SERUM ADENOSINE DEAMINASE ACTIVITY – DOES IT PREDICT GLYCAEMIC STATUS IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Diabetes mellitus (DM) is a metabolic disorder characterised by chronic hyperglycemia resulting from deficiency of insulin or insulin resistance. Adenosine Deaminase [ADA] is an enzyme involved in purine nucleoside metabolism and plays a vital role in maintaining adenosine concentration. Oxidative stress gets more pronounced in chronic hyperglycemia which further increases ADA activity aggravating insulin resistance. Recently, growing evidence suggests an association of uric acid with diabetes mellitus. The current study is an attempt to assess ADA as a predictor of glycaemic status and to evaluate the role of serum uric acid levels in type 2 Diabetes mellitus [T2 DM].

AIM AND OBJECTIVES

To determine the activity of serum ADA and uric acid levels in type 2 diabetes patients and correlate them with HbA_1c.

MATERIALS AND METHODS

A cross sectional study was done on 135 subjects and were divided into 3 groups. Group A: 45 normal healthy adults, Group B: 45 Type 2 Diabetes mellitus patients with HbA_1c <7% and Group C: 45 Type 2 Diabetes mellitus patients with HbA_1c >7%. Serum ADA, HbA_1c, fasting and postprandial blood glucose and uric acid levels were measured.

RESULTS

In our study, fasting blood glucose [FBG], post prandial blood glucose [PPBG], HbA_1c, ADA, uric acid were found to be increased in group B. In group C, FBG, PPBG, HbA_1c, ADA were increased except uric acid level which is decreased compared to group B. A bell shaped curve was obtained when mean serum uric acid levels of all the three groups were observed.
A significant positive association was found between serum ADA and HbA_1c in group B ($r=0.405$, $p=0.006$) and group C ($r=0.465$, $p=0.001$). A positive correlation was observed between uric acid and HbA_1c in group B which was not statistically significant ($r=0.199$, $p=0.189$), whereas a significant negative correlation was observed between uric acid and HbA_1c in group C ($r= -0.3$, $p=0.046$).

CONCLUSION

From the present case control study, it is concluded that there was an increase in serum Adenosine deaminase activity with increase in HbA_1c. Raised serum uric acid was observed with moderately raised levels of HbA_1c [<7%], but Uric acid levels lowered with further increases in HbA_1c [>7%].

KEYWORDS

Adenosine Deaminase, Uric acid, HbA_1c, Type 2 Diabetes Mellitus.

HOW TO CITE THIS ARTICLE: Kandaswamy VC, Rangasamy S, Panneerselvam S. Serum adenosine deaminase activity – does it predict glycaemic status in type 2 diabetes mellitus. J. Evid. Based Med. Healthc. 2016; 3(28), 1288-1291.
DOI: 10.18410/jebmh/2016/296

INTRODUCTION: Diabetes mellitus is the most prevalent endocrine disorder characterised by metabolic derangements and long term complications.

Financial or Other, Competing Interest: None.
Submission 14-03-2016, Peer Review 28-03-2016,
Acceptance 04-04-2016, Published 06-04-2016.
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DOI: 10.18410/jebmh/2016/296

The incidence of type 2 diabetes mellitus across the world is increasing and is becoming a major health problem in many countries. It is calculated that 80 million people in India would be having Diabetes by the year 2030.[1] Long term blood glucose level is assessed by HbA_1c. The HbA_1c reflects blood glucose level of previous 8–10 weeks. It is formed by two steps by non-enzymatic reaction.[2]

ADA is an enzyme, catalysing irreversible deamination of adenosine and 2 deoxyadenosine to inosine and 2 deoxyinosine in purine catabolic pathway. Both inosine and

deoxyinosine are converted to hypoxanthine, xanthine and finally to uric acid.[3,4] ADA also plays a vital role in lymphocyte maturation and activation. High lymphocyte ADA activities were found in diseases with cell mediated immune response. Immunological disturbances in Type 2 diabetes mellitus have an association with cell mediated immunity. In studies conducted in India, it has been reported that increased ADA activity is seen in patients with type 2 diabetes mellitus.[3]

Uric acid is the end product of purine metabolism.[5,6] There is a biochemical interaction between glucose and purine metabolism. Serum uric acid status in type 2 DM varies between different studies, but no conclusive results could be established. Due to this lacunae, the present study aims at estimating serum ADA and uric acid levels and its correlation with HbA_1c in type 2 diabetes mellitus patients.

MATERIALS AND METHODS: This study was a hospital based case control study conducted during the year May 2015 to December 2015. The cases were selected from the outpatient and inpatient department of Vinayaka Missions Kirupananda Variyar Medical College hospital, Salem, Tamilnadu, India. Forty five healthy individuals were selected as controls form Group A, Forty five type 2 Diabetes mellitus with HbA_1c <7% form Group B. Forty five type 2 Diabetes mellitus with HbA_1c >7% form Group C.

Inclusion Criteria: Type 2 diabetes mellitus cases were included for the study. Type 2 diabetes mellitus patients were either newly diagnosed or old patients on treatment with oral hypoglycaemic drugs.

Exclusion Criteria: Patients on insulin treatment, gestational diabetes mellitus, haemolytic anaemia, Hb variants, uricosuric drugs, chronic diseases such as tuberculosis, rheumatoid arthritis, gout, renal failure, immunological disorders which alters ADA level were excluded from the study.

Institutional ethical committee clearance was obtained. Written informed consent was taken from the study subjects. All study subjects were interviewed using a questionnaire containing age, gender, family history, duration of diabetes and drug history.

Biochemical Analysis: After 12 hours of fasting, 4 ml of blood sample was collected for biochemical parameter quantification and 2ml was collected for postprandial blood glucose analysis. The blood samples were subjected to centrifugation at 3000 rpm for 10 minutes for separation of plasma and serum. The plasma thus obtained was analysed for biochemical parameters such as glucose, serum for adenosine deaminase and uric acid using a semi-autoanalyser. The ADA levels were estimated by enzymatic method. This procedure is based on Purine nucleoside phosphorylase and Xanthine oxidase method. Adenosine deaminase hydrolyse adenosine to ammonia and inosine. Inosine is converted to hypoxanthine by purine nucleoside phosphorylase. Hypoxanthine is then converted to uric acid and hydrogen peroxide by xanthine oxidase. H_2O_2 is further reacted with N-Ethyl–N-3- methylaniline and 4-amino-antipyrine in the presence of peroxidase to generate Quinone dye which is measured. Glucose is estimated by Glucose oxidase peroxidase method. Uric acid is estimated by Uricase peroxidase method and HbA_1c by Ion exchange resin method.

STATISTICAL ANALYSIS: The statistical analysis was performed using the SPSS software version. Differences between the groups were analysed by student t test. Pearson correlation analysis was used to find out the relationship of HbA_1c with ADA and Uric acid within the groups. P value <0.05 was taken as significant.

RESULTS: Table 1 shows the comparison of mean and the standard deviation of biochemical parameters - fasting blood glucose, post prandial blood glucose, HbA_1c, ADA and uric acid levels between the study groups. Table 2 shows Pearson correlation analysis of ADA with fasting blood glucose, post prandial blood glucose, HbA_1c and uric acid in all the three groups. Table 3 shows the Pearson correlation analysis of HbA_1c and Uric acid in group A, group B and group C.

Parameter	Group A	Group B	Group C	P Value		
				Group A & B	Group A & C	Group B & C
Fasting Blood Glucose (FBG) (mg/dl)	89.8±11.27	163.11±41.02	231.49±64.61	<0.001	<0.001	<0.001
Post prandial blood Glucose (PPBG) (mg/dl)	122.29±12.74	326.4±43.80	403.44±53.74	<0.001	<0.001	<0.001
HbA1c (%)	5.13±0.42	6.35±0.44	9.25±1.54	<0.001	<0.001	<0.001
Adenosine deaminase (ADA) level (U/I)	18.25±4.75	29.16±8.55	43.29±12.56	<0.001	<0.001	<0.001
Uric Acid (mg/dl)	5.16±1.03	6.42±0.88	4.66±0.76	<0.001	<0.001	0.0277

Table 1: Comparison of data in study groups

Correlation between		Group A	Group B	Group C
Serum ADA(U/I)and FBG(mg/dl)	Correlation coefficient r	0.246	0.612	0.462
	Significance (P value)	0.103	<0.001	<0.001
Serum ADA(U/I) and PPBG (mg/dl)	Correlation coefficient r	0.074	0.649	0.523
	Significance (P value)	0.631	<0.001	<0.001

Serum ADA(U/I) and HbA1c (%)	Correlation coefficient r	0.116	0.405	0.465
	Significance (P value)	0.448	0.006	<0.001
Serum ADA(U/I) and Uric Acid(mg/dl)	Correlation coefficient r	0.072	0.503	-0.537
	Significance (P value)	0.638	<0.001	<0.001

Table 2: Correlation of ADA with Biochemical parameters

		HbA1c (%)		
		Group A	**Group B**	**Group C**
Uric Acid (mg/dl)	Correlation coefficient r	0.162	0.199	-0.3
	Significance (P value)	0.287	0.189	0.046

Table 3: Correlation of Uric acid with HbA1c

Statistical analysis showed, Adenosine deaminase activity was significantly increased in patients with type 2 diabetes mellitus compared with the control group and increase was more in Group C (43.29±12.56 U/L) compared to Group B (29.16±8.55 U/L). Uric acid level is increased in group B (6.42±0.88 mg/dl) but the levels were decreased in group C (4.66±0.8 mg/dl). The mean uric acid levels showed a bell shaped curve among the three groups.

Pearson correlation analysis showed a significant positive association between serum ADA and HbA_1c in group B and group C. A positive correlation was observed between uric acid and HbA1c in group B(r=0.199) which was not statistically significant (p=0.189), whereas a significant negative correlation was observed between uric acid and HbA_1c in group C. (r= -0.3, p=0.046).

DISCUSSION: Diabetes mellitus is a metabolic disorder characterised by chronic hyperglycaemia resulting from genetic, environmental factors, insulin resistance and defective secretion of insulin. Globally, it has been estimated that 438 million people will be affected with type 2 DM in 2030.[7]

In the present study, serum ADA activity is increased in patients with type 2 diabetes mellitus and it further increased in type 2 DM with poor glycaemic control. Serum ADA level had a significant positive correlation with FBS, PPBS and HbA_1c in type 2 diabetes mellitus patients. This correlation was specifically strong in diabetes patients with poor glycaemic control which is similar to the findings of Hosino et al.[8] Adenosine is needed for the uptake of glucose by the cells. In diabetes mellitus increase of ADA activity will deplete adenosine, thus glucose uptake by the cells are affected.[9] Also, chronic hyperglycaemia increases free radical activity and reactive oxygen species formation, resulting in the elevation of ADA.[10-13] Another reason behind the increase of ADA activity is increased expression due to inflammation in diabetes mellitus.[14]

When serum Uric acid levels were compared within the three groups, Group A and Group C study subjects had lower serum uric acid levels compared to group B. Although group B levels were higher than group A and group C, they were well within the physiological range. It probably reflects the biochemical interaction between serum glucose and purine metabolism. The probable reasons for the decreased uric acid level in group C may be (1). Increased excretion of uric acid in type 2 DM patients due to hyperglycaemia and glycosuria[15] (2). More oxidative stress leading to a decrease of the antioxidant, uric acid. Uric acid exerts its antioxidant function in T_2DM by improving beta cell function and thus, stimulates insulin secretion.[16-18]

Choi et al[19] and Kaur et al,[20] concluded serum uric acid level increased with HbA_1C <7% and then serum uric acid decreased with increase of HbA_1c >7%.

Further studies are required to confirm the antioxidant role of uric acid in diabetes mellitus. The limitation of the present study is that this is a hospital based study, whereas community based study yields more information. The number of participants can be increased to confirm the present study findings.

CONCLUSION: Serum ADA level increases with increase in HbA_1c and can be used to determine the glycaemic status of type 2 diabetes mellitus patients. Serum uric acid increases with moderately increasing levels of HbA_1c and then decreases with further increases in HbA_1c. Thus, Serum uric acid may serve as a potential marker of deterioration of glucose metabolism.

REFERENCES:

1. Havilah I, Pandit Vinodh B, Durga Prasad K. Adenosine Deaminase Activity in Type-2 Diabetes Mellitus- An Independent Marker of Glycemic Status and Stimulator of Lipid Peroxidation. Int J. Chem and Life Sciences. 2013; 2(6); pg.1175-8.
2. Santigo JV, Davis JE and Fisher F. Haemoglobin A1c levels in diabetic detection. J Clin Endocrinol 1978; 47: pg.578-81.
3. Mon Mohan Boro, Deepika Lahon, Barnali B Thakur. A study of serum deaminase activity in type 2 diabetes mellitus with and without complications and its correlation with serum uric acid level in glycemic control. Indian Journal of Basic and Applied Medical Research. December 2015; 5(1), Pg.619-633.
4. Nisha Subhashchandra Ramani, Krishnamurthy N, Raghavendra Prasad B N, Ashakiran S et al. Role of Adenosine Deaminase to Predict Glycemic Status in Type 2 Diabetes Mellitus. J Clin Biomed Sci 2012; 2 (3); pg.123-133.
5. Nagendra.S, Kashirnath R.T, Srinivas. Hyperuricemia in Type 2 Diabetes Mellitus. Global Journal of Medical Research: B Pharma, Drug Discovery, Toxicology and Medicine. 2014;14(3); pg.18-24.
6. Sahiba Kukreja, Amandeep Kaur, Namrata Chhabra, Manmeet Kaur. Relationship between serum uric acid levels and glycaemic control in patients of type 2 Diabetes Mellitus. Journal of Medical Science & Technology. 2012;1(3); pg.3-8.

7. Dr Shivam Khare, Dr Jogesh Kumar Vishandasani, Dr Archna Kansal. To Study Serum Uric Acid In Type 2 Diabetes Mellitus Patient. IOSR Journal of Dental and Medical Sciences. Sep 2015; 14(9) Ver III;Pg.82-86.
8. Hoshino T,Yamada K,Masuoka K et al. Elevated adenosine deaminase activity in serum of patients with DM. Diabetes Res Clin Pract.1994;25;Pg.97–102.
9. Dr. A. Poddar, Dr. S. Das, Dr. B. Singh, Dr. A. K. Sahoo et al., Serum Adenosine Deaminase Activity- A promising Glycemic Marker in Uncomplicated Type 2 Diabetes Mellitus. International Journal of Pharmaceutical Research and Bio science. 2015; Vol 4(2);Pg.71-79.
10. Gohel MG, Sirajwala HB, Kalaria TR, Kamariya CP. A study of serum adenosine deaminase level in patient with type 2 diabetes mellitus and its correlation with glycemic control.International journal of medical and applied sciences.2013;2(3);pg.259-267.
11. M. N. Vanitha Gowda, K. C. Vasudha, S Reshma, K. J. Sujatha. Serum Adenosine Deaminase activity in type 2 Diabetes Mellitus Patients. International Journal of Diabetes in Developing Countries. September 2012;32;pg 176-181.
12. Priti Singh, Salman Khan, Mittal Rabindra Kumar. Adenosine Deaminase Activity and its Relation with Glycated Hemoglobin and Uric Acid in Type 2 Diabetic Patients. Iranian journal of diabetes and obesity. 2013; 5(1).pg1-6.
13. Bhavithapatel, Dilip Taviad, Brahmareddy Malapti, Mitul Chatriwata et al. Serum Adenosine Deaminase in patients with Type 2 Diabetes Mellitus and its Relation with Blood Glucose and Glycated Haemoglobin levels. Int Journal of Biomedical Research. 2014;Vol 14(9);Pg.556-558.
14. Amandeep Kaur, Sahiba Kukreja, Naresh MAlhotra, Neha. Serum Adenosine Deaminase Activity and its Correlation with Glycated Haemoglobin Levels in Patients of Type 2 Diabetes Mellitus. Journal of Clinical and Diagnostic Research. 2012 April;Vol-6(2);Pg.252-256.
15. Sudhindra Rao M, Bino John Sahayo. A Study of Serum Uric Acid in Diabetes Mellitus and Pre-Diabetes in a South Indian Tertiary Care Hospital. Nitte University Journal of Health Sciences. 2012; Vol 2 (2). Pg.18-23
16. Muhammad Fahmi Hidayat, Santi Syafril, Dharma Lindarto. Elevated Uric Acid level Decreases glycated hemoglobin in type 2 DiabetesMellitus. Universa Medicina. 2014;Vol 33(3);Pg.199-204.
17. Amruta Bakshi, Shilpa Asegaonkar, Jayshree Bavikar, Mangesh Tekade et al., Evaluation of serum uric acid levels in type 2 diabetes mellitus: Complex interplay with demographic and Clinical Parameters. International Journal of Recent Trends in Science And Technology, 2015;14(1);Pg.20-24.
18. K.Gawlik, J.W.Naskalski, D.Dedak, D.Pawlca-Gosiewska et al. Markers of Antioxidant Defense in Patients with Type 2 Diabetes. Oxidative Medicine and Cellular Longevity.2016;pg1-6.
19. Choi HK, De Vera MA, Krishna E. Gout and the risk of type 2diabetes among men with a high cardiovascular risk profile.Rheumatology 2008;Vol 47;Pg.1567-70.
20. Kaur, Kukreja S, Malhotra N, Neha. Serum adenosine deaminase activity and its correlation with glycated haemoglobin levels in patients of type 2 diabetes mellitus. J Clin Diagns Res. 2012;Vol 6;Pg.252-6.