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Serum Adiponectin: A Novel Biomarker of Glucose Intolerance in Prediabetic Obese Subjects

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ABSTRACT

Background: Prediabetes is an intermediate hyperglycemic and insulin resistant state. It includes subjects with impaired fasting glucose and/or impaired glucose tolerance. Adiponectin is a peptide hormones synthesize exclusively from adipose tissues and has insulin sensitizing property. Decreased adiponectin level was observed in prediabetes and in insulin resistant states in various studies. Adiponectin has been proposed as a biomarker of metabolic syndrome.

Objective: The aim of our study was to evaluate adiponectin level in prediabetic obese subjects and to compare it with the glucose tolerance in control subjects. We also studied correlation of adiponectin level with lipid profile.

Methods and methods: Study included 200 prediabetic subjects and 100 control subjects. Blood samples were analyzed for fasting blood glucose, lipid profile and adiponectin. According to BMI, control subjects were separated into obese (BMI ≥ 30) and control (BMI < 25) groups. **Results:** Mean serum adiponectin levels were statistically significant and were different in control and obese prediabetic groups (11.61 ±1.97 µg/ml) vs. (18.12 ± 9.27 µg/ml), $p<0.001$). Serum Adiponectin level was significantly lower in obese prediabetic group as compared to control group. Impaired glucose tolerance levels in control and obese prediabetics were (109.93 ± 10.78 mg/dl) and (156.10 ± 8.23 mg/dl) respectively. This difference was statistically very significant ($p<0.001$). Adiponectin showed inverse correlation with HOMA-IR ($p = 0.0011$).

Conclusions: Serum adiponectin level was decreased in obese prediabetics as compared with control subjects. Whereas impaired glucose tolerance was statistically significantly higher in subjects with prediabetic obese as compared to the healthy controls.

Keywords: adiponectin, glucose tolerance, prediabetes, obesity.

INTRODUCTION

Prediabetes is an intermediate metabolic state between normal glucose tolerance and type 2 diabetes [1]. It includes subjects with impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and both [2]. Every year, approximately 11% individuals with prediabetes progress to type 2 diabetes [3]. Thus for reducing the prevalence of type 2 diabetes it is very important to diagnose prediabetes. Moreover diagnosis of prediabetes is also important for reducing the cardiovascular risks that develop even before development of type 2 diabetes [4]. Conventionally prediabetes can be diagnosed by

fasting plasma glucose and or OGTT [3]. However these tests have certain limitations [5]. Adiponectin is a proinflammatory cytokine secreted from adipocytes, found to have insulin sensitizing property [6]. Circulating levels of Adiponectin decrease in patients who are obese and those with insulin resistance and type 2 diabetes. Present study thus aimed to find out the role of adiponectin as a biomarker of prediabetes in obese subjects as it shares the same underlying mechanism of insulin resistance [3].

MATERIAL AND METHODS

This study was conducted on 200 prediabetic obese subjects, selected via screening through survey in the Gwalior (M.P.) and the samples were processed in the Department of Biochemistry, G.R. Medical College & J. A. group of hospitals, Gwalior (M.P.). We had excluded the Patients with current insulin use or any medication that can affect blood glucose level, other diseases & agents that altered glucose metabolism and pregnant women. The screening questionnaires and written consents were taken from all the subjects. The study proforma which includes the anthropometric parameters like age, sex, height, weight etc. were noted during screening time using standardized techniques [7]. Ethical approval was taken from Institutional Ethical Committee, G.R. Medical College Gwalior. The serum adiponectin was measured by ELISA method. Fasting blood sugar (FBS) and lipid profile were estimated by Mindray BS-400 fully autoanalyser. BMI was calculated using the formula, weight in kilograms divided by the square of height in meters. The homeostasis model assessment of insulin resistance (HOMA-IR), an index of insulin resistance, was calculated using an equation as described by Matthews DR et al. [8].

STATISTICAL ANALYSIS:

As the reference value of adiponectin for this population is not established, we have taken the mean values of the control subjects as a reference. Data were summarized using standard procedures. All the data of overall status of anthropometric and biochemical parameters of obese prediabetic subjects were expressed as mean ± standard deviation (SD). Linear regression analyses were used to estimate the significance of adiponectin with BMI, W/H ratio, impaired glucose tolerance (IGT) and HOMA-IR. All analyses were performed using Statistical Package for the Social Sciences, version 23.0 (SPSS software). The graphs were prepared by using Excel and graph pad prism7. The p value < 0.05 was considered significant.

RESULTS

A total of 200 patients aged 31-69 years old were taken in the analysis with impaired glucose tolerance. Prediabetic subjects had elevated BMI, W/H, IGT, total cholesterol, triglycerides, LDL-C and VLDL but adiponectin and HDL-C were decreased significantly (Table 1). Table no. 2 showing the correlation of adiponectin with BMI, W/H ratio, IGT, insulin resistance (HOMA-IR) & lipid profile. Adiponectin was correlated negatively with BMI, W/H ratio, IGT and HOMA-IR as shown in figures 1 to 4.

Table 1: Overall status of anthropometric and biochemical parameters of control and prediabetic obese subjects.

Parameters	Mean ± SD (Control)	Mean± SD (Case)	P value
BMI (Kg/m^2)	24.87 ± 3.05	30.80 ± 1.93***	< 0.001
W/H Ratio	0.91 ± 0.06	0.94 ± 0.04***	< 0.001
IGT (mg/dl)	104.27 ± 10.06	155.34 ± 8.81***	< 0.001
Serum Adiponectin (µg/ml)	18.12 ± 9.26	11.61 ± 1.97***	< 0.001
HOMA IR	2.62 ± 0.86	3.40 ± 2.28***	0.0011

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Total cholesterol (mg/dl)	164.49 ± 18.04	178.16 ± 20.77***	< 0.001
Triglyceride (mg/dl)	105.33 ± 23.70	150.28 ± 28.46***	< 0.001
HDL-C (mg/dl)	45.24 ± 4.75	38.27 ± 4.74***	< 0.001
LDL-C (mg/dl)	94.92 ± 21.20	108.85 ± 21.18***	< 0.001
VLDL (mg/dl)	28.48 ± 6.70	28.05 ± 5.69NS	0.5620

Table 2: Pearson's correlation of adiponectin with BMI, W/H ratio, IGT, HOMA-IR and lipid profile

S/No.	Parameters	Adiponectin (r value)
1	BMI	-0.536
2	W/H	-0.52
3	FBG	-0.52
3	IGT	-0.494
4	HOMA-IR	-0.393
5	TC	-0.478
6	HDL-C	0.441
7	TG	-0.494
8	LDL	-0.39
9	VLDL	-0.494

** Correlation is significant at the 0.01 level.

Figure no. 1 Linear regression of Adiponectin vs W/H ratio

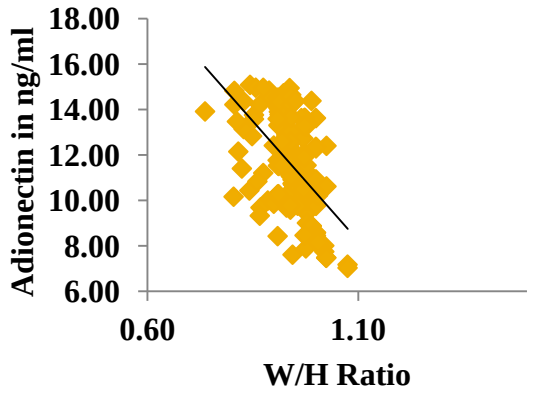

Figure no. 2 Linear regression of Adiponectin vs BMI

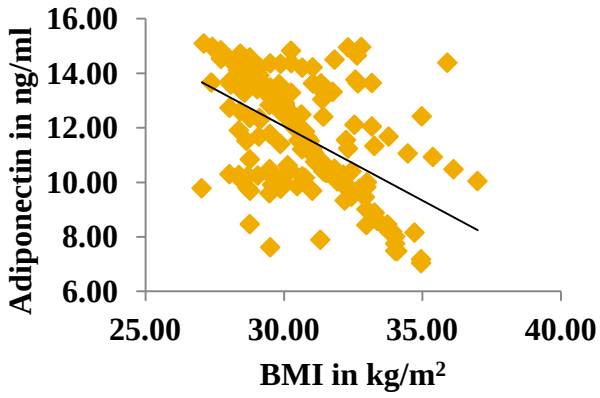

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Figure no.3 Linear regression of Adiponectin vs IGT

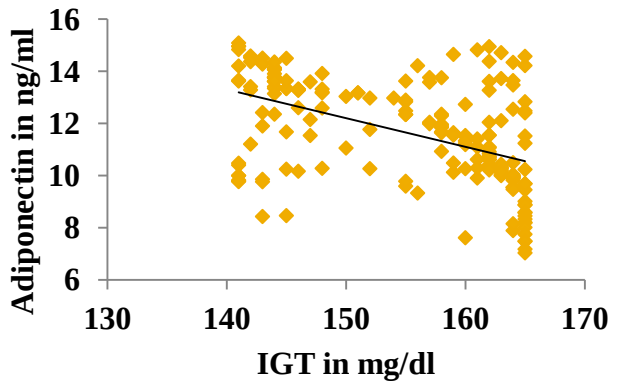
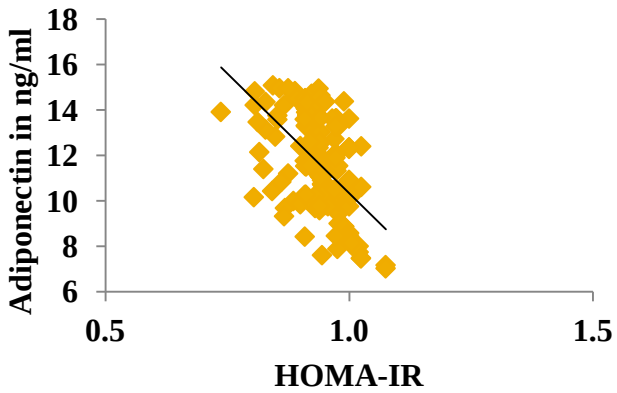


Figure no. 4 Linear regression of Adiponectin vs Homa-IR



DISCUSSION

Prediabetes is a metabolic state in between normal glucose tolerance and diabetes mellitus. It includes IFG and/or IGT subjects [2]. Adiponectin is one of the adipocyte secreted hormone [9]. Adiponectin level was found to be decreased in obese subjects. Plasma adiponectin levels have also been reported to be reduced in obese humans, particularly those with visceral obesity, and to correlate inversely with Insulin resistance [10, 11, 20, 21, 22, 23]. In this study we demonstrated that adiponectin level was decreased significantly in prediabetic obese subjects when compared with control subjects. Strong negative correlation was found among BMI, W/H ratio, IGT and HOMA-IR with adiponectin in prediabetic obese subjects. Similar findings were quoted by Urbanavičius V et al., 2008 [12]; Jiang Y et al., 2016 [13]; Kong SE et al., 2015[14]. One of the previous study conducted by Nakashimaet Y et al., 2008 in Japan showed that the decreased levels adiponectin were associated with impaired glucose tolerance (IGT) [15]. The results of our study suggest that adiponectin secretion is already altered in pre-diabetic conditions, and as the majority of subjects with IGT eventually will develop type 2 diabetes. Our data also suggest that metabolic alterations seen in IGT state are strong enough to further lead to diabetes development. Clinical and experimental studies have indicated that adiponectin directly affects obesity-related disorders, insulin resistance and atherosclerosis [16-19]. Kong SE et al., 2015 showed that the low adiponectin levels are associated with significant increases in waist-to-hip ratio in prediabetic subjects [14]. We observed significant relationships between adiponectin and several metabolic variables in our study. Plasma adiponectin concentration was negatively correlated with BMI, waist circumference, FPG, triglycerides, fasting insulin, HOMA-IR and positively correlated with HDL cholesterol.

Conclusion

The study supports the assumption that adiponectin may play an important role in the impaired glucose tolerance. From the above results, it may conclude that prediabetic subjects have decreased levels of adiponectin and altered metabolism is responsible for impaired glucose tolerance, thus producing insulin resistance in prediabetic obese subjects. Adiponectin can be used as a marker for diagnosis of prediabetes in obese subjects but it needs validation.

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