



COMPARITIVE STUDY OF SERUM ADENOSINE DEAMINASE AND DYSLIPIDEMIA IN TYPE II DIABETES MELLITUS

KEYWORDS

Diabetes mellitus type-2, lipid profile, serum adenosine deaminase (ADA).

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ABSTRACT *Introduction: Type 2 Diabetes Mellitus is a common metabolic disorder characterized by high plasma glucose levels. Adenosine Deaminase(ADA) is an enzyme which catalyses the irreversible deamination of adenosine to inosine. Adenosine is known to exert potent metabolic effects acting through its receptors. Increased levels of serum ADA has been shown in individuals with Type 2 Diabetes Mellitus. The study aims to understand the relationship between serum ADA, Lipid profile and blood glucose levels. Objective: To estimate the level of serum adenosine deaminase (ADA), fasting blood glucose and lipid profile in patients with uncomplicated type -2 diabetes mellitus through case control study and also to know any correlation between plasma glucose values with ADA and lipid profile. Method: This study was conducted at Government General Hospital, Kurnool. We took total 50 patients in our study, out of which 25 patients were with uncomplicated type-2 diabetes mellitus and other 25 were as healthy control group. Blood sample were taken and Adenosine deaminase levels were measured calorimetrically, based on the method described by Giusti and Galanti. Other routine investigation like- FBS, PPBS, lipid profile, Blood urea, Serum creatinine were also measured. Results: Elevation of the serum ADP was found in diabetic patients as compared to controls and also strong correlations were found between serum ADA, lipid profile and plasma glucose levels. Conclusions: ADA level is significantly related with the type -2 diabetes mellitus. Any change of ADA level is an indirect expression of tissue adenosine levels. In pathophysiology of diabetes, ADA has its multimetabolic effects.*

INTRODUCTION

Diabetes mellitus (DM) is the most common endocrinological disorder characterized by metabolic abnormalities and

long term complications. The incidence and prevalence of type 2 DM is globally increasing and becoming a major public health problem for health care providers¹ Diabetes is projected to increase significantly in the coming period and is estimated that 80 million people in India would be having Diabetes by the year 2030² As the obesity increase, the risk of cardiovascular diseases, DM 2, renal function, cancer, impaired respiratory function, osteoarthritis, liver and gall bladder diseases are also increases³ diabetes account for 60% of all death in non-communicable disease. The most common age group are currently affected by Diabetes are 40-59 years.⁴ After bringing the long term glucose level by a single point reduces the risk of kidney failure and blindness by 37%.⁴ Hyperglycemia causes serious breakdown in lipid dynamics, often reflected by the elevated levels of circulating free fatty acids (FFAs) and triglycerides⁵ Adenosine deaminase (ADA), an enzyme of purine metabolism modulates energy metabolism and is crucial in regulating the steady concentrations of adenosine. Emerging studies have shown ADA as a proinflammatory biomarker of various diseases especially in immunology, neurological and cardiovascular systems.^{6,7,8,9} ADA was found as a producer of reactive oxygen species (ROS), stimulator of lipid peroxidation.^{10,11} Marker of both T-cell activation and glycemic status in diabetes mellitus (DM). ADA activity is high in lymphoid tissues and it increases lymphocyte proliferation and differentiation¹². In 1980, ADA was using as diagnostic tool in meningitis and TB. Elevated ADA levels were found in obesity, type 2 DM, Metabolic syn-

drome, liver cirrhosis and hepatoma¹³, TB, Brucellosis, Typhoid fever, Hypoxic states and cell mediated immune responses¹⁴ Several studies have demonstrated elevated of adenosine deaminase in individuals with Type 2 Diabetes mellitus, but exact Pathologic role of elevated ADA activity in type 2 DM remains to be elucidated.^{12, 17,18,19} Studies have shown that ADA which reduces adenosine levels, increases basal and nor adrenaline stimulated lipolysis in adipocytes.^{15,16} Insulin administration has been shown to reduce the elevated ADA levels in Type-2 diabetes.¹⁷ Adenosine has got insulin like activity on glucose and lipid metabolism particularly in adipose tissue and skeletal muscles. In view of increasing burden of Diabetes and mimicking action of adenosine like insulin we studied ADA as a new marker for detecting diabetes and its association with dyslipidemia and glycemic status (FBS) in Type -2 DM.

MATERIAL AND METHODS

The study was conducted at Dept. of Biochemistry in Kurnool medical College and Government General Hospital, Kurnool. Total number of patients is 50. Total number of controls is 25. Total number of patients without complication of type-2 diabetes mellitus is 25. Male and female both the patients were included under the age of 30-70 years of age in this study. A through clinical examination and appropriate investigations were done before selecting the cases and controls for the study. A detailed clinical history and physical examination was done. Routine investigation (blood urea, creatinine, lipid profile, serum adenosine deaminase, urine protein ECG, Fundoscopy) were done before selecting the subject for this study.

RESULTS

Table 1: Comparison of serum adenosine deaminase in cases and controls

SL.NO.	SERUM ADA	
	CASES	CONTROLS
1	30	6
2	29	4.8
3	26	4.0
4	32	18.2
5	36	7.6
6	13	12.4
7	34	5.2
8	11	9
9	27	7
10	28	6.6
11	45	9.1
12	50.1	7.2

13	28	7.9
14	16	8.4
15	11	9.1
16	39	8.1
17	24.4	7.5
18	26	13.4
19	25.6	9.1
20	43.8	8.2
21	26	8.6
22	43.8	7.4
23	26	8.0
24	25	7.9
25	28	7.2
TOTAL	723.7	207.9
MEAN	28.95	8.31
SD	10.18	2.87
P value		<0.0001

The mean value of serum ADA is 28.948 ± 10.182 and 8.316 ± 2.875 respectively for cases and controls. The difference is statistically significant with respect to p value < 0.0001.

Table 2: Lipid profile in cases and control										
SL.NO.	T. CHOL		TG		HDL		LDL		VLDL	
	CASE	CONT								
1	172	174	264	139	29	38	128	108	53	27
2	220	139	258	134	28	38	140	74	52	26
3	182	147	224	184	30	39	107	71	45	36
4	256	174	280	215	32	33	168	98	56	43
5	280	142	324	162	28	39	187	71	65	32
6	120	182	119	139	41	37	55	118	24	27
7	276	193	311	188	28	39	186	117	62	37
8	190	158	186	132	30	36	123	96	37	26
9	300	214	280	169	30	39	214	141	56	34
10	280	141	311	138	29	35	189	78	62	27
11	286	164	336	179	27	39	192	89	67	36
12	246	157	326	144	29	35	152	93	65	28
13	230	136	286	167	30	38	143	64	57	33
14	156	206	180	139	35	40	85	138	36	27
15	121	180	152	216	36	37	55	99	30	43
16	196	159	226	241	31	33	120	77	45	48
17	156	148	180	194	36	38	84	71	36	38
18	244	199	146	132	39	40	175	132	29	26
19	208	142	158	162	42	39	134	71	31	32
20	280	139	324	115	29	39	187	77	65	23
21	182	139	134	37	38	117	74	74	27	26
22	180	120	125	145	42	35	113	56	25	29
23	210	117	165	127	50	35	127	57	33	25
24	223	141	109	126	37	32	165	83	21	25
25	204	176	168	147	37	39	154	109	33	29
TOTAL	5398	3987	5577	3968	842	930	3500	2262	1112	783
MEAN	215.92	159.48	223.08	158.72	33.68	37.2	140	90.48	44.48	31.32
SD	51.51	26.00	76.31	32.49	5.86	2.30	42.86	24.54	15.39	6.58
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Mean ± SD of total cholesterol in cases is 215.92 ± 51.51 and in controls it is 159.48 ± 26.003 with p value <0.0001.

Mean +- SD of the triglycerides in cases is 223.08 +- 76.315 and in controls it is 158.72+-32.496 with p value <0.0001. Mean +- SD of HDL in cases is 33.68 +- 5.865 and in controls it is 37.2+-2.309 with p value <0.0001. Mean SD of LDL in cases is 140.0 +- 42.863 and in controls it is 90.48+- 24.546 with p value <0.0001. Mean SD of VLDL in cases is 44.48 +-15.39 and in controls 31.320 +- 6.587 with p value <0.0001.

Table 3: comparison of FBS with ADA in diabetic population

SL.NO.	FBS	SERUM ADA
1	249	30
2	286	29
3	235	26
4	310	32
5	376	36
6	141	13
7	381	34
8	157	11
9	284	27
10	271	28
11	408	45
12	356	50.1
13	258	28
14	136	16
15	126	11
16	390	39
17	114	24.4
18	135	26
19	140	25.6
20	288	43.8
21	126	26
22	280	43.8
23	165	26
24	126	25
25	210	28
TOTAL	5948	723.7
MEAN	237.56	28.94
SD	96.53	10.18
P Value		< 0.001

As the FBS is increasing ADA is increasing. Elevated glucose levels show increase in serum ADA in diabetic population. P< 0.001, considered very significant. The correlation of ADA and Blood Glucose parameters is positive and significant.

Table 4: Mean ADA level for different ranges of FBS in diabetic population

FBS RANGE	FBS mean +- SD	ADA(U/L) Mean +-SD	P value
101-200	136.6+-15.291	20.4+-6.742	< 0.001
201-300	262.33-26.828	31.511+-7.056	< 0.001
301-400	368.67+-32.197	39.35+- 6.949	<0.001
Inference	As the FBS increasing, ADA is significantly with p< 0.001		

As the FBS is increasing ADA is increasing. Elevated glucose levels show increase in serum ADA in diabetic population. p <0.001, considered very significant.

Table 5: Correlation of serum ADA with TG/HDL

PARAMETER	MEAN	SD
Serum ADA	28.948	10.182
TG/HDL	6.805	3.185
R value	0.5156	
P value	0.0083	

ADA Vs TG/HDL r value is 0.5156 and p value is 0.00001 showing that it is extremely significant. Considered very significant.

Table 6: Pearson correlation of age, BMI, FBS, TG/HDL with ADA in cases

VARIABLES	RELATION WITH ADA		
	R	P	Significance
Age	-0.05383	0.7983	Not significant
BMI	-0.05738	0.7853	Not significant
FBS	0.7764	< 0.001	significant
TG/HDL	0.5156	0.0083	significant

The correlation of ADA values with age and BMI is found to be insignificant. The correlation of ADA with FBS and TG/HDL is significant.

DISCUSSION

The world- wide burden of the diabetes has been increasing day by day and has reached in epidemic proportions. Being a chronic metabolic disorder, it's long term complications could have devastating consequences.

BLOOD GLUCOSE

The diagnosis of type 2 diabetes rests on the measurement of plasma glucose values. According to American Diabetes Association FBS >126 mg/dl is diagnostic of Diabetes. In our study the mean +- SD of FBS values of type 2 diabetes cases was 237.56+-96.53 well above the American Diabetes Association criteria to diagnose Diabetes and the PPBS which was higher than the upper limit 291.76+- 94.035 where the cut off value is 140 mg/dl. The control group had blood glucose values as 93.576 +- 9.479 and 136.56+- 3.809 for FBS and PPBS respectively suggestively of normoglycemia. These values correlate well with clinical diagnosis.

SERUM ADENOSINE DEAMINASE

The present study found an elevated serum Adenosine deaminase (ADA) activity in cases of type 2 Diabetes Mellitus when compared to age and sex matched controls. Similar reports were given by Hoshino *et al*⁸. Type 2 DM with chronic hyperglycemia favours auto oxidation and also increases free radical activity. These results of elevated ADA in type -2 diabetes also correlated with studies done by Kurtul *et al* (2006)⁶. Lee *et al* and Shiva Prakash *et al*¹² found type 2 DM patients with relatively good glycemic control have low ADA activity compared to individuals with poor glycemic control. The Pearson correlation between the serum ADA and TG/ HDL ratio correlation between the serum ADA and TG/ HDL ratio in type 2 diabetes showed a significant correlation (r=0.5156; p= 0.0083). These findings are in accordance with Nisha subhas Chandra Ramani *et al*¹⁴. Increased lipolysis associated with increased levels of cyclic AMP (cAMP)^{15, 16}. It has been shown that in the adipose tissue most of adenosine is formed extracellularly. Extracellular adenosine is metabolised only by adenosine deaminase. The source of extracellular adenosine in the adipose tissue is currently unknown. It is possible that the extracellular adenosine may

act in a retaliatory manner and try to inhibit lipolysis stimulated by increased levels of cyclic AMP. This pathway is known as the extracellular CAMP –adenosine pathway and has been shown in kidney, heart, brain, oviduct cells and also in the skeletal muscle.

LIPID PROFILE

Dyslipidemia was an obvious feature in the present study among the study group. TG and VLDL were significantly elevated in the study group when compared to controls. HDL was reduced among diabetics when compared to nondiabetics. These findings collaborated with the study conducted by Mazzone *et al* (2000)²⁰ where he documented increase in triglycerides. In this study it was observed that apart from an increase in triglycerides and VLDL and decrease in HDL, total cholesterol was also found to be raised in the study. A study conducted by V siva Prabodh *et al* (2012)²¹ also documented an increase in TG, total cholesterol, LDL, and decrease in HDL which was similar to the findings in the study. Study such as Adigun *et al* (2007)²², Albrki WM *et al* (2007)²³ also documented increased levels of TG, VLDL and decreased levels of HDL which has pretty much the picture in the study. P.K Bijlaani *et al* (1983)²⁴ and Barr *et al* (1951) found that HDL levels were depressed in diabetics which was one of the finding in this study as well mean HDL level of (33.68+_- 5.865) among the diabetic population compared to HDL level of (37.2+_- 2.309) among the nondiabetics. The combination of high TG, low HDL, and central obesity are the hall marks of the metabolic syndrome, which occurs in 80% of the people with diabetes mellitus. The frightening sig-

nificance of this combination of risk factors is the marked incidence in these people of premature death from heart disease. Association between the elevated total cholesterol and insulin resistance was also statistically significant in the

study conducted by Menik *et al*. In the study by H. Surekha Rani *et al*²⁵, an attempt has been made to evaluate the risk factors for coronary heart disease in DM patients. It is observed that FBS, PPBS, total cholesterol, triglyceride VLDL and LDL were high and the levels of HDL were low compared to controls.

CONCLUSION

Serum adenosine deaminase (ADA) levels were evaluated in type 2 Diabetes mellitus cases through a case control study using age and sex matched controls. Individuals who had developed complications of Diabetes were not included in the study. Serum levels of ADA were found to be significantly higher in type-2 diabetics when compared to controls. A very large correlation was found to exist between serum ADA and blood glucose values. Body mass index, age and sex were not found to significantly influence the ADA level. The diabetic patients had a higher prevalence of high serum cholesterol, high triglyceride, high LDL-C, and low HDL-C than in controls, indicating that diabetic patients were more prone to cardiovascular diseases. These findings clearly project that serum Adenosine deaminase reflects the current glycemic status in the diabetic individual, indicating a possible involvement of the enzyme substrate Adenosine, in the diabetic processes.

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