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STUDY OF ADENOSINE DEAMINASE (ADA) LEVELS IN TRUNCAL OBESITY WITH AND WITHOUT THE CARDIOMETABOLIC RISK

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ABSTRACT

Background: Obesity is a leading cause for mortality and morbidity in world wide. Previous literature demonstrated high adenosine deaminase activity in obese than non-obese individuals. Despite, obesity is not a homogenous but it is heterogeneous like metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO).

Aim and Objective: To estimate the adenosine deaminase activity in metabolically healthy and unhealthy truncal obese subjects and its clinical significance in predicting the pathogenesis of obesity at an early stage.

Materials and Method: A group of 50 adult subjects with truncal obesity and 40 age and sex matched healthy subjects without truncal obesity as controls were adopted for this study.

The parameters of modified NECP ATP III criteria to identify cardiometabolic risk and Serum Adenosine deaminase activity were performed in all the subjects. Based on the cardiometabolic syndrome risk factors the obese subjects were grouped into metabolically healthy and metabolically unhealthy subjects. Waist circumference was taken as common metabolic risk factors in both the groups. Comparison of metabolically healthy vs. unhealthy, control vs. metabolically healthy and metabolically healthy vs. control was done. Finally Pearson's correlation of number of cardiometabolic syndrome risk factors and adenosine deaminase activity was done.

Results: The cardiometabolic risk parameters were significantly elevated in obese individuals. The mean ADA in subjects with truncal obesity is 34.92±17.75, it was significantly higher than in controls 18.97±3.42. In subjects with MHO the mean ADA is found to be 20.82±5.22 whereas it is 45.2±13.71 in MHO subjects. Pearson's correlation of number of cardiometabolic syndrome risk factors against adenosine deaminase showed positive correlation and it was statistically significant (r=0.5524; p=0.0001).

Conclusion: Elevated adenosine deaminase activity in metabolically healthy obese individuals may predict immunopathological transition of healthy obese to metabolically unhealthy.

KEYWORDS Adenosine deaminase, Immunopathogenesis, Cardiometabolic syndrome, Obesity.

INTRODUCTION

Biochemical parameters are playing crucial role in diagnostic era of modern medicine. They are sensitive enough to identify the pathological transition of most of the diseases. The estimation of cytokines and adipokines provides a better insight on obesity and its pathological transition from healthy to unhealthy state. But it requires accurate, sensitive methods those are not faceable for small laboratories. It shows the necessity to study the predictivity of various available low cost parameters to replace the high cost parameters.

Adenosine deaminase (ADA) is a known marker for tuberculosis[1], type 2 diabetes mellitus [2]and other conditions like hepatotoxic state, liver cirrhosis, and immunosuppression. The recent study has revealed that serum levels of ADA are increased in obese subjects than normal individuals.

However, obesity is heterogeneous i.e., metabolically healthy obese (MHO) and metabolically unhealthy (MUHO). In MHO scenario, the metabolic andimmunological dysfunctions such as insulin resistance,hypertriglyceridemia, low high-density lipoprotein(HDL) cholesterol, hyperglycemia and hypertension arenot present. Whereas increased inflammatory cytokines and adipokines in MHO individual will lead to accumulation of macrophages in adipose tissuethere by dysfunction of metabolic and immune systems due to adipose tissue inflamation,considered being as MUHO.

Since ADA is playing a major role in pathological transition of adipose tissue as CD-26 ecto-ADA complex [3, 4]. We have under taken a study to estimate and compare the ADA levels in MHO and MUHO subjects. This study helps to enlighten the existing knowledge on ADA clinical importance to identify the truncal obese individuals under pathological progression at an early stage.

MATERIALS AND METHODS

The study was conducted at Department of Clinical Biochemistry, Konaseema Institue of Medical Sciences, Amalapuram. A total of 50 adult obese subjects with truncal obesity were taken selectively for this study. Truncal obesity was defined by BMI ≥25.0 with waist circumference >90cm in males, >80cm in females. And cardiometabolic risk defined by subjects who are satisfying any 3 conditions in NCEP ATP III criteria. A subject satisfying ≥3 cardiometabolic risk parameters were considered as MUHO and with≤ 2 parameters were considered as MHO. And a group of 40 age and sex matched healthy individuals without truncal obesity and with no history of diabetes were served as controls.

Under aseptic conditions, the required fasting blood (5ml) was collected and serum was separated under aseptic condition. The parameters of modified NECP ATP III criteria for cardiometabolic syndrome and adenosine deaminase activity (ADA) were estimated in all the subjects and controls using standard kit procedures on chem. V7 analyzer. Systolic / diastolic blood pressure was defined as mean of the second and third reading of the consecutive blood pressure measurements.

During the entire study the utmost care was taken according to Helsinki Declaration about patient confidentiality[5]. The study was approved by Institutional Ethical Committee (IEC). Written Informed consent of participants was taken prior to study.

Criteria to identify for cardiometabolic syndrome:
Presence of any three following risk factors is considered as positive for risk of cardiometabolicsyndrome. Central obesity - WC > 90 cm (men), > 80 cm (women); BP - SBP 130 mmHg and / or DBP 85 mmHg or medical treatment for previously diagnosed hypertension; hypertriglyceridemia - TG 150 mg/dL; low HDL-C < 40 mg/dL (men), < 50 mg/dL (women); impaired FBS 100 mg/dl.

Adenosine deaminase activity:
The normal reference range for ADA was consider to be <30 IU/L, suspect 30-40 IU/L, strong positive >40 – 60 IU/L and > 60 IU/L positive.

Statistical Analysis:
Statistical analysis was done by student't' test using Graph pad prism version 6.0 software and results were expressed as mean + SD. Pearson's bivariate correlation analysis was used to correlate risk factors with ADA activity. P value <0.05 were considered as statistically significant.

RESULTS
Table 1: Showing the comparison of mean and SD values of studied parameters among control and truncal obese subjects. All parameters taken for study were found to be increased significantly in cases than controls.

Table-1 comparision of mean and SD of study parameters in control and obese groups

VARIABLE	CONTROLS (Mean±SD)	Obese (Mean±SD)			CONTROL vs OBESE
		MALE (N=30)	FEMALE (N=20)	TOTAL (N=50)	
WC	89.30±12.59	108.86±7.70	105.88±6.19	107.78±7.33	P=0.001
BP SBP	120.08±5.76	126.86±10.16	127.05±9.84	126.93±10.05	P=0.0025
DBP	76.24±4.7	79.23±7.03	79.88±6.63	79.46±6.89	P=0.0410
TGL	135.88±11.56	173.53±41.31	181.52±34.80	176.42±39.27	P=0.001
HDL	48.16±8.12	41.16±8.33	43.17±9.46	41.89±8.81	P=0.0049
FBS	88.3±8.25	104.76±25.74	100.88±23.33	103.56±24.96	P=0.0038
ADA	18.97±3.42	36.55±17.75	35.18±17.45	34.92±17.75	P=0.0001

Table 2: Showing the comparison of ADA and cardiometabolic risk factors among metabolically healthy obese (MHO) and metabolically unhealthy subjects (MUHO).All the values have shown significant difference between MHO and MUHO.

Table-2: Mean and standard deviation of cardiometabolic syndrome risk factors and ADA levels in obese groups

Group	WC	Blood pressure		TGL	HDL	FBS	ADA
		SBP	DBP				
Metabolically un-healthy N=26	107.73±7.41	129.03±11.0	85.83±7.39	199.7±28.9	38.2±8.56	112.06±27.23	46.2±13.70
Metabolically healthy N=21	105.71±7.23	119.23±6.6	77.05±5.09	135.35±11.82	48.41±4.33	88.0±6.67	17.82±5.22

Table 3: Showing the comparison of mean and SD of all the studied parameters among control, MUHO and MHO. It gives an impression that ADA levels were significantly high in MUHO when compared to MHO.

Table-3: Comparison of Mean and Standard Deviation among the Studied Group

Comparision Between	WC	Blood pressure		TGL	HDL	FBS	ADA
		SBP	DBP				
Control Vs MUHO	0.0001*	0.005	0.0016	0.0001	0.0001	0.0001	0.0001*
Control Vs MHO	0.001*	0.6575	0.5957	0.8848	0.9080	0.9173	0.1076 (NS)
MUHO vs MHO	0.6498 (NS)	0.0017	0.0225	0.0001	0.0001	0.0009	0.0001*

DISCUSSION
Adenosine deaminase (ADA) is an enzyme of purine metabolism, which has been the subject of great interest because of its fine modulation of inflammatory immune responses[6]. And it was an important biochemical marker of the inflammatory response and immune and metabolic disturbances. Estimation of adenosine deaminase activity in serum, plasma and cavity fluids using sensitive biochemical method gives accurate information to assess the immunopathogenesis of various diseases[7]. In previous studies [8,9] it was found that ADA activity will be elevated in overweight and obesity. In the present study also adenosine deaminase and cardiometabolic syndrome risk factors of modified NECP ATP III criteria were significantly elevated in obese individuals when compared to controls.

The mean ADA level in control is found to be (18.97±3.42). Where as in obese subjects it was (34.92±17.75) and it was high in males (36.55±17.75) than females (35.18±17.54). It was already established that not all obese individuals exhibit increased risk of inflammation and not all normal weight individuals are metabolically healthy or free from dyslipidemia or cardiometabolic risk factors.[10] So in this study, we did comparison of cardiometabolic syndrome risk factors and adenosine deaminase activity among MHO subjects, MUHO subjects. The results have shown that mean ADA levels were significantly high in MUHO individuals 45.2±13.71 compared to MHO subjects 20.82±5.22. All the cardiometabolic syndrome risk factors were absent in MHO subjects except waist circumference (105.71±7.23) when compared to control (89.30±12.59) [Table: 2 & 3].

The pathogenesis behind the increased ADA levels in obesity can be explained by adenosine. Adenosine, regulates adipokines secretion by adipose tissue they will regulates free fatty acid oxidation and it has the capacity to act like insulin on adipose tissue. Increased adenosine deaminase activity MUHO state leads decrease in adenosine in adipose tissue. This will lead to dysregulation of adipokines secretion. This in turn causes development of insulin resistance (IR) and dysregulation of fatty acid oxidation. The Elevated free fatty acid in blood leads to higher levels of both triglyceridesand low density lipoprotein (LDL).

Hypertriglyceridemia leads to decrease high density lipoprotein (HDL). Decreased adenosine leads to positive regulation of rennin secretion from juxtaglomerular cells there by dysregulation of hypertension[11-13].The correlation of number of cardiometabolic syndrome risk factors and ADA was done. The results have revealed that adenosine deaminase levels were significantly elevated in accordance with number of metabolic risk factors (r=0.5524 p=0.0001).

The high activity of this enzyme may be because of immunological disturbances and it indicates immune pathogenesis of MHO into MUHO. This study on adenosine deaminase activity metabolically healthy and metabolically unhealthy individuals is the first kind of description.

The estimation of adenosine deaminase activity (ADA) is a cost effective process and the efficient exploitation of this strategy may helps better establishing this enzyme as a good marker for predicting immune pathogenesis of metabolically healthy subjects.

CONCLUSION
Therefore, we conclude that elevated adenosine deaminase activity may be important indicators for the immune pathogenesis of obesity among the subjects with cardiometabolic risk. Estimation of ADA in obese subjects without cardiometabolic risk

can give a strong indication about the transition to from MHO to MUHO.

However further studies on ADA activity in MUHO and MHO individuals is required to consider ADA as an effective predictive immune marker for establishment of cardiometabolic syndrome in metabolically healthy subjects.

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