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Adiponectin as a biomarker of Metabolic Syndrome: A hospital based case control study

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ABSTRACT:

Background: Adiponectin levels are decreased in patients with metabolic syndrome (MetS). Thus, adiponectin can be a useful indicator for early diagnosis of metabolic syndrome. There are few studies from India using adiponectin as a marker of MetS.

Objective: To study the correlation of adiponectin with other markers of metabolic syndrome.

Methods: Hospital based, case control study was carried out among 80 cases (having MetS) and 80 healthy controls. Detailed history, clinical examination, anthropometry was carried out. Fasting blood sugar and lipid profile was estimated by enzymatic methods. Low density lipoprotein cholesterol was calculated by using Friedewald formula and Serum Adiponectin was assayed by ELISA kit.

Results: Cases and controls were similar for age and sex. Mean body mass index (BMI), waist circumference (WC), weight, fasting blood sugar (FBS), total cholesterol, serum triglycerides (TG), were significantly higher in cases compared to controls ($p<0.05$). Serum HDL and serum adiponectin were significantly lower in cases compared to controls ($p<0.05$). Serum adiponectin was significantly correlated with all components of MetS ($p<0.05$). It was negatively correlated with WC, FBS, TG, whereas it was positively correlated with HDL. Serum adiponectin level was significantly higher among the normal weight individuals compared to the overweight and obese individuals ($p<0.05$).

Conclusion: Hypoadiponectinemia is closely associated with the clinical phenotype of the metabolic syndrome and measuring the plasma concentration of adiponectin may be useful for the diagnosis of the metabolic syndrome.

Key words: Adiponectin, correlation, metabolic syndrome, lipid profile

INTRODUCTION

Metabolic syndrome is also known as syndrome X or visceral fat syndrome. It is a group of disorders which include resistance to insulin, obesity and the risk factors of cardiovascular disease. Adiposity is central to the metabolic syndrome. However, it has been stated that not all people with abdominal obesity will have it. [1]

The global prevalence of metabolic syndrome (MetS) varies from 15-40%. It has been found to be more prevalence in developing countries but it is often under-reported. Thus, it is an important public health problem. Individuals having metabolic syndrome are five times more at risk of developing diabetes and two times more risk of developing cardiovascular disease. [2]

Adiponectin is produced and secreted by the adipose tissues. It is an adipokine. It has certain important characteristics like anti-inflammatory, anti-diabetic and anti-atherogenic. It is well known for its cardio protective effect. [3, 4] In individuals with obesity, the adiponectin levels are decreased and at the same time, its expression is also reduced. [5]

According to the Adult Treatment Panel III (ATPIII) criteria of the National Cholesterol and Education Program (NCEP) for MetS; the presence of any three of the following characteristics: dysglycemia, low plasma high-density lipoprotein cholesterol (HDL-C), increased triglycerides (TG), elevated blood pressure, and abdominal obesity (AO). There is

international agreement on using the ATPIII criteria. However, the cut-off values of waist circumference differ by ethnicity, country, and region. [6]

People with metabolic syndrome have increased risk of type 2 diabetes mellitus, coronary heart disease and other cardio metabolic diseases. India has the highest number of people with type 2 diabetes mellitus i.e. 41 million. Globally, every fifth individual with type 2 diabetes mellitus is from India. This number is expected to be 82 million by 2030. [7, 8]

Those with metabolic syndrome are at an increased risk of atherosclerotic cardiovascular disease (ASCVD). It consists of an atherogenic dyslipidemia, elevation of blood pressure and glucose, prothrombotic and pro-inflammatory states. There is double the risk of atherosclerotic cardiovascular disease in people with metabolic syndrome compared to people without the metabolic syndrome. There are multiple pathways for the development of atherosclerotic cardiovascular disease in people with the metabolic syndrome. Compared to healthy controls, those with type-2 diabetes mellitus have higher levels of highly sensitive C reactive protein and at the same time low levels of adiponectin. [9]

As mentioned above, the adiponectin levels are decreased in patients with metabolic syndrome. Thus, adiponectin can be a useful indicator for early diagnosis of metabolic syndrome. Moreover, there are few studies from India using adiponectin as a marker of metabolic syndrome. Therefore, present study was carried out to study the correlation of adiponectin with other markers of metabolic syndrome.

MATERIAL AND METHODOS

Present study was single centre, hospital based, case control study was carried out in the Department of Biochemistry in collaboration with department of General Medicine from November 2016 to October 2018 among 80 cases (having metabolic syndrome) and 80 healthy controls.

Yosaee S et al [10] found that the mean adiponectin levels were 4.85 ± 1.8 in those with metabolic syndrome and 7.25 ± 3.2 in those without metabolic syndrome. Taking these values for sample size calculation, with 95% of confidence level, 80% power and ratio of cases to controls as 1:1, the sample size came out to be 26 for each group. However, we were able to include 80 cases and 80 controls.

Ethical clearance was obtained from the institutional research and ethics committee (No. 2016/I-F-CT-01/006). Written informed consent was taken from all the study participants.

The case definition was as per the ATP III 2001 guidelines – with any three of the following 1. Waist circumference: males >102 cm and females > 88 cm, raised triglycerides: $\geq$ 150 mg/dl, 3. Reduced HDL cholesterol: < 40 mg/dl in males and < 50 mg/dl in females, 4. Raised blood pressure (BP): systolic BP $\geq$ 130 mmHg or diastolic BP $\geq$ 85 mmHg or on treatment, 5. Raised fasting plasma glucose: $\geq$ 100 mg/dl. Controls were age, sex and socio-economic status matched non-obese individuals without metabolic syndrome.

Individuals of age 20-60 years of either gender or willing to participate were included. Those having type-1 diabetes mellitus, taking thiozolidinediones, insulin therapy, anti- inflammatory drugs, ACE inhibitors, ARBs, liver and renal failure and who were critically ill were excluded from the present study.

Blood pressure was measured by standard sphygmomanometer with right arm supine position.

Body mass index (BMI) was calculated by dividing the body weight in kilogram by the square of height in square meter. Following aseptic precautions five ml of blood was collected from each participant into a grey top vacutainer and plain vacutainer, after 20 minutes it was centrifuged at 4500 rpm for 10 minutes then the plasma and serum was separated.

Fasting blood sugar and lipid profile was estimated by enzymatic methods, Low density lipoprotein cholesterol was calculated by using Friedewald formula and Serum Adiponectin was assayed by ELISA kit.

Statistical analysis:

The data was expressed as proportions and means with standard deviation. Comparison of mean in two groups was tested applying t test and in more than two groups by analysis of variance test. Pearson correlation coefficient was calculated to study the correlation. Probability value of less than 0.05 was considered as statistically significant.

RESULTS

Table 1: Age and sex distribution of the study group

Characteristics	Case	Control	P value
Age	51.05±8.8	48.90±8.66	0.121
Sex(F:M)	37:43	34:46	

The mean age was not significantly different in cases and controls. The female to male ratio was also not significantly different in them. As they were matched for age and sex, they were similar for age and sex. (Table 1)

Table 2: Comparison of various parameters in cases and controls

Parameters	Cases	Controls	P value
BMI(kg/m^2)	27.77±3.82	26.28±2.64	**0.005**
Waist Circumference(cm)	102.80±6.10	93.61±8.17	**0.001**
Height(cm)	163.08±8.10	161.64±8.07	0.262
Weight(kg)	73.56±8.54	68.98±9.67	**0.002**
FBS(mg/dl)	110.35±35.19	83.4±11.06	**0.001**
Serum Urea(mg/dl)	30.33±4.73	28.39±6.06	0.290
Serum Creatinine (mg/dl)	0.806±0.198	0.878±0.156	0.233
Total Cholesterol(mg/dl)	164.34±39.66	148.83±34.5	**0.009**
Triglycerides(mg/dl)	162.24±60.24	117.65±40.99	**0.0001**
HDL(mg/dl)	36.93±7.9	41.43±7.82	**0.0004**
LDL(mg/dl)	96.21±29.23	86.31±33.62	0.065
Serum Adiponectin(ug/ml)	2.43±0.83	7.54±0.94	**0.0001**

The mean body mass index, waist circumference, weight, fasting blood sugar, total cholesterol, serum triglycerides, were significantly higher in cases compared to controls ($p<0.05$). Serum HDL and serum adiponectin were significantly lower in cases compared to controls ($p<0.05$).

Other parameters like height, serum urea, serum creatinine, and serum LDL were not significantly different among the cases and the controls (p>0.05). (Table 2)

Table 3: Correlation of serum adiponectin with components of metabolic syndrome

Components of metabolic syndrome	Correlation coefficient (r)	P value
Waist circumference (cm)	-0.806	<0.05
Fasting plasma glucose (mg/dl)	-0.576	<0.05
Triglycerides (mg/dl)	-0.298	<0.05
HDL (mg/dl)	0.562	<0.05

The serum adiponectin was found to be significantly correlated with all components of metabolic syndrome (p<0.05). It was negatively correlated with waist circumference, fasting plasma glucose and triglycerides, whereas it was positively correlated with HDL. (Table 3)

Table 4: Comparison of adiponectin across different categories of body mass index

	Normal weight	Over weight	Obese	P value
Age	45.13±11.9	50.6±10.04	47.40±11.42	0.646
Sex (F:M)	26:28	21:32	24:29	0.665
BMI (kg/m^2)	22.8±1.462	27.83±1.512	32.03±7.92	**<0.001**
Waist circumference (cm)	93.2±7.22	100.53±7.08	106.8±7.92	**<0.024**
Adiponectin (ug/ml)	7.211±0.40	3.396±0.93	2.844±0.143	**<0.001**

The body mass index and the waist circumference was significantly more in the obese individuals compared to overweight and the normal weight individuals. The serum adiponectin level was significantly higher among the normal weight individuals compared to the overweight and obese individuals (p<0.05). (Table 4)

DISCUSSION

In the present study, the mean age was not significantly different in cases and controls. The female to male ratio was also not significantly different in them. As they were matched for age and sex, they were similar for age and sex. The mean body mass index, waist circumference, weight, fasting blood sugar, total cholesterol, serum triglycerides, were significantly higher in cases compared to controls (p<0.05). Serum HDL and serum adiponectin were significantly lower in cases compared to controls (p<0.05). Other parameters like height, serum urea, serum creatinine, and serum LDL were not significantly different among the cases and the controls (p>0.05). The serum adiponectin was found to be significantly correlated with all components of metabolic syndrome. (p<0.05) It was negatively correlated with waist circumference, fasting plasma glucose and triglycerides, whereas it was positively correlated with HDL. The body mass index and the waist circumference was significantly more in the obese individuals compared to overweight and the normal weight individuals. The serum adiponectin level was significantly higher among the normal weight individuals compared to the overweight and obese individuals (p<0.05).

Rubin D et al [11] assessed serum adiponectin in 110 non-diabetic males after oral glucose tolerance test. They found that there was a significant decline two hours after giving load of glucose and five to six hours after giving load of lipid. Serum adiponectin measured after mixed

meal had a very good correlation with the components of metabolic syndrome. This correlation was not much evident when serum adiponectin was correlated after fasting values. They also found that after multivariate analysis, triglycerides independently predicted the levels of serum adiponectin. Thus, the authors concluded that postprandial adiponectin is significantly correlated with postprandial triglycerides.

St-Pierre AC et al [12] estimated cholesterol levels in small and large low density lipoproteins sub-fractions in 2072 males and followed them for 13 years. The incidence of ischemic heart disease was found in 262 cases. the authors found an independent association between LDL-C < 255 A levels with IHD in the first seven years of follow up. Values of this marker more than this limit were not found to have any kind of association.

Ryo M et al [13] enrolled 479 males and 182 females of age range 43-66. They found that there was a negative correlation of serum adiponectin with that of waist circumference, triglycerides, visceral fat, fasting blood sugar, systolic blood pressure, fasting insulin and diastolic blood pressure. They found that there was a positive correlation of serum adiponectin with that of high density lipoprotein. These findings are similar to the findings of the present study. They also reported that as the average number of components of metabolic syndrome increased, the serum adiponectin decreased significantly. We also found a significant association between serum adiponectin levels and the components of metabolic syndrome. The authors concluded that the low levels of serum adiponectin are significantly associated with metabolic syndrome clinical phenotypes and therefore for the management of metabolic syndrome, it may be useful to measure the serum adiponectin.

Mohan V et al [14] assessed the association between serum adiponectin with that of the components of metabolic syndrome in Asian Indians among 100 cases with diabetes and 100 matched controls without diabetes. They found that the levels of serum adiponectin were significantly lower in patients with diabetes and those having metabolic syndrome compared to their healthy counterparts. We also reported similar findings which are in accordance with this study. On linear regression analysis, the authors found that the serum adiponectin was significantly associated with waist circumference, body mass index, triglycerides, glycated haemoglobin and the fasting blood sugar. On logistic regression analysis, they found that there was a negative association between serum adiponectin and metabolic syndrome. We also found similar results.

Ogawa Y et al [15] investigated the relation between the serum adiponectin and metabolic syndrome among 100 boys with obesity of age 8-13 years. They formed three groups of this population based on the serum adiponectin percentiles. They found that there was significant difference in the prevalence of visceral fat, high level of serum insulin, raised values of low density lipoproteins and metabolic syndrome. They found that the area under curve was 0.672 with a cut-off value of 6.65 mcg/ml for serum adiponectin.

Arita Y et al [16] found from their study that the levels of the serum adiponectin ranged from 1.9 to 17 mg/ml among the healthy people. But, they were significantly lower among those with obesity. We also found a significant association between the serum adiponectin levels and the overweight and the obese cases.

Hotta K et al [17] analyzed the relation between the insulin resistance and the serum adiponectin in the rhesus monkeys. They found that the serum adiponectin levels were significantly lower in diabetic and obese monkeys. They also observed that during the early phase of obesity, the serum adiponectin levels decreased and remained so after development of diabetes.

CONCLUSION

Hypoadiponectinemia is closely associated with the clinical phenotype of the metabolic syndrome and measuring the plasma concentration of adiponectin may be useful for the diagnosis of the metabolic syndrome. The serum adiponectin values were significantly lower in cases which indicates its effectiveness as a potential biomarker of metabolic syndrome. Larger trials have to be done for determining the average value of serum adiponectin in our population.

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