Evaluation of serum adenosine deaminase levels with components of metabolic syndrome

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Abstract

Introduction: Metabolic syndrome is a major worldwide health problem leading to markedly increased mortality and serious morbidity. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hyperglycemia, and hypertension. Adenosine, regulates adipokines secretion by adipose tissue. They will regulate free fatty acid oxidation and it has the capacity to act like insulin on adipose tissue. Increased Adenosine Deaminase(ADA) activity leads to decrease in adenosine in adipose tissue. Since a relationship exists between adenosine deaminase and metabolic syndrome, we have undertaken a preliminary study to determine its plasma activity in metabolic syndrome cases and highlight its importance by comparing its activity with each component of metabolic syndrome.

Objectives: To estimate serum ADA, Fasting blood sugar (FBS), Triglyceride (TG), HDL, Waist circumference (WC) & Blood pressure (BP) in cases and controls and to correlate serum ADA with FBS, TG, HDL, WC & BP in cases of Metabolic syndrome.

Materials & Methods: The study was conducted on 50 diagnosed cases of Metabolic syndrome and 50 age and sex matched healthy subjects. ADA estimated by Guisti and Gulanti method, FBS by GOD - POD method, HDL-C by Immunoinhibition method, TG by GPO-PAP method, Waist circumference & BP measured as per WHO criteria. Statistical analysis was done using SPSS-17.

Results: Serum ADA, FBS & TG levels, waist circumference, Blood Pressure levels were significantly elevated in cases compared to controls. Serum HDL levels was significantly decreased in cases compared to controls. Correlation was positive and significant when ADA activity was compared with FBS, TG, WC & BP and correlation was negative and significant when ADA activity was compared with HDL in cases.

Conclusion: These findings clearly project an early detection of elevation of ADA levels may help in early prevention and management of metabolic syndrome and its complications.

Keywords: Metabolic syndrome, Adenosine, Adenosine Deaminase, Hyperglycemia, Hypertension, Dyslipidemia & Obesity

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Introduction

The metabolic syndrome (Syndrome X, insulin resistance syndrome) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and cerebrovascular disease[1]. The criteria for the metabolic syndrome have evolved since the original definition by the World Health Organization in 1998, reflecting growing clinical evidence and analysis by a variety of consensus conferences and professional organizations. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low high density lipoprotein (HDL) cholesterol, hyperglycemia and hypertension.[1]

The rise in the prevalence of obesity in India is threatening to increase the burden of atherosclerotic cardiovascular disease (ASCVD). The prevalence of metabolic syndrome worldwide is 20-25% as per International Diabetes Federation(IDF)[2,3]. Among the complications, cardiovascular events produce the greatest morbidity and mortality. A significant portion of the latter occurs in persons in whom obesity precedes type II diabetes. But diabetes is only one of several conditions that associate strongly with obesity. Others include dyslipidemia, hypertension, systemic inflammation and a thrombotic tendency.

Recently there has been a trend in the cardiovascular field to group all of these factors together under the heading of metabolic syndrome[1]. In this sense, metabolic syndrome can be taken to represent a multiplex cardiovascular risk factor. This syndrome does not include, but is strongly associated with, other complications of obesity, for example, fatty liver, cholesterol gallstones, obstructive sleep apnoea, and polycystic ovarian syndrome[4]. The current definition generally regards hyperglycemia in the range of type II diabetes to be one of the components of metabolic syndrome. The clustering of CVD risk factors that typifies metabolic syndrome is considered to be the driving force behind a CVD epidemic. There has been a consistent effort to evaluate biochemical

markers to predict an early onset of metabolic syndrome and subsequently intervene appropriately by means of lifestyle changes and drug therapy and thereby reduce cardiovascular morbidity and mortality. Studies are lacking in the adult Indian population.

Markers like adiponectin have been studied as a measure of increased adipose tissue but have not proven to be cost effective and easily available. Clearly a prompt, cost effective and easily available biochemical marker is required to predict an early onset of this syndrome. Adenosine Deaminase (ADA) is one such marker which is cost effective, easily available[5]. Adenosine deaminase is a purine catabolic enzyme, that specifically catalyses irreversible deamination of adenosine to inosine. It contributes to regulation of intracellular and extracellular concentrations of adenosine and modifies adenosine action on its receptors. Increase in serum ADA activity depletes adenosine concentration. ADA seems to be an important enzyme for modulating the bioactivity of insulin. Rise in serum ADA activity is associated with obesity, insulin resistance, abnormal lipid profile and hypertension[5,6,7]. Hence the present study was done to evaluate the relation of serum Adenosine deaminase activity with major features of metabolic syndrome.

Objectives of this study were to measure Waist circumference and Blood pressure and to estimate serum Adenosine Deaminase activity, Fasting Blood Glucose, Triglyceride, HDL levels in cases and controls and to compare and correlate serum Adenosine Deaminase activity with Waist circumference and Blood pressure, Fasting Blood Glucose, Triglyceride and HDL levels in cases of metabolic syndrome.

Materials and Methods

This case control study was conducted at Basaveshwar Teaching & General Hospital, Gulbarga for a period of one year from January 2013 to January 2014, on 30 to 60yrs age matched (30 Male and 20 Female) 50 healthy subjects and (30 Male and 20 Female) 50 diagnosed metabolic syndrome cases. Patients informed consent & Institutional Ethical clearance was obtained.

Sample Collection

Blood sample: 4 ml of overnight fasting venous blood was collected aseptically from antecubital vein for estimations. One ml in fluoride containing tube & 3ml in plain tube. Serum was separated by centrifugation at 3000 rpm for 10 min and was stored at 4˚C to prevent bacterial action until analysis.

Materials

The present study included 100 subjects both male and female with mean age 53±10 years. Fifty healthy controls and fifty diagnosed metabolic syndrome cases. Exclusion criteria includes age <30yrs & >60yrs, pregnant and post-menopausal women, liver diseases, any diseases or drugs affecting blood pressure, carbohydrate and lipid metabolism.

Method of Estimation

Estimations were done in Semiautoanalyser Erba Chem-7, ADA by colorimetric method of Giusti and Galanti method[8], Blood Glucose by GOD-POD method[9,10], Serum Triglycerides by GPO-PAP method[11,12,13] and Serum HDL by Immunoturbidimetric method[14]. Blood pressure measured by standard Mercury sphygmomanometer[15] and waist circumference measured in horizontal plane midway between the inferior margin of the ribs and superior border of iliac crest with measuring tape in cms[15].

Statistical Analysis

The results were expressed as mean ± standard deviation. Student ‘t’ test was used to compare mean values. Pearson's correlation coefficient for association between the parameters was done using the statistical package of social sciences (SPSS-17, Chicago, USA).

Results

The present study was undertaken to study the levels of serum Adenosine Deaminase (ADA) in individuals with Metabolic Syndrome, and the correlation of serum ADA with the components of Metabolic Syndrome. A series of statistical tables and graphs have been used to present the results. The Table 1 shows comparison of serum ADA, FBS, TG, HDL, SBP, DBP and WC between controls and cases. The correlation of serum ADA with Waist circumference, Blood pressure, Fasting blood glucose, Triglyceride, HDL-C in cases and pictorial representation of results is done by scatter diagrams. Table 1 shows Mean and Standard Deviation of parameters among cases and controls**.** Mean and Standard Deviation for serum Adenosine deaminase of cases and controls were 26.51±3.603 U/L and 8.614±3.52 U/L respectively. Significant positive difference ($p<0.01$) was observed in relation to serum Adenosine deaminase in cases compared to controls. Mean and Standard Deviation for Fasting Blood Sugar of cases and controls were 165.30±54.26 mg/dl and 87.52±5.33 mg/dl respectively. Significant positive difference ($p<0.01$) was observed in relation to Fasting Blood Sugar in cases compared to controls. Mean and Standard Deviation for Triglycerides of cases and controls were 211.25±49.76 mg/dl and 121.28±16.69 mg/dl respectively. Significant positive difference ($p<0.01$) was observed in relation to Triglycerides in cases compared to controls. Mean and Standard deviation for HDL of cases and controls were 38.40±5.15 mg/dl and 51.80±6.369 mg/dl respectively. Significant Negative difference ($p<0.01$) was observed in relation to HDL in cases compared to controls. Mean and Standard Deviation for Waist circumference of cases and controls were 104.31±6.61cms and 83.39±18.79 cms

respectively. Significant positive difference ($p<0.01$) was observed in relation to Waist circumference in cases compared to controls. Mean and Standard Deviation for Systolic Blood Pressure of cases and controls were 132.42±10.54 mmHg and 119.56±5.58 mmHg respectively. Significant positive difference ($p<0.01$) was observed in relation to Systolic Blood Pressure in cases compared to controls. Mean and Standard Deviation for Diastolic Blood Pressure of cases and controls were 85.69±5.22 mmHg and 77.92±4.36 mmHg respectively. Significant positive difference ($p<0.01$) was observed in relation to Diastolic Blood Pressure in cases compared to controls. Table 2 shows correlation of serum ADA levels with FBS, Triglycerides, HDL, blood pressure and waist circumference in cases. Fig. 1, 2, 4, 5 and 6 depicts positive correlation of serum Adenosine Deaminase with Fasting blood sugar, Triglyceride, Waist circumference, Systolic Blood Pressure and Diastolic Blood Pressure respectively in cases. Fig. 3 depicts negative correlation of serum Adenosine Deaminase with HDL-C in cases.

Table 1: Mean and Standard deviation (SD) of Parameters in cases and controls

Parameters	Metabolic syndrome cases	Normal healthy controls	Z test	p-value
ADA (U/L)	26.51±3.603	8.614±3.52	24.69	<0.01
FBS (mg/dl)	165.30±54.26	87.52±5.33	10.01	<0.01
TG (mg/dl)	211.25±49.76	121.28±16.69	5.86	<0.01
HDL (mg/dl)	38.40±5.15	51.80±6.369	11.65	<0.01
WC (cm)	104.31±6.61	83.39±18.79	7.289	<0.01
SBP (mm Hg)	132.42±10.54	119.56±5.58	7.65	<0.01
DBP (mm Hg)	85.69±5.22	77.92±4.36	6.138	<0.01

Table 2: Adenosine Deaminase Vs components of metabolic syndrome in cases

ADA Vs FBS	r = +0.014	p < 0.05
ADA Vs TG	r = +0.112	p < 0.05
ADA Vs HDL-C	r = - 0.02	p < 0.05
ADA Vs WC	r = + 0.034	p < 0.05
ADA Vs SBP	r = + 0.108	p < 0.05
ADA Vs DBP	r = + 0.092	p < 0.05

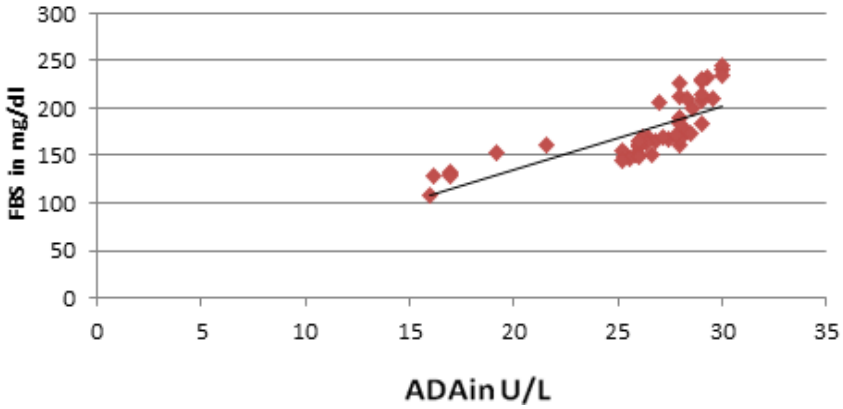

Fig. 1: Correlation of serum Adenosine Deaminase with Fasting Blood Sugar in cases

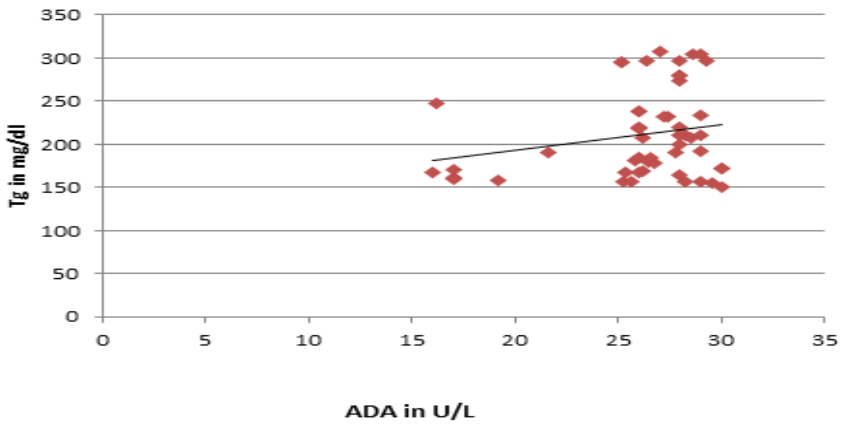

Fig. 2: Correlation of serum Adenosine Deaminase with Triglyceride in cases

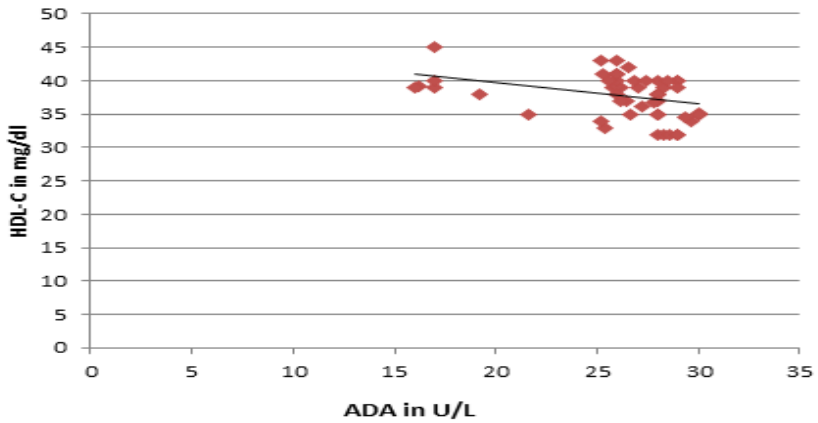

Fig. 3: Correlation of serum Adenosine Deaminase with HDL in cases

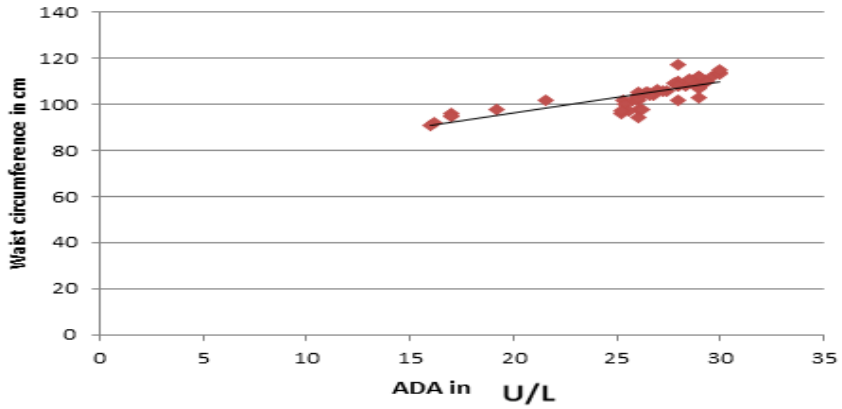

Fig. 4: Correlation of serum Adenosine Deaminase with Waist circumference in cases

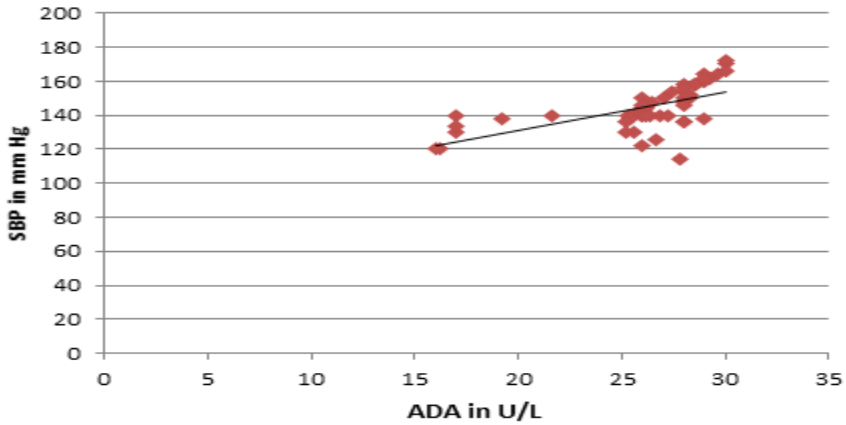

Fig. 5: Correlation of serum Adenosine Deaminase with SBP in cases

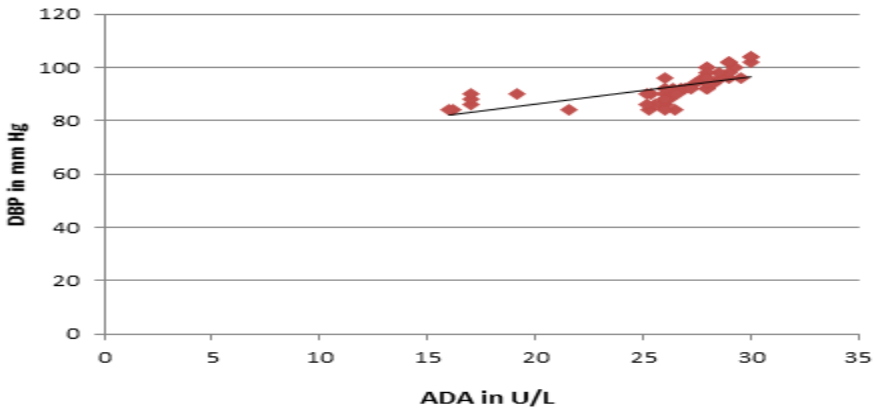

Fig. 6: Correlation of serum Adenosine Deaminase with DBP in cases

Discussion

The major component of Metabolic syndrome include central obesity, hypertriglyceridemia, decreased HDL, hyperglycemia & hypertension. The need for early indicators of Metabolic syndrome complications is essential to prevent late complications and their detrimental/ deleterious effects. There is a need for sensitive serum markers that are associated with Metabolic syndrome and its complications. Estimation of these parameters helps in early intervention, thereby delaying/ reverting the chronic complications of metabolic syndrome in the early stages. The present study was aimed to assess the Serum Adenosine Deaminase levels in Metabolic syndrome patients in comparison to age and sex matched normal healthy controls and also to correlate serum Adenosine Deaminase activity with the components of Metabolic syndrome in cases.

The pathogenesis behind the increased serum ADA levels in metabolic syndrome can be explained by

adenosine. Adenosine is called as retaliatory metabolite. Adenosine regulates adipokines secretion by adipose tissue. This explains its anti-lipolytic property & through this effect it reduces FFA level. Due to decrease in FFA levels there is increased in insulin sensitivity. This explains its capacity to act like insulin on adipose tissue. Adenosine will decrease the release of rennin secretion from juxta glomerular cells & thus regulates blood pressure levels. Adenosine production & utilization are primarily dependent on activity of producing enzymes 5' nucleotidase and 2 utilizing enzymes adenosine deaminase and adenosine kinase. It has been shown that in the adipose tissue most of the adenosine is formed extracellularly. Extracellular adenosine is metabolized by ADA. Thus increased formation of adenosine leads to increased adenosine deaminase. The source of extracellular formation of adenosine is via an enzyme cascade for breakdown of ATP, ADP and AMP which appears to be major mechanism that leads to elevated extracellular adenosine[16].

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 leads to decrease in adenosine in adipose tissue. This will lead to dysregulation of adipokines secretion. This leads to increase in FFA levels. Increase in FFA inturn causes elevation of insulin resistance. It is now a well-known fact that there is elevation of free fatty acid levels in diabetes consequent to increased lipolysis which leads to a vicious cycle of worsening insulin resistance and consequent hepatic beta cell failure; in addition to the other features of diabetes[17].

Excess non-esterified fatty acids is carried to liver & converted to TG & cholesterol. TG & cholesterol released its circulation as VLDL, leading to high circulating levels of both TG & LDL, Increased TG leads to decrease in HDL level. Decreased adenosine leads to positive regulation of rennin secretion from juxtaglomerular cells there by dysregulation of hypertension. This study shows that there is significant increase of ADA levels in cases of metabolic syndrome when compared to controls. It also shows that there is a significant positive correlation between increase in ADA levels with increase in FBS, TG, WC, SBP and DBP and significant negative correlation between increased ADA levels with decreased HDL levels. Thus early detection of elevation of ADA levels may help in early prevention and management of metabolic syndrome and its complications and may also help in monitoring further progression of complications in metabolic syndromes.

The public health impact of high serum ADA levels may be larger than currently thought. 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 metabolic syndrome and its complications[16,17].

Conclusion

Metabolic syndrome is a major worldwide health problem leading to markedly increased mortality and serious morbidity. The need for early indicators of Metabolic syndrome complications is essential to prevent late complications and their detrimental/ deleterious effects. There is a need for sensitive serum markers that are associated with Metabolic syndrome and its complications. Estimation of these parameters helps in early intervention, thereby delaying the chronic complications of metabolic syndrome in the early stages. 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 metabolic syndrome and its complications.

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