Research Article

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ADENOSINE DEAMINASE ACTIVITY IN METABOLICALLY HEALTHY AND UNHEALTHY OBESE INDIVIDUALS IN RELATION TO METABOLIC SYNDROME

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Abstract: Obesity is a major worldwide health problem leading to markedly increased mortality and serious morbidity. Literature demonstrates high Adenosine deaminase activity in overweight and obesity than non-obese individuals. It was known that obesity is not a homogenous but it was heterogeneous like metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO). Accordingly we have undertaken a preliminary comparative study to estimate the adenosine deaminase activity in metabolically healthy and unhealthy subjects and its clinical significance in predicting the pathogenesis of obesity at an early stage. A group of 47 adult obese subjects having increased waist circumference [males >90cm, females >80cm] were selected. A group of 40 age and sex matched healthy individuals were served as controls. Serum Adenosine deaminase activity and parameters of modified NECP APT III criteria of metabolic syndrome were performed in all the subjects. Based on the metabolic 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 metabolic syndrome risk factors and adenosine deaminase activity was done. All metabolic syndrome parameters were significantly elevated in obese individuals. The mean ADA in obese (35.93±17.76) was significantly elevated than controls (19.98±3.41). In metabolically healthy subjects the mean ADA was found to be 17.82±5.22 whereas it was 46.2±13.70 in metabolically unhealthy obese subjects. Pearson's correlation of number of metabolic syndrome risk factors against adenosine deaminase showed positive correlation and it was statistically significant (r=0.6524 p=0.0001). Elevated adenosine deaminase activity in metabolically healthy obese individuals may predict immunopathological transition of healthy obese to metabolically unhealthy.

Keywords: Adenosine deaminase, Immunopathogenesis, Metabolic syndrome, Obesity.

INTRODUCTION

In modern medicine, the estimation of biochemical parameters is playing a critical role in prediction, diagnosis and treatment monitoring of a disease. The sensitive biochemical estimates to diagnose pathological transition of obesity at an early stage includes estimation of cytokines and adipokines. But it requires accurate, sensitive methods and it was high cost. The recent research on adenosine deaminase activity has revealed that seric and plasmic levels of this enzyme were increased in obese individuals than in non-obese. It is also estimated that elevated serum ADA were found in Type 2 D.M, acute hepatitis, chronic-active hepatitis, liver cirrhosis, and hepatoma [1], T.B. brucellosis, Typhoid fever, hypoxic states and cell mediated immunoresponses. [2] However obesity is not homogenous but heterogeneous-metabolically healthy obese (MHO) and metabolically unhealthy (MUHO). [3] In MHO scenario, the metabolic and immunological dysfunctions such as insulin resistance, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hyperglycemia and hypertension are not present. [4] Whereas increased inflammatory cytokines and adipokines in MHO individual will leads to accumulation of macrophages in adipose tissue there by dysfunction metabolic and immune systems, considered to be as MUHO otherwise used as metabolic syndrome (Mets).

Adenosine is an endogenous anti-inflammatory metabolite that is increased in response to inflammation of adipose tissue (visceral) in obesity. The pro inflammatory cytokines such as TNF-α and IL-6 positively regulate CD-26 ecto-ADA complex of adipose tissue thereby increase the expression of adenosine deaminase activity, which will convert the adenosine to inosine in the course pathological transition of obese individuals from healthy to unhealthy. [5,6] Since a relationship exists between adenosine deaminase and inflammatory condition of adipose tissue, we have taken a preliminary comparative study to determine adenosine deaminase activity in metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO) and to highlight its clinical importance in diagnosis of pathogenesis of obesity at an early stage.

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MATERIALS AND METHODS

This preliminary comparative study was conducted in Department of Clinical Biochemistry, Santhiram Medical College and General Hospital (SRMC&GH) Nandyal. We selected a group of 47 adult obese subjects who are having increased waist circumference measured at the level of umbilicus [males >90cm, females >80cm] were selected from outpatient department of Santhiram medical college and General hospital.; none of the subjects have a history of infection or other ailments at the time of the study. And a group of 40 age and sex matched healthy individuals with no history of diabetes, confirmed by fasting blood glucose estimate served as controls.

Informed consent was taken from all the 47 subjects before conducting the clinical and biochemical evaluation.

Criteria for metabolic syndrome:

In this study, the parameters of modified NECP ATP III criteria [Table 1] and adenosine deaminase activity (ADA) were estimated in all the subjects and controls.

Table.1: Modified NECP ATPIII criteria for metabolic syndrome screening. [7]

RISK FACTOR	CUT OFF VALUE
Waist circumference (WC)	–males >90 cm –females >80cm
Blood pressure (BP)	≥ 130/≥ 85 mmHg
Triglycerides (TGL)	≥ 150 mg/dL
HDL-cholesterol (HDL-C)	–males < 40 mg/dL –females < 50 mg/dL
Fasting glucose (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.

Sample collection:

Under aseptic conditions, the required fasting blood (5ml) was collected and serum was separated under aseptic conditions using standard procedure.

Biochemical evaluation:

All blood investigations like adenosine deaminase (ADA), fasting blood sugar (FBS), triglycerides (TGL), and high density lipoprotein (HDL-C) were done on chem. V7 analyzer using standard kits.

Clinical evaluation:

Systolic / diastolic blood pressure was defined as mean of the second and third reading of the consecutive blood pressure measurements.

Statistical Analysis:

Statistical analysis was done by student't' test using Graph pad 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: shows NECP ATP III criteria.

Table 2: Shows the comparison of mean and SD of controls and cases. All parameters taken for study were found to be increased significantly in cases than controls. Thus, showing adenosine deaminase activity will increased in obesity.

Table 3: Shows the comparison of ADA and metabolic syndrome risk factors among metabolically healthy obese (MHO) and metabolically unhealthy subjects (MUHO). It gives and impression that the entire metabolic syndrome risk factors and ADA were elevated in MUHO when compared to MHO.

Table 4: Shows the comparison of mean and Standard deviation 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.

Graph 1: Shows that correlation of adenosine deaminase levels with number of metabolic syndrome risk factors. It has shown that ADA levels were positively correlated with increased metabolic syndrome risk factors.

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. And it was an important biochemical marker of the inflammatory response and immune and metabolic disturbances. Estimation adenosine deaminase activity in serum, plasma and cavity fluids using sensitive biochemical method gives accurate information to assess the immunopathogenesis of various diseases. [8]

In previous studies [9, 10] it was found that ADA activity will be elevated in overweight and obesity. In the present study also adenosine deaminase and metabolic syndrome risk factors of modified NECP ATP III criteria were significantly elevated in obese individuals when compared to non-obese individuals. The mean ADA level in control is found to be 19.98± 3.41 where as in obese subjects it was 35.93±17.76. And it was high in males (36.66±17.85) than females (35.17±17.58) [Table no: 2].

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.[11] So in this study, we did comparison of metabolic syndrome risk factors and adenosine deaminase activity among metabolically healthy (MHO), metabolically unhealthy subjects (MUHO). The results have shown that mean ADA levels were significantly high in MUHO individuals (46.2±13.70)

compared to MHO subjects (17.82±5.22). All the metabolic syndrome risk factors were absent in MHO subjects except waist circumference (106.71±7.24) when compared to control (90.30±12.59) [Table: 3 & 4].

Table.2: Anthropometric and Biochemical Parameter Status of the Participants.

PARAMETER STUDIED	CONTROLS (N=40) (MEAN ±SD)	OBESITY (N=40) (MEAN ±SD)			Control vs. Total obese
		Male (n=30)	Female (n=17)	Total (n=47)	
Waist circumference (WC)	90.30±12.59	108.86±7.70	105.88±6.19	107.78±7.33	P=0.001
Blood pressure Systolic (SBP)	120.08±5.76	126.86±10.16	127.05±9.84	126.93±10.05	P=0.0025
Blood pressure Diastolic (DBP)	76.24±4.7	79.23±7.03	79.88±6.63	79.46±6.89	P=0.0410
Triglycerides (TGL)	135.88±11.56	173.53±41.31	181.52±34.80	176.42±39.27	P=0.001
High density lipoprotein (HDL)	48.16±8.12	41.16±8.33	43.17±9.46	41.89±8.81	P=0.0049
Fasting blood sugar (FBS)	88.3±8.25	104.76±25.74	100.88±23.33	103.56±24.96	P=0.0038
Adenosine deaminase (ADA)	19.98±3.41	36.36±17.85	35.17±17.58	35.93±17.76	P=0.0001

Table.3: Mean and standard deviation of metabolic syndrome risk factors and ADA levels in MUHO and MHO

Groups	WC	Blood pressure		TGL	HDL	FBS	ADA
		SBP	DBP				
MUHO (n=30)	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
MHO (n=17)	106.71±7.24	119.23±6.6	77.05±5.09	135.35±11.82	48.41±4.33	88±6.67	17.82±5.22

Table.4: Comparison of Mean and Standard Deviation among the Studied Group

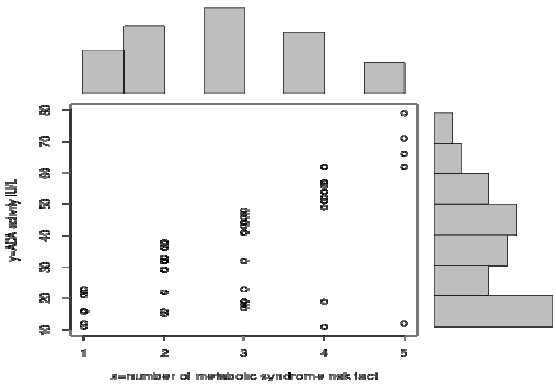
Groups	WC	Blood pressure		TGL	HDL	FBS	ADA
		SBP	DBP				
Cont vs. MUHO p-value	0.001	0.005	0.0016	0.0001	0.0001	0.0001	0.0001
Cont vs. MHO p-values	0.001	0.6575 *	0.5957 *	0.8848 *	0.9080 *	0.9173 *	0.1076 *
MUHO vs. MHO P-value	0.6498 *	0.0017	0.0225	0.0001	0.0001	0.0009	0.0001

Cont= control; MUHO=metabolically unhealthy obese; MHO=metabolically healthy obese;
*=statistically insignificant

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 triglycerides and 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. [12-14]

The correlation of number of metabolic 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=0.6524 p=0.0001) [graph1].

Graph.1: Correlation of Adenosine Deaminase Activity against Number of Metabolic Syndrome Risk Factors.



The high activity of this enzyme may 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 help 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 in the immune pathogenesis of obesity and a good immune marker to predict establishment of metabolic syndrome in metabolically healthy obese individuals. 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 metabolic syndrome in metabolically healthy subjects.

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