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SERUM ADENOSINE DEAMINASE LEVEL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract:

Objective: *to evaluate the serum adenosine deaminase level in patients with type 2 diabetes mellitus at tertiary care hospital Hyderabad.*

Patients and Methods: *This six month cross sectional descriptive study was conducted in the department of medicine at tertiary care hospital Hyderabad. The inclusion criteria of this cross sectional study (six months duration) were the individuals with uncomplicated type 2 diabetes mellitus had ≥35 years of age and both male and female gender. The study diabetic population was screened for serum adenosine deaminase level by taking 2 cc venous blood sample and sent to laboratory for analysis. The frequency and percentages was calculated while the mean ±SD was computed for numerical variables.*

Results: *Total fifty type 2 diabetic individuals were studied during six months study period, the mean age ± SD for whole population was 52.87±8.85 while mean ±SD for fasting and random blood glucose and HBA1C was 131.21±4.82 and 230.63±9.94 and 10.72±2.43 respectively. The male population was predominant 35 (70%) while the serum ADA was raised in 29 (58%) type 2 diabetic populations and also correlates with HBA1C 23 (79.3%)*

Conclusion: *serum ADA levels play an important role in evaluating the glycemic status and an indicator in the immuno-pathogenesis of diabetes mellitus.*

Keywords: *Diabetes mellitus, adenosine deaminase and Metabolism*

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INTRODUCTION:

The prevalence of type 2 diabetes mellitus and obesity is increasing rapidly and has been reported that approximately 2.3 billion people will be overweight and more than 700 million people obese worldwide. [1, 2] Type 2 diabetes mellitus has two facets, the insulin resistance and malfunction of ß-cells of pancreas [3]

Adenosine deaminase (ADA) is an enzyme involved in the metabolism of purine nucleosides catalyses the irreversible hydrolytic deamination of adenosine (Ado) and 2´-deoxyadenosine (2´-dAdo) to inosine and 2´-deoxyinosine, respectively. [4] Former studies shown that ADA reduces adenosine levels, increases basal and lipolysis in adipocytes stimulated by noradrenaline. [5, 6] Several studies have found elevated levels of adenosine deaminase in subjects with type 2 diabetes mellitus but the exact pathogenesis is unknown and should be explored whereas the insulin administration has been shown to reduce the ADA levels in type 2 diabetic population. [7-9] Adenosine has multiple effects and acts through its receptors following its release affects different tissue and organ functions including skeletal muscle, pancreas, hepatic, renal and cardiovascular vascular tissues. The expression level of adenosine nucleoside transporters and adenosine receptors has been shown to be different in diabetes. [10, 11] Chronic energy imbalance leads to hypertrophy and hyperplasia of adipocyte, stress for endoplasmic reticulum and dysfunction of mitochondria. In reaction the adipocytes produce huge amounts of inflammatory cytokines that impaired the immune cells exist in close proximity of the macrophages and adipocytes, such inflammation is also associated with insulin resistance in diabetes mellitus.[12] Adenosine is also acts as endogenous regulator of various functions in the immune system, thus the adenosine receptors are also important for drug targets in the adipose tissue to reduce the underlying inflammation in obesity and increase insulin sensitivity.

Therefore the present study was hospital based cross sectional study wherein the adenosine deaminase was measured in diabetic populations and helped ascertain the existence of correlation between serum ADA and blood sugar level.

PATIENTS AND METHODS:

The inclusion criteria of this cross sectional study (six months duration) were the individuals with uncomplicated type 2 diabetes mellitus had ≥35 years of age and both male as well as female gender while the exclusion criteria of the study were subjects with diabetic complications neuropathy, nephropathy, retinopathy and vascular complications, acute or chronic infection and pregnant and lactating ladies were excluded from the study. All the relevant individuals were stratified and after taking the informed consent the subjects were enrolled and recruited in the study. The history was taken, examination was performed and the routine investigations were advised. The study diabetic population was screened for serum adenosine deaminase level by taking 2 cc venous blood sample and sent to laboratory for analysis. The normal adenosine deaminase level is ≤30 U/L and the value > 30 U/L was considered as raised / high. The data was collected on pre-designed proforma and analyzed in SPSS version 16. The frequency and percentages (%) was computed and the numerical variables were presented as mean ± SD. The chi-square test was used to compute the categorical variables with p-value ≤0.05 as statistical significance.

RESULTS:

Total fifty type 2 diabetic individuals were studied during six months study period, the mean age ± SD for whole population was 52.87±8.85 while mean ±SD for fasting and random blood glucose and HBA1C was 131.21±4.82 and 230.63±9.94 and 10.72±2.43 respectively. The male population was predominant 35 (70%) while the serum ADA was raised in 29 (58%) type 2 diabetic populations. The results of the study are presented in Table 1-7.

Table 1: The Demographical and Clinical Data of the Study Population

AGE (yrs)	**FREQUENCY (n=50)**	**PERCENTAGES (%)**
35-39	10	20
40-49	12	24
50-59	10	20
60-69	15	30
70+	03	06
GENDER		
Male	35	70
Female	15	39
BMI (kg/m^2)		
19-25	18	36
25-30	20	40
>30	12	24
DURATION OF DIABETES (yrs)		
<1	07	14
1-5	14	28
5-10	20	40
>10	09	18

Table 2: The Age and Gender Distribution

	GENDER		Total
AGE (yrs)	Male	Female	
35-39	6	4	10
	17.1%	26.7%	20.0%
40-49	9	3	12
	25.7%	20.0%	24.0%
50-59	8	2	10
	22.9%	13.3%	20.0%
60-69	10	5	15
	28.6%	33.3%	30.0%
70+	2	1	3
	5.7%	6.7%	6.0%
Total	35	15	50
	100.0%	100.0%	100.0%

Table 3: The Age Distribution In Relation To HBA1C

		HEMOGLOBIN A1C		Total
	AGE (yrs)	Raised	Normal	
	35-39	9	1	10
		30.0%	5.0%	20.0%
	40-49	4	8	12
		13.3%	40.0%	24.0%
	50-59	7	3	10
		23.3%	15.0%	20.0%
	60-69	9	6	15
		30.0%	30.0%	30.0%
	70+	1	2	3
		3.3%	10.0%	6.0%
Total		30	20	50
		100.0%	100.0%	100.0%

*p-value = 0.05; statistically significant

Table 4: The Age Distribution In Relation To Adenosine Deaminase

		SERUM ADENOSINE DEAMINASE		Total
	AGE (yrs)	Raised	Normal	
	35-39	9	1	10
		31.0%	4.8%	20.0%
	40-49	5	7	12
		17.2%	33.3%	24.0%
	50-59	4	6	10
		13.8%	28.6%	20.0%
	60-69	10	5	15
		34.5%	23.8%	30.0%
	70+	1	2	3
		3.4%	9.5%	6.0%
Total		29	21	50
		100.0%	100.0%	100.0%

*p-value: 0.04; statistically significant

Table 5: The Gender In Relation To Glycated Hemoglobin

		HEMOGLOBIN A1C		Total
	GENDER	raised	Normal	
	Male	24	11	35
		80.0%	55.0%	70.0%
	Female	6	9	15
		20.0%	45.0%	30.0%
Total		30	20	50
		100.0%	100.0%	100.0%

*p=0.05; significant

Table 6: The Gender and Adenosine Deaminase Level

		SERUM ADENOSINE DEAMINASE		Total
	GENDER	Raised	Normal	
	Male	21	14	35
		72.4%	66.7%	70.0%
	Female	8	7	15
		27.6%	33.3%	30.0%
Total		29	21	50
		100.0%	100.0%	100.0%

*p-value: 0.66; statistically non-significant

Table 7: The Glycated Hemoglobin In Relation To Adenosine Deaminase

		SERUM ADENOSINE DEAMINASE		Total
	HBA1C	Raised	Normal	
	Raised	23	7	30
		79.3%	33.3%	60.0%
	Normal	6	14	20
		20.7%	66.7%	40.0%
Total		29	21	50
		100.0%	100.0%	100.0%

*p-value: 0.001; statistically significant

DISCUSSION:

The diabetes mellitus is a common disorder characterized by increase blood glucose due to variable interaction of environmental and hereditary factors along with of insulin resistance leads to long term complications with devastating consequences. The present study observed elevated serum adenosine deaminase (ADA) level in subjects with type 2 diabetes mellitus consistent with the former several studies. [13, 14] In addition former literature observed that the serum ADA levels back to normalize after insulin infusion [15], although the pharmacological activity of insulin treatment on serum ADA levels not evaluated in the present study. In present study the positive correlation was identified between the blood glucose level and serum ADA level and also detected the positive associations between the long term index of glycemic control via glycated haemoglobin (HbA1c) and serum ADA and consistent with the previous studies. [16, 17] This positive correlation between glycemic status and ADA level suggest its major role in carbohydrate and fat metabolic derangements observed in diabetic individuals and the finding was also reported by former studies. [18, 19] The pathogenesis of increased ADA levels in Type 2 DM is due to extra cellular Cyclic AMP adenosine pathway. ADA inhibits adenosine and leads to lipolysis and causes accumulation of Cyclic AMP accumulation. During insulin deficiency glucose and lipids spread through blood and are taken by liver, pancreas and adipose tissue which stores triglycerides leads to hypertrophy of adipocyte. This in turn causes cellular dysfunction, elevated free fatty acids and a pro-inflammatory state. The hepatocytes exposure to excusive glucose and fat causes insulin resistance and steatohepatitis worsening the insulin resistence and β-cell dysfunction.[20, 21] The chronic hyperglycemia causes increase in oxidative stress by producing free radicals and increases ADA levels further leads to Insulin resistance. Another mechanism of insulin resistance is down regulation of GLUT4 receptors due to deficiency of adenosine. Several studies observed the elevated serum adenosine deaminase activity in diabetes mellitus but the exact mechanism yet to be explored. [22-24] Furthermore serum adenosine deaminase level and its correlation with the insulin activity and the glucose tolerance test should be conducted to strengthen the concept and to evaluate its role as a prognostic and pathological marker in type 2 diabetes mellitus.

CONCLUSION: The study observed that increase HbA1c and blood sugar levels, serum ADA levels also increased shown its important role in evaluating the glycemic status and a indicator in the immuno-

pathogenesis of diabetes mellitus suggests that ADA plays a vital role in the pathophysiology of type 2 DM and its complications, although Further advance studies are needed to support these observations.

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