. On the other hand Uric acid (UA) is the end product of the purine metabolism. The association between the blood glucose and the serum uric acid levels has been known for quite sometime[12]. A positive association between the serum uric acid levels and the development of type 2 diabetes mellitus (T2DM) has been reported[13]. In individuals with an impaired glucose tolerance, an elevated serum uric acid (SUA) level was found to increase the risk for developing T2DM [14]. Uric acid can act as a prooxidant and it may thus be a marker of oxidative stress, but it may also have a therapeutic role as an antioxidant[15]. Urate, the soluble form of uric acid, can scavenge the superoxide and the hydroxyl radicals and it can chelate the transition metals [16]. Hyperuricaemia has been also added to the set of metabolic abnormalities which are associated with insulin resistance and/or hyperinsulinaemia in the metabolic syndrome[17]. While an increase in the uric acid levels in prediabetes and diabetes was demonstrated by some studies, a declining trend of the serum uric acid levels with increasing blood glucose levels was observed by other research workers[18].Taking into consideration of above points, the present study has been undertaken to determine the oxidative stress by measuring the antioxidant levels in diabetes mellitus patients. The level HbA1C, Malondialdehyde (MDA) and uric acid concentration in serum of normal and diabetic subjects has been studied.

Material and method

A total of 100 participants were taken in this study. Out of which 50 were normal age matching control and 50 were known cases of diabetes mellitus. Patients were identified by the principal investigator general OPD of hospital. Complete history and physical examination were taken to confirm diagnosis and cases were also confirmed from treating doctors. If participants meet the inclusion criteria, informed written consent was taken from the participant after explaining to him or her about the study. Venous blood was drawn from the antecubital vein from each patient. The blood samples were then transported to the central laboratory within an hour of collection for analysis. HbA1c was measured using Nycocard reader, MDA was measured by semi automated analyser and serum uric acid was analysed by using fully automated analyser and test value were recorded for further analysis.

Statistical analysis of collected data has been determined by using SPSS (16.0). The results of laboratory tests of this study have been summarized as mean ± standard deviation. Mean

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

difference (both participating groups) have be analysed by using student's t-test and chi-square test was used to show the co-relation. P value <0.05 was considered as statistically significant.

Inclusion criteria

For Cases:

1. Clinically confirmed cases of diabetes.

Control

1. Age matching normal individual
2. Patient having no history of cardiovascular disease.
3. Patients with no history of CKD.

Exclusion criteria

1. Patients with associated history of acute illness
2. Pregnant women
3. Recent surgery

Result

Comparison of HbA1C level between controls and patients of diabetes mellitus by Student's t-test

Parameter	Diabetic Patients (n=50) Mean ± SD	Control group (n=50) Mean ± SD	p-value
HbA1C %	8.2± 2.7	4.17± 0.6	0.001

Statistically significant differences were observed in the mean HbA1C level of diabetic patient (8.2± 2.7 %) and normal Individuals(4.17± 0.7 %). (p = 0.001)

Comparison of Serum uric acid between controls and patients of diabetes mellitusby Student's t-test

Parameter	Diabetic Patients (n=50) Mean ± SD	Control group (n=50) Mean ± SD	p-value
Serum uric acid (mg/dl)	8.78 ± 2.1	5.4± 1.7	0.001

Statistically significant differences were observed in the mean serum uric acid level of diabetic patients(8.78± 2.1mg/dl) and normal Individuals (5.4± 1.7). (p = 0.001)

Comparison of serum MDA level between controls and diabetic patient by Student's t-test

Parameter	Diabetic patients (n=50) Mean ± SD	Control groups (n=50) Mean ± SD	p-value
Serum MDA nmol/dl	430± 23.1	195± 14	0.001

Statistically significant differences were observed in the mean serum MDA level of diabetic patients (430± 23.1nmol/dl) and normal Individual(195 ± 14 nmol/dl). (p = 0.001)

Tabular representation showing Pearson correlation coefficient (r) and p-value

Parameters	r- value	p-value
HbA1c and MDA(in Cases)	0.510	0.001
HbA1c and MDA(in Control)	0.027	0.007

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

HbA1c and Uric acid(in Cases)	0.417	0.002
HbA1c and Uric acid(in Control)	0.123	0.05

After applying Pearson's correlation coefficient it was found that there is a positive correlation between serum MDA and HbA1C level (r = 0.510) in cases and slight positive correlation in controls at the significant level (p=0.007). Similarly, uric acid also shows positive relation in cases and control (r=-0.417), (r=0.123) at the significant level (p=0.002) and (0.05) respectively. According to the result of this study we can state both uric acid and MDA level are increase in diabetic patients in relation to HbA1C. So, monitoring of these parameters and its treatment can influence the better health of an individual.

Discussion

Diabetes mellitus is characterized by hyperglycemia resulting from defects in insulin secretion and insulin action or both. Hyperglycemic condition is known to generate ROS, which in turn cause damage to the cells in many ways that leads to secondary complications in diabetes mellitus[19].The lipid peroxidation product, MDA has been recognized as a primary biomarker of free radical mediated lipid damage and oxidative stress[20].On the other handUA is also a physiological free radical scavenger and one of the major contributors of the plasma antioxidant capacity. Thus, UA plays a dual role, both as a prooxidant and as an antioxidant[21,22]. T2DM is associated with oxidative stress and increased free radical formation[23]. Under the condition of increased oxidative stress, there occurs the depletion of the local antioxidants, which causes a reduction in the antioxidant status of the body [24]. In thisstudy, the MDA levels have been measured in diabetic and healthy control subjects. Higher level of MDA in diabetic subjects were observed which could be attributed to higher ROS.Increased level of MDA in diabetics suggests that peroxidative injury may be involved in the development of diabetic complications. The increase in lipid peroxidation is also an indication of decline in defense mechanisms of enzymatic and non-enzymatic antioxidants[25].Clinical studies have reported that significantly higher lipid peroxidation is associated with high glucose levels as observed by the fasting glucose and HbA1c levels[26].The plasma antioxidant level is significantly lower in diabetic subjects with poor glycaemic control than healthy subjects, while patients with good glycaemic control had plasma antioxidative values similar to controls. Another study has reported significant reduction in biological antioxidant potential in sciatic nerve homogenates of diabetic animals[27].The increased level of oxidative stress biomarkers such as MD in diabetic patients accompanied with decreased level of non enzymatic antioxidants such uric acid were observed in the present work could cause complications in patients leading to oxidative damage to proteins, lipid and nucleic acids. This may also cause insulin resistance in type 2 diabetic patients[28].Therefore, earlier identification of these markers in diabetes mellitus patient can play a life saving role to patients.

Conclusion

From this study we can conclude knowing the inter-relation between hyperglycemia and parameters like HbA1C, MDA and Uric acid can provide useful information about the degree of oxidative stress and antioxidant level in human body. This can be beneficial during treating patients.

Reference

1. Shah PB, Acharya A, Shrestha S et al. Role of HbA1c and microalbumin as an early risk marker of diabetic nephropathy. Int J Health Sci Res. 2017; 7(2):141-145.
2. American Diabetes Association (2010) Diabetes Care, 33: S62-S68.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

3. Pyorala K, Laakso M, Uusitupa M: Diabetes and atherosclerosis: an epidemiologic view. *Diabetes Metab Rev* 1987, 3(2):463-524.
4. Laakso M: Hyperglycemia and cardiovascular disease in type 2 diabetes. *Diabetes* 1999, 48(5):937-942.
5. American Diabetes Association: National diabetes fact sheet. 2002 [http://www.diabetes.org/diabetes-statistics.jsp].
6. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin dependent diabetes mellitus. *N Engl J Med* 1993, 329 (14):977-986.
7. Ramachandran A, Das AK, Joshi SR, Yajnik CS, Shah S, Kumar KMP. Current status of diabetes in India and need for novel therapeutic agents. J AssocPhysc India 2010;58: 7-9.
8. Halliwell B, Gutteridge J Free Radicals in Biology and Medicine. Oxford University Press, New York, NY, USA. 2007.
9. Yoshikawa T. Science of free radicals. KoudanShaSaientifikku, Tokyo. 1997.
10. Wang X, Martindale JL, Liu Y, Holbrook, NJ. The cellular response to oxidative stress: influences of mitogen activated protein kinase signalling pathways on cell survival. Biochem J 1998; 333: 291-300.
11. Purves T, Middlemas A, Agthong S, Jude EB, Boulton AJ, Fernyhough P *et al*., A role for mitogen-activated protein kinases in the etiology of diabetic neuropathy. FASEB J 2001; 15: 2508-2514.
12. Herman JB, Medalie JH, Goldbourt U. Diabetes, prediabetes and uricaemia.*Diabetologia*.1976;12(1):47–52.
13. Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. The association between serum uric acid and the development of type 2 diabetes mellitus. *A meta-Analysis. Diabetes Care*. 2009;32(9):1737-42
14. Caroline K, Denise V, Simerjot K, Elizabeth B. The serum uric acid levels improve the prediction of the incident type 2 diabetes in individuals with impaired fasting glucose levels. *The Rancho Bernardo Study. Diabetes Care*.2009;32(7):1272-73.
15. Patterson RA, Horsley E TM,Leake DS. The prooxidant and the antioxidant properties of the human serum ultrafiltrates towards LDL: the important role of uric acid. *J Lipid Res*. 2003;44(3):512–21
16. Ames BN, Cathcart R, Schwiers E, Hochstein P. Uric acid provides an antioxidant defence mechanism in humans against oxidants and radicals which cause aging and cancer: a a hypothesis. *Proc Natl AcadSci USA* 1981;78:6858-62.
17. Nakagawa T, HuH, Zharikov S, Tuttle KR, Short RA, Glushakova O, et al. A causal role of uric acid in the fructose- induced metabolic syndrome. *Am. J. Physiol. Renal. Physiol*. 2005;290:F625-31.
18. Nan H, Dong Y, Gao W, Tuomilehto J, Qiao Q. Diabetes, which was associated with a low general Chinese population. *Diabetes Res and ClinPract*.2007;76:68–74.
19. Jaganjac M, Tirosh O, Cohen G, Sasson S, Zarkovic N. Reactive aldehydes second messengers of free radicals in diabetes mellitus. Free Radical Res 2013; 47: 39-48.
20. Shodehinde SA, G Oboh. (2013) Antioxidant properties of aqueous extracts of unripe Musa paradisiaca on sodium nitroprus- side induced lipid peroxidation in rat pancreas in vitro. Asian Pac J Trop Biomed 2013; 3:449–457.
21. Bagnati M, Cristina P, Cristiana CAU, Roberta B, Emanuele A, Giorgio B. When and why a water-soluble antioxidant becomes pro-oxidant during a copper-induced, low-density lipoprotein oxidation : a study which was done by using uric acid. *Biochem J*. 1999; 340: 143-52.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 07, 2022

22. Strasak AM, Rapp K, Hilbe W, Oberaigner W, Ruttmann E, Concin H. The role of serum uric acid as an antioxidant which protects against cancer: a prospective study in more than 28 000 old Austrian women. *Ann Oncol*2007;18:1893-97.
23. Maritim AC, Sanders RA, Watkins JB. Diabetes, oxidative stress, and antioxidants: a review. *J BiochemMolToxicol*; 2003;17:24-38.
24. Bonnefont-Rousselot D and associates. Consequences of the diabetic status on the oxidant/antioxidant balance. *Diabetes Metab (Paris)*. 2000;26:163-76
25. Saddala RR, Thopireddy L, Ganapathi N, Kesireddy SR. Regulation of cardiac oxidative stress and lipid peroxidation in streptozotocin-induced diabetic rats treated with aqueous extract of *Pimpinellatirupatiensis*tuberous root. ExpToxicolPathol 2013; 65: 15-19.
26. Catanzaroa O, Capponia JA, Michielia J, Labala, Martinoa ID, Sirois P. Bradykinin B1 antagonism inhibits oxidative stress and restores Na+, K+ ATPase activity in diabetic rat peripheral nervous system, Peptides 2013; 44: 100-104.
27. Turk A, Nuhoglu I, Mentese A, Karahan SC, Erdol H, Erem C. The relationship between diabetic retinopathy and serum levels of ischemia modified albumin and malondialdehyde. Retina 2011; 31:602–608.
28. Lodovicia M, Giovannellia L, Pitozzia V, Bigaglia E, Bardinib G, Rotellab CM. Oxidative DNA damage and plasma antioxidant capacity in type 2 diabetic patients with good and poor glycaemic control. Mutat Res 2008; 638:98-102.