Original Research Article

Study of glycated haemoglobin and serum adenosine deaminase in patients with type II diabetes mellitus with and without diabetic nephropathy or retinopathy

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Abstract

Background: Diabetes Mellitus refers to a group of common metabolic disorders that share phenotype hyperglycemia. Several distinct types of DM are caused by complex interaction of genetic and environmental factors such as lifestyle, alcohol, diet, smoking, obesity etc. **Aims and objective:** To study and compare concentrations of HbA1c and sr. ADA in DM type 2 with and without DM retinopathy or nephropathy, and Dm without microangiopathy. **Materials and methods:** The present study was a hospital based cross sectional observational study. Prior to study approval of IEC of BVDU medical college sangli. Data of type 2 DM indoor patients, was collected over a period of 1 year from 1st march 2015 to 29th Feb. 2016. All patients blood samples from selected patients fasting Blood sugar (FandPP), Hba1C,sr, ADA send to Bharati Hospital Biochemistry lab. HbA1c was measured using Nephlometery and sr. ADA was estimated using Hypoxanthine Method and urine microalbumin test was done using dip test, fundoscopy was done by Senior ophthalmologists, statistics using mean and standard deviations t and chi-square test. Observations, **results and conclusion:** Results of the present study suggest of a positive correlation of Sr. ADA with microvascular complications in DM retionopathy and nephropathy. Raised levels of sr. ADA can be considered as chronic microvascular complications. And HbA1c is better more reliable and specific.

Key Word: Glycated Hb, ADA, Retinopathy, Nephropathy

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INTRODUCTION

Diabetes Mellitus refers to a group of common metabolic disorders that share phenotype hyperglycemia. Several distinct types of DM are caused by complex interaction of genetic and environmental factors such as lifestyle, alcohol, diet, smoking, obesity etc. Depending upon the etiology of DM factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization and increased glucose production[1]. Type2 Diabetes Mellitus Diabetes mellitus is one of the most important metabolic disorders associated with increased morbidity and mortality. It is associated with serious complications, macrovascular (coronary artery disease, Cerebrovascular Accidents, Peripheral Artery Disease) as well as microvascular diseases (retinopathy, Nephropathy, Neuropathy)[2,3]. Approximately 285 million people worldwide are diabetic. This number is likely to double by 2030. More than 80 per cent of diabetes deaths occur in low- and middle-income countries. Currently, 4.0-11.6 per cent of India's urban population and three per cent of the

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rural population above the age of 15 has diabetes. Nearly 44 lakh Indians in their most productive years aged 20 to 79 years aren't aware that they are diabetic. Glycated Haemoglobin (HbA1c) has been the key measure of glycaemic control in diabetic patients for last two to three decades[5]. It is considered to be the gold standard test, and most widely used and accepted test of glycemia among clinicians. HbA1c is produced by a non-enzymatic glycation of Haemoglobin A, the adult haemoglobin. Hemoglobin A1c (HbA1c) is a result of the nonenzymatic attachment of a hexose molecule to the N-terminal amino acid of the hemoglobin molecule. The HbA1c level reflects the mean glucose concentration over the previous period (approximately 8-12 weeks, depending on the individual) and provides a much better indication of long-term glycemic control than blood and urinary glucose determinations. The current study was undertaken to understand relation between activity of Serum Adenosine Deaminase in type 2 DM in patients with good glycaemic control, with poor glycaemic control, those with microvascular complications and those without. Microvascular complications of diabetes mellitus, i.e Retinopathy, Nephropathy, Neuropathy, have direct associated with duration of diabetes mellitus as well as glycaemic control. Development of microvascular complications is earlier in patients with poorly controlled sugar levels. Various environmental and genetic factors with hyperglycemia at center are involved in pathogenesis of microvascular complications.

MATERIALS AND METHODS:

The present study was a hospital based cross sectional observational study. It was conducted getting approval from Ethical Committee (Bharati Vidyapeeth Deemed University Pune. Subjects: Patients of both sex and of any age were selected for the study. The inclusion and exclusion criteria were laid down.

Inclusion Criteria

- Type 2 DM patients hospitalized in the hospital.
- Patients diagnosed with Type 2 DM patient of any duration, any age group, and both sexes.
- Patients suffering from non-infectious disease were included in the study
- Patients suffering from Tuberculosis and other chronic or acute infectious conditions were excluded.
- Patients with established other causes of renal failure or CKD, other than diabetic nephropathy were also excluded in the study.
- Patients admitted for infectious conditions like pneumonia, urinary tract infection, abscess, cellulitis etc were excluded from the present study.

Data of Type 2 DM indoor patients admitted in Bharati Vidyapeeth Medical College Hospital, Sangli, 173 Type 2 DM was collected over a period of 1 year from 1st march 2015 to 29th Feb. 2016. All study patients Venous blood samples were collected from selected patients subjected for Fasting Blood Sugar, Post Prandial Blood Sugar, Glycated Haemoglobin and Serum ADA. HbA1c was measured using Nephlometery and Seum ADA was estimated using Hypoxanthine Method. Morning urine sample were collected for screening of microalbumin in urine using dip test and biochemical testing in laboratory was also performed on the same samples. Microalbumin dip test kits were used. Screening for diabetic retinopathy was done by dilated fundoscopy using ophthalmoscope. Senior ophthalmologists in the present hospital confirmed the findings.

Table 1: Age Distribution of Patients In The Present Study

Age Group (In years)	Total	Male	Female	Percentage
25-35	5	2	3	2.8%
36-45	27	13	14	15.6%
46-55	45	25	20	26%
56-65	54	31	23	31.6%
66-75	24	15	9	14%
>75	18	9	9	10%
TOTAL	**173**	**95**	**78**	100%
PERCENTAGE	**100%**	**54.1%**	**45.9%**	

In the present study, data of total of 173 patients, which fit the inclusion criteria, were studied. Out of 173 patients 54.9% patients were males and 45.1% were females. Most patients were from the age group of 56-65 years i.e 31.6%. The mean age for males was 58.4±12.6 years and that for females was 58.1±12.7.

Table 2: Sex Distribution of Patients In Current Study

Sex	Number	Percentage	Mean HbA1c S.D	Mean Sr. ADA S. D
Males	95	54.90%	8.71 1. 12%	24. 14 7.68IU/L
Females	78	45.10%	8.73 1.13%	23.92 7.58 IU/L

There were a total of 95 male patients and 78 female patients in the study. Male to female ratio in this study was 1.2:1. There was no significant difference in Mean HbA1c or serum ADA between both the sexes

Table 3: Duration of type2 DM in study population.

DURATION (YEARS)	Total	Males	Females	Total Percentage
1-5	70	34	36	40.4%
6-10	53	32	21	30.6%
11-15	32	16	16	18.8%
15-20	12	8	4	6.9%
21-25	5	4	1	2.8%
25+	1	1	0	0.5%
			Total	100%

In the present study 70 (40.4%) patients suffered from type 2 DM for less than 5 years. 53 (30.6%) patients had duration of type 2 DM between 6-10 years, 32 patients (18.4%) had duration between 11-15 years, 12 (7%) patients between 15-20 years and 6 (3.5%) patients above 20 years were found.

Table 4: Body Mass Index Distribution Of Study Population

BMI	Males	Females	Total	Percentage
<18.5	8	1	9	5.20%
18.5-23	29	23	52	30.1%
23-30	43	42	85	49.10%
>30	15	12	27	15.60%
			Total	100%

In the present study, diabetic patients with normal BMI (18.5-23) were 52 (30.1%), underweight (<18.5) were 9 (5.2%), overweight (23-30) were 85 (49.1%) and obese (>30) were 27 (15.6%). Obesity was equally prevalent in both males and females.

Table 5: Mean HbA1c and Sr. ADA in different weight categories

Weight Category	N=	Mean HbA1C S.D		Mean Serum ADA S.D	
Underweight (BMI<18.5)	**9**	8.80 1.1%		24.80	7.6 IU/L
Normal Wieght (BMI =18.5-23)	**52**	8.40 1.1%		22.80	7.6 IU/L
Overweight (BMI=23-30)	**85**	8.80%	1.1%	24.30	7.6 IU/L
Obese (BMI >30)	**27**	8.80%	1.1%	24.70	7.6IU/L

There was no statistically significant correlation of BMI with serum ADA and HbA1c.

Table 6: HbA1c levels in study population

HbA1c	no. of Patients	Percentage
5.5-6.5	5	3%
6.6-7.5	25	14.40%
7.6-8.5	45	26%
8.6-9.5	68	39.30%
9.6-10.5	18	10.40%
10.5+	12	6.90%

The minimum HbA1c was 6.2% while maximum was 13% with a mean value of 8.6 ± 1.1 in the study population in all patients with type2 DM. In the present study the minimum RBS was 70 mg/dl and maximum was 450 mg/dl with a mean

RBS value of 176±62.4 mg/dl. The minimum FBS value was 90 mg/dl and maximum value was 370 mg/dl with a mean value of 169.6±54.6 mg/dl. The minimum PPBS value was 130 mg/dl and maximum value was 460 mg/dl with a mean value of 220.1±78.2 mg/dl.

Out of total 173 type2 DM patients in the present study 102(58.9%) were also having hypertension. 55.8 % of patients with hypertension had microvascular complications. While 47.8 % patients of patients without hypertension had microvascular complications. Incidence of microvascular complications was more in patients with hypertension

Table 7: Mean HbA1c and Mean Sr. ADA in relation to presence of Hypertension

	HbA1c		Sr. ADA	
HTN	YES	NO	Yes	NO
N	102	71	102	71
Mean	8.81	8.60	24.39	23.55
Std. Deviation	1.24	0.97	8.48	6.39
Std. Error Mean	0.12	0.11	0.84	0.76
t value	1.232		0.745	
p value	0.22		0.457	

There was no statistically significant correlation of Se. HbA1c or Sr. ADA in relation to presence or absence of hypertension.

47.3% (82) of total patients did not suffer from any of the microvascular complications under study. 52.6% (91) Patients suffered from any or both of the complications. 22.5% (39) patients suffered from DR, while 19.6 % (34) had albuminuria (microalbuminuria or macroalbuminuria) and 10.4 % (18) suffered from both.

Table 8: Association of Albuminuria with HbA1c and Sr. ADA

Details	**HbA1c**		**Sr.ADA**	
Albuminlinuria	**Yes**	**No**	**Yes**	**No**
N	52	121	52	121
Mean	9.32	8.47	28.81	22.00
Std. Deviation	1.26	0.98	7.56	6.80
Std. Error Mean	0.17	0.09	1.05	0.62
z value	**4.334**		**5.594**	
p value	**<0.005**		**<0.005**	

There was statistically significant association of both HbA1c level and Serum ADA in relation to presence of albuminuria.

Table 9: Association of Diabetic Retinopathy in relation to Sr. ADA and HbA1c

	HbA1c		Sr.ADA	
Diabetic Retinopathy	Yes	No	Yes	No
N	/57	116	57	116
Mean	/8.87	8.65	27.40	22.40
Std. Deviation	1.02	1.19	7.69	7.15
Std. Error Mean	0.14	0.11	1.02	0.66
z value	**1.245**		**4.119**	
p value	**0.216**		**<0.005**	

There was statistically significant association of Serum ADA, but no significant association was found for HbA1c in relation to presence of diabetic retinopathy.

DISCUSSION

Mean HbA1c in T2DM patients with Diabetic Retinopathy was 8.87% with a standard deviation of 1.02% when compared to a mean of 8.65% with a standard deviation of 1.19% in T2DM patients without Diabetic Retinopathy. Mean serum ADA in patients with albuminuria was 27.40 IU/L with standard deviation of 7.69 IU/L against Mean Serum ADA of 22.4 IU/L with standard deviation of 7.15 IU/L in patients without microalbuminuria. Thus level of serum ADA was statistically significant in relation to presence of diabetic retinopathy but no significant association of HbA1c was found in relation to diabetic retinopathy. (Table 8). Various studies have been carried out in India and abroad to study Serum ADA levels in respect to various aspects of Diabetes Mellitus in last two decades. Various studies conducted have shown increased

activity of ADA in diabetic population. Serum ADA showed a positive correlation with HbA1c. Mean Serum ADA was lowest in group of patients with HbA1c 6.6-7.5% was 16.08 IU/L with Standard Deviation of 7.6 IU/L. It was the highest in group of patients with HbA1c more than 10.5 %. i.e 27.5 IU/L with a standard deviation of 7.5 IU/L. This suggests a possible positive correlation between HbA1c representing glycaemic control and Serum ADA. (Ref. 16 and17) In a study conducted by Venkateswarlu *et al* showed elevated serum ADA activity in T2DM patients as compare to age and sex matched controls. The study showed significant correlation between fasting blood sugar level and serum ADA. Similar results were given by Hoshino *et al* and kurtul *et al.* (Ref. 18) Study conducted by Patel *et al*, Serum ADA levels were studied in relation to glycaemic control. Their study showed that with increase in blood glucose levels and HbA1c, serum ADA also increased suggesting a role of ADA in immune pathogenesis of T2DM.

CONCLUSION

Results of the present study suggest of a positive correlation of Sr. ADA with microvascular complications in the present study viz. diabetic retinopathy and diabetic nephropathy. Raised ADA levels in these patients may be considered as early marker for chronic microvascular complications. It might also have a role in determining glycaemic control but HbA1c is better more reliable and specific.

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