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Association of Serum Adiponectin with Dysglycemia and Dyslipidemia in Impaired Glucose Tolerance and Type 2 Diabetes Mellitus

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Abstract **Original Research Article**

Background*:** The association of low adiponectin concentration and type 2 diabetes is well studied but the association of adiponectin with prediabetes is still unresolved. Data from Bangladeshi population shows that both insulin secretory defect and insulin resistance are present in T2DM subjects, but the secretory defects seem to have a predominant role. In a search for the downward factors regulating the basic defects attention has also been focused to inflammatory markers and adipocytokines. Adiponectin is one of the major targets for such studies and few studies have already been conducted on the association of adiponectin with prediabetes in our population. ***Objective*:** The objective of our study was to evaluate adiponectin level in subjects with pre-diabetes and to compare it with the levels in newly diagnosed type 2 diabetes and healthy (normal glucose tolerance) subjects. ***Method*:** It was an observational analytic study with a group compare design. The study was conducted in the Biomedical Research Group and Department of Biochemistry & Cell Biology of the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka. This study was done during the period of July 2012 to June 2013. ***Results: IGT and Controls subjects were age and BMI matched. Mean (±SD) age of Control, IGT and T2DM subjects were 38.75±8.40, 42.71±7.65 and 44.61±7.00 years respectively. Age of T2DM subjects were higher compared to controls (p=0.022). Mean (±SD) BMI of the Control, IGT and T2DM subjects were 20.53±2.43, 20.89±2.22 and 21.14±2.23 respectively. ***Conclusion:*** From our study we can conclude that, type 2 DM subjects have lower adiponectin level compared to controls. Prediabetic subjects do not have lower adiponectin level, but they have a lower adiponectin- glucose ratio compared to controls.

Keywords: Serum adiponectin, dysglycemia, dyslipidemia, impaired glucose.

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. When fully expressed, diabetes is characterized by fasting hyperglycemia, but the disease can also be recognized during less overt stages, most usually by the presence of glucose intolerance.

Although a number of specific causes of DM have been identified, the etiology and pathogenesis of the more common types are less clearly understood. The majority of cases of diabetes fall into two broad etiopathogenetic categories, now called type 1 and type 2 diabetes (WHO Consultation Group 1999) but the extent of heterogeneity among these types remains uncertain[1]. Because of the increasing number of types of diabetes for which a specific etiology can be recognized, the current clinical classification, proposed by the American Diabetic Association (ADA) in 1997

and adopted by the World Health Organization (WHO) in 1999 and that supersedes the previously internationally recognized 1985 WHO classification [1].

The clinical staging reflects that diabetes progresses through several stages during its natural history and that individual subjects may move from one stage to another in either direction. The global prevalence of T2DM is expected to be double in the period 2000-2025 and may reach a level of almost 300 million people [2].

The global prevalence of T2DM is expected to be double in the period 2000-2025 and may reach a level of almost 300 million people[2].The progressive deterioration of pancreatic insulin secretion has been implicated as the proximate cause of the progressive increase in plasma glucose level [3]. Thus decrease in insulin secretion is a major contributor to the development of the overt T2DM state.

Type 2 diabetes develops through the stage of IFG and/or IGT, which are asymptomatic and unassociated with any manifested morbidity. Their sole significance lies in the fact that they predict future diabetes or cardiovascular disease [4]. Recently, it has been found that insulin resistance and insulin secretory defect appears in the prediabetes stage i.e., before the onset of diabetes [5].

The association of low adiponectin concentration and type 2 diabetes is rather well studied, only few studies investigated adiponectin level in prediabetes (e.g. impaired glucose tolerance and impaired fasting glucose) [6, 7]. The results of some studies are rather conflicting, one study showing similar levels of adiponectin in pre-diabetes and type 2 diabetes and another study reporting significantly higher levels of adiponectin in pre-diabetes as compared to type 2 diabetes [6, 7]. It seems that association of adiponectin with insulin resistance occurs early in obesity development; however it remains unclear if this association is of further importance in prediabetes and early stages of type 2 diabetes and remains the same through all glucose intolerance development stages.

From the basic scientific point of view, association of serum adiponectin with impaired glucose regulation has got practical relevance in designing appropriate management and prevention policies. Although, the present investigation covers only a section of prediabetic subjects in our population it may give important methodological and technical tools for further studies in this direction.

OBJECTIVE

General Objective

The general objective of the study was association of serum adiponectin with dysglycemia and dyslipidemia among IGT and T2DM subjects

Specific Objectives

1. The specific objectives of the study were:
2. To measure serum adiponectin level. ; in control, IGT and T2DM subjects
3. To explore association of serum adiponectin with IGT and T2DM.
4. To investigate the association of serum adiponectin with fasting and postprandial plasma glucose and fasting lipids in control, IGT and T2DM subjects.

METHODOLOGY

Study design

It was an observational analytic study with a group compare design.

Place of the study

The study was conducted in the Biomedical Research Group and Department of Biochemistry & Cell Biology of the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka.

Study period: This study was done during the period of July 2012 to June 2013.

Sampling Method: A purposive sampling method

Sample Size

A group of 71 subjects were included in this study and they were recruited from the Out-Patient Department of the BIRDEM Hospital.

Inclusion criteria

- Adult subjects with age ranging from 22-57 years.
- Voluntarily agreed to include in this study by providing informed consent.

Exclusion criteria

- Patients with serious co-morbid diseases (severe infection, stroke, myocardial infarction, major surgery, mal-absorption etc).
- History of using drugs significantly affecting glucose metabolism (glucocorticoids, oral contraceptives containing levonorgestrel or high-dose estrogen, phenytoin, high-dose thiazide diuretics etc.)
- Pregnancy.

Statistical Analysis

Data were expressed as mean ±SD and/or median (range) where appropriate. Comparison between two groups was done using Students ‘t’ test (paired and unpaired), Mann-Whitney ‘U’ test and Wilcoxon ‘Z’ test. Bivariatte correlation analysis was done by using Spearman’s Correlation analysis. To adjust the effects of confounder variables multiple linear regression analysis was done taking serum adiponectin level and

fasting glucose as a dependent variable. Data were managed and statistical analyses were performed using Statistical Package for Social Science (SPSS) for Windows version 11.5. A p value <0.05 was taken as level of significance.

RESULTS

Clinical and anthropometric characteristics of the study subjects

Table 1: Clinical and anthropometric characteristics of the study subjects

Variable	Control(22)	IGT(36)	T2DM(13)	t/p value		
				Control/IGT	Control/T2DM	IGT/T2DM
AGE(years)	38.75±8.40	42.71±7.64	44.61±7.00	1.774/ 0.076	-2.449/ 0.022	-0.727/ 0.473
BMI (kg/m^2)	20.53±2.43	20.89±2.22	21.14±2.23	0.556/ 0.581	-0.796/ 0.430	-0.322/ 0.749
WHR	0.905±0.03	0.927±0.03	0.922±0.02	2.465/ 0.019	-2.102 0.048	0.399/ 0.693
Creatinine (mg/dl)	0.936±0.16	0.957±0.17	0.981±0.17	0.459/ 0.648	0.787/ 0.436	0.394/ 0.696
SGPT(u/l)	22.22±8.99	26.00±19.57	27.00±15.74	0.987 /0.327	1.276 /0.208	-0.145/ 0.886

Results were expressed as Mean±SD. n=number of subjects; BMI, body mass index; WHR, waist to hip ratio;serum creatinine,serum SGPT:serum glutamate pyruvate kinase IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus.

Table 1 shows that mean (±SD) age in the Control, IGT and T2DM subjects were 38.75±8.40, 42.71±7.65 and 44.61±7.00 years respectively. Mean (±SD) BMI in the Control, IGT and T2DM subjects were 20.53±2.43, 20.89±2.22 and 21.14±2.23 respectively. Mean BMI of IGT and T2DM did not show statistically significant differece compared to the Control (Table 1). Mean WHR in the IGT and T2DM group were statistically significant difference compared to the Control (p=0.019,p=0.048) but T2DM group did not show any statistically significant to IGT (Table 1). Mean (±SD) serum creatinine value of Control, IGT and subjects were 0.936±0.16 ,0.957±0.17 and 0.95±0.15 respectively. The value did not show statistically significant with each other. Mean (±SD) value of SGPT of Control, IGT and subjects were 22.22±8.99,26.00±19.57 and 27.00±15.74 respectively.

Glycemic and lipidemic status of the study subjects

Table 2: Glycemic and lipidemic status of the study subjects

Variable	Control(22)	IGT(36)	T2DM(13)	t/p value		
				Control/ IGT	Control/ T2DM	IGT/ T2DM
F Glucose (mmol/l)	5.08±0.56	5.67±1.19	7.05±2.09	2.131/ 0.043	-3.354/ 0.005	-2.165/ 0.045
postprandial Glucose (mmol/l)	6.17±0.91	8.95±0.93	12.99±3.81	10.88/ 0.0001	-6.375/ 0.0001	-3.746/ 0.002
TG(mg/dl)	153.69±84.11	190.09±107.34	191.23±75.24	1.422/ 0.161	-1.419/ 0.162	-0.036/ 0.971
Choesterol(mg/dl)	187.25±36.28	203.04±31.16	194.07±45.01	1.667/ 0.089	-0.545/ 0.588	0.688/ 0.497
HDL-c(mg/dl)	37.30±7.93	40.95±8.93	33.23±10.00	1.598/ 0.130	1.480/ 0.146	2.278/ 0.032
LDL-c(mg/dl)	119.20±31.01	124.07±24.35	122.41±43.67	0.616/ 0.514	-0.286/ 0.776	0.143/ 0.887

Results were expressed as Mean±SD. n=number of subjects; F Glucose, fasting serum glucose; 2hrs Glucose, postprandial serum glucose (serum glucose 2 hours after 75g glucose load); TG, triglyceride; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; IGT, Impaired glucose tolerance; T2DM, type 2 diabetes mellitus

Table 2 shows that mean fasting glucose in IGT and T2DM group show statistically significant difference compared to the Control (p=0.043,p=0.005 and p=0.045 respectively). Mean (±SD) postprandial serum glucose in the Control, IGT and T2DM subjects were 6.17±0.91, 8.95±0.93 and 12.99±3.81 respectively. Mean (±SD) TG in the Control, IGT and T2DM subjects were 153.69±84.11, 190.09±107.34 and 191.23±75.24 respectively. Mean TG value in the

T2DM and IGT group did not show statistically significance difference compared to control. Mean (±SD) total cholesterol in the Control, IGT and T2DM subjects were 187.25±36.28, 190.09±107.54 and 191.23±75.24 respectively. Mean total HDL of T2DM statistically difference significant compared to the IGT subjects (P=0.032). Mean (±SD) serum LDL-c value in the Control, IGT and T2DM subjects were 119.20±31.01, 124.07±24.35 and 122.41±43.67 respectively. Mean value of IGT and T2DM did not show statistically significant compared to the Control.

Ratio analysis of ADIPONECTIN with various parameters:

Table-3: Adiponectin level of the study subjects

Variable	Control(22)	IGT(36)	T2DM(13)	t/p value		
				Control/IGT	Control/T2DM	IGT/T2DM
Adiponectin	11.22±2.78	11.13±3.26	8.44±1.82	-0.114/ 0.909	4.059/ 0.0001	3.081/ 0.004
F-Adipo : FGlu	2.24±0.616	2.04±0.726	1.29±0.445	-1.096/ 0.278	5.909/ 0.0001	3.738/ 0.OO1
F-Adipo : PGlu	1.83±0.424	1.26±0.418	0.682±0.188	-4.90/ 0.0001	13.05/ 0.0001	5.517/ 0.0001
F-Adipo : FTG	0.0915±0.047	0.078±0.046	0.050±0.022	-0.979/ 0.332	4.139/ 0.0001	2.40/ 0.023
F-Adipo : FCHOL	0.625±0.019	0.056±0.017	0.467±0.018	-1.212/ 0.231	2.615/ 0.015	1.480/ 0.149

Table 3 shows that mean (±SD) value of serum fasting adiponectin value in the Control, IGT and T2DM subjects were 11.22±2.78, 11.13±3.26 and 8.44±1.82 respectively. T2DM value showed statistically significant difference compared to the control and IGT groups (p=0.0001,p=0.001). Serum fasting adiponectin and fasting TG ratio in Control, IGT and T2DM were 0.091±0.04, 0.078±0.046 and 0.050±0.022 respectively. Serum fasting adiponectin and fasting cholesterol ratio in Control, IGR and T2DM were 0.625±0.019, 0.056±0.017, 0.047±0.018 respectively. T2DM value showed statistically significant difference compared to the control group (p=0.015). Serum fasting adiponectin and postprandial glucose ratio in Control, IGT and T2DM were 1.83±0.424,1.26±0.418, 0.682±0.188 respectively. The value showed statistically significant difference between these groups (p=0.0001, p=0.0001.p=0.0001).

Biochemical and anthropometric value among the male and female subjects:

Table-4: Biochemical and anthropometric measurements of the male and female subjects

Variables	Male (n=48)	Female (n=23)	*t/p value*
Age (yrs)	41.02±8.21	39.95±7.64	-0.500/0.619
BMI (kg/m^2)	20.64±2.22	20.78±2.52	0.230/0.819
WHR	0.916±0.31	0.912±0.028	-0.672/0.504
Fasting glucose(mmol/l)	5.66±1.51	5.42±0.79	-0.672/0.504
Postprandial(mmol/l)	8.22±3.52	8.17±2.07	-0.057/0.955
TG(mg/dl)	181.81±97.26	149.80±75.78	-1.313/0.194
Cholesterol (mg/dl)	200.08±36.91	179.20±32.44	-2.320/0.025
HDL-c(mg/dl)	36.85±9.50	40.10±6.88	1.381/0.172
LDL-c(mg/dl)	126.86±31.08	109.14±30.40	-2.176±0.036
S Creatinine(mg/dl)	0.989±0.156	0.855±0.153	-3.273/0.002
SGPT(u/l)	26.29±15.99	19.05±5.84	-2.730/0.008

Table IV shows that mean (±SD) age of the male subjects and female subjects were 41.02±8.21 and 39.95±7.64 respectively. Mean (±SD) BMI of the male and female subjects were 20.64±2.22 and 20.78±2.52 respectively. The value did not show any statistically significant (p=0.819). Mean (±SD) WHR of male subjects and female subjects were 0.91±0.03 and 0 .91±0.02 respectively. Mean (±SD) value of fasting serum glucose (FSG) of male and female subjects were 5.66±1.51 and 5.42±0.79 respectively. Mean (±SD) value of 2 hours after serum glucose (PSG) of Male and female subjects were 8.22 ±3.52and 8.17±2.07 respectively. These value did not show statistically significant (p=0.955). Mean(±SD) TG value of male and female subjects were 181.81±97.28 and 149.80±75.78 respectively. The value did not show statistically significant (p=0.194). Mean(±SD) value of total cholesterol of male and female subjects were 200.08±36.91 and 179.20±32.44 respectively. The value showed statistically significant difference (p=0.025). Mean (±SD) value of HDL-c of male and female subjects were 36.85±9.50 and 40.10±6.88

respectivelyMean(±SD) value of serum LDL-c of male and female subjects were 126.86±31.08 and 109.14±30.40 respectively. The value showed statistically significant (p=0.036). Mean (±SD) value of serum creatinine of male and female subjects were 0.989±0.156 and 0.85±0.15 respectively. The value showed statistically significant (p=0.002). Mean (±SD) value of SGPT of male and female subjects were 26.29±15.99 and 19.05±5.84 respectively.

DISCUSSION

Adipose tissue was found to produce a variety of adipocytokines including leptin, adiposin and tumor necrosis factor [8-10]. Adiponectin is the recently identified most abundant among of them – is a 30. kDa protein [11, 12]. Mechanisms of regulation of adiponectin proposed to be multifactorial. Involvements of genetic factors, glucocorticosteroids, body fat distribution and insulin have been shown in different studies.

Data from Bangladeshi population shows that both insulin secretory defect and insulin resistance are present in T2DM subjects, but the secretory defects seem to have a predominant role [13]. In a search for the downward factors regulating the basic defects attention has also been focused to inflammatory markers and adipocytokines. Adiponectin is one of the major target for such studies. Few studies have already been conducted on the association of adiponectin with prediabetes and also with T2DM subjects [14].

Each of the basic defects of diabetes mellitus, in turn, are determined and modulated by a number of factors. In particular, subclinical chronic inflammation, linked with a number of proinflammatory adipocytokines (TNF-α, IL-6) have been implicated with insulin resistance in these conditions. Excess adiposity is another most important risk factor for the development of insulin resistance and IGT (Wilding, 2003) [15]. Several features render adiponectin, an attractive and tractable biomarker for large epidemiologic studies, such as its long half-life, high ex vivo stability, and minimal diurnal variability and it is negatively correlated with markers of inflammation in vivo and is the link between adiposity, inflammation, and IGT [16].

The results of these studies are rather conflicting. one group showing similar levels of adiponectin in pre-diabetes and type 2 diabetes (Bluher *et al*., 2007), while the other one reporting significantly higher levels of adiponectin in pre-diabetes as compared to type 2 diabetes [6, 7]. It seems that association of adiponectin with insulin resistance occurs early in obesity development. However it remains unclear if this association is of further importance in prediabetes and early stages of type 2 diabetes. The objective of the present study was to evaluate adiponectin level in subjects with pre-diabetes and to compare it with the levels in newly diagnosed type 2 diabetes and healthy (normal glucose tolerance) subjects.

CONCLUSION

I conclusion we can say that type 2 DM subjects have lower adiponectin level compared to controls. Prediabetic subjects do not have lower adiponectin level, but they have a lower adiponectin-glucose ratio compared to controls.

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