Original Article

Serum level of adiponectin and leptin in type 2 diabetic Cigarette smokers.

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Summary:

Background: Cigarette smoking is the leading avoidable cause of morbidity and mortality in the general population; however its effects on people with diabetes are even more profound. The adipocytokines leptin and adiponectin play an important role in regulating glycemia, lipidemia, endothelial dysfunction, and proinflammatory mechanisms .

Objective: We aimed to investigate the profile of adiponectin and leptin in type 2 diabetic smokers and non- smokers.

Patients and Methods: Ninety overweight males attending the Teaching Laboratories, Medical City were enrolled in this study, they were arranged as 30 diabetics non smoker, 30 diabetics smokers and 30 age matched apparently healthy control group.The mean age of participants was 48.3 ± 5 years.
Fasting venous blood samples were collected from all the subjects. The serum was used for analyzing Fasting Blood Glucose (FBG), Total cholesterol (TC), HDL-cholesterol (HDL-C), Triglycerides (TG).HbA1c was estimated by high performance liquid chromatography, LDL-cholesterol was calculated by Friedwald and Frederickson formula. Enzyme linked immune assay were used to measure Insulin, Adiponectin and leptin . BMI was calculated as weight in kilograms divided by height in meters squared. Insulin resistance was calculated using HOMA-IR . Analysis of data was performed using the statistically package for social science (SPSS) version 17.0.

Results: Serum adiponectin and leptin level were significantly lower in the diabetics group as compared to age and BMI matched control group (7.25 ± 0.5 vs 9.15±0.3 and7.1 ±0.6 vs.23.5±6.3 respectively), Serum adiponectin and leptin level were significantly lower in diabetics who were smokers compared to the non smokers (5.5 ±0.7 vs 8.8 ±0.9; p=0.005) and (5.02 ±0.6 vs 8 ± 0.9;p=0.01 respectively), Adiponectin correlate negatively with BMI and positively with age .

Conclusion: The level of serum leptin and adiponectin were lower in diabetics who were cigarette smokers.

Keywords: Adiponectin, leptin, smoking, Diabetes mellitus.

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Introduction:

Cigarette smoking is the leading avoidable cause of morbidity and mortality in the general population; however its effects on people with diabetes are even more intricate and profound. All-cause mortality is increased in smokers with diabetes, and the risk of macrovascular and microvascular complications is also increased, cigarette smoke contains thousands of potentially bioactive constituents, including free radicals, furthermore smoking has been linked to worsening diabetes control [1].The adipocyte is an active endocrine secretary cell releasing several cytokines, free fatty acids and hormones as leptin, adiponectin, tumor necrosis factor, which play an important role in regulating glycemia, lipidemia, endothelial dysfunction, and proinflammatory mechanisms [2].Leptin is primarily involved in central regulation of food intake and energy expenditure and acts on a specific receptors located in the hypothalamus to decrease appetite and increase energy expenditure . Leptin also regulates vascular function, bone and cartilage growth as well as the immune system and systemic inflammatory response . Leptin action is mediated by cell surface leptin receptors, and participates in several mechanisms of diseases associated with obesity [3, 4].Adiponectin is a novel collagen like protein synthesized by the adipocytes that circulates at relatively high serum and accounting for about 0.01% of total plasma proteins [5, 6] ,and are inversely associated with obesity, , as well as with hyperlipidemia and insulin resistance In addition, adiponectin seems to have antiatherogenic and anti-inflammatory properties [7,8] .

Objective: to investigate the profile of adiponectin and leptin in smokers and non- smokers type 2 diabetic patients

Patients and methods:

Ninety (90) male attending the Teaching Laboratories, Medical City were enrolled in this study. They were recruited as 30 apparently healthy male (control group), 30 smoker diabetic,30 non smokers diabetic.The mean age of the studied population

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(was 48.3 ± 5 years) .Inclusion criteria: age 30–65 yr, type 2 DM, male, overweight ,no treatment with insulin or with any other drug known to influence glucose or lipid metabolism; no history of recent acute illness or clinical evidence suggestive of kidney, liver, or other endocrine diseases; no severe chronic diabetic complications (retinopathy , macroalbuminuria, symptomatic neuropathy, coronary and other vascular diseases).Cigarette smokers group had been smoking about 8-10 cigarettes per day for 10-15 yr, the control and the other group had never smoked.The groups were matched for age, BMI(all were overweight), diabetic duration, and treatment. All participants underwent a medical history and physical examination. The smoking group was selected to match the nonsmoking group in several clinical aspects, including chronic diabetic complications. This selection process might have eliminated the possibility of finding more striking metabolic differences between the two groups. Fasting venous blood samples were collected from all the subjects. The serum was used for analyzing Fasting Blood Glucose (FBG), Total cholesterol (TC), HDL-cholesterol (HDL-C), Triglycerides (TG).HbA1c was estimated by high performance liquid chromatography(supplied by Variant company, USA). Glucose level was determined using kits supplied by Randox, UK . Total cholesterol, triglycerides, high density lipoprotein were determined using kits (Biomaghrab,Sa,France). LDL-cholesterol was calculated by Friedwald and Frederickson formula,Enzyme linked immune assay were used to measure insulin (DRG kit, Germany),adiponectin (DRG kit, USA) and leptin (DRG kit, Germany) . Insulin resistance was measured according to the following formula [9]:HOMA-IR: Homeostasis Model of Assessment - Insulin Resistance=fasting Glucose(mg/dl) x fasting Insulin(µU/mL) / 405 Statistical analysis: Statistical analysis was done by SPSS version 17.0. Independent samples t-test (2-tailed) was used to compare means of different parameters. All values are expressed as mean ± standard error of mean. Pearson's correlation test was performed to examine correlations between various parameters, the results were considered statistically significant when $P < 0.05$.

Results:

Serum adiponectin and leptin level were significantly lower in the diabetics group as compared to age and BMI matched control group (table 1) in addition insulin resistance as measured by HOMA- IR was higher in diabetics, no significant difference in the lipid profile between the control and diabetic group, however TG,TC,LDL-C were higher and HDL-C was lower in T2DM patients.Serum leptin and adiponectin were significantly lower in diabetics who were smokers compared to the non smokers, insulin resistance was higher; no significant difference was observed in the glycemic control or the lipid profile between these two groups.Negative significant correlation was found between adiponectin and BMI, positive significant correlation was found between adiponectin and age.

Table 1: Baseline, demographic and biochemical characteristics of the diabetics and the control group

	Control	Diabetics	P-value
Age (years)	47.1±2.2	48.4±1.9	0.6
BMI(kg/m^2)	27± 0.5	26.5± 0.7	0.6
FBG(mg/dl)	96.4±3	184.2±7	0.000**
HbA_{1C} (%)	5.2 ±1.7	9.62± 2.03	0.000**
Leptin(ng/ml)	23.53±6.3	7.1 ±0.6	0.001**
Adiponectin(µg/ml)	9.15±0.3	7.25±0.5	0.009*
Insulin(µIU/ml)	10.76±0.4	13 ±1.3	0.16
Homa-IR	2.57±0.1	5.72±0.6	0.000**
TC(mg/dl)	178±4.5	183±4.7	0.48
TG(mg/dl)	129±9	149±12	0. 15
HDL-C (mg/dl)	31.6±1.6	34±1.9	0. 12
LDL-C (mg/dl)	124± 4.2	113±5.6	0.166

Results are expressed as mean ± SD ,P value less than 0.05 is considered statistically significant*, P value less than 0.001 is highly significant**

Table2: Baseline, demographic and biochemical characteristics of the diabetic smokers and non-smokers

	Diabetics-Non Smoker	Diabetics Smokers	P-value
number	30	30	
Age (years)	50.5±2.5	46.6±3	0.3
BMI(kg/m^2)	26.6± 0.9	26.3±1.1	0.8
FBG(mg/dl)	178 ± 14	190 ± 12	0.6
HbA_{1C} (%)	9.5±2.2	9.75±2.1	0.8
Leptin(ng/ml)	8 ± 0.9	5.02±0.6	0.012*
Adiponectin(µg/ml)	8.8 ± 0.7	5.5±0.7	0.005*
Insulin(µIU/ml)	12.2± 2.4	14.1± 0.6	0.4
Homa-IR	4.5 ± 0.75	7.1± 0.95	0.04*
TC(mg/dl)	183.5±7	183±5	0.9
TG(mg/dl)	177±17	168±18	0.7
HDL-C (mg/dl)	39.1±3	38.7±2	0.9
LDL-C (mg/dl)	111.2±9	115.2±5	0.7

Results are expressed as mean ± SD ,P value less than 0.05 is considered statistically significant*, P value less than 0.001 is highly significant**

Table 3: Correlation between different parameters

	R	P-value
Adiponectin and age	0.316	0.006*
Adiponectin and BMI	0.572-	0.001**

* Correlation is significant at 0.05 level (2-tailed)

** Correlation is highly significant at 0.001 level (2-tailed)

Discussion:

Type 2 diabetes mellitus has become a worldwide epidemic and a major public health burden. It is one of the most common non-communicable diseases, the World Health Organization estimates that 366 million people would have T2DM by 2030 [10].The study showed that the level of serum adiponectin in diabetics was lower than its level in the control group, comparable to the results of others[11,12] hypoadiponectenemia has many adverse clinical consequences as adiponectin has anti-atherogenic and anti-inflammatory properties [7,8] .In the present study serum leptin level also was lower in diabetics compared to weight matched control subjects; the level of leptin in diabetics in other studies had shown discrepant results showing no effect [13,14] or a decrease in serum leptin level [15,16] .The reduction in serum leptin level in diabetic may have metabolic consequences because leptin enhance whole body insulin sensitivity, increase glucose turnover, improve glucose uptake by muscle, and decrease hepatic glucose production[17]. The present study showed the serum adiponectin level to be significantly lower in smokers, smoking has been identified as a source of reactive oxygen species, and associated with increased levels of inflammatory markers, inflammation might down-regulate adiponectin expression in adipose tissue. In addition insulin resistance was significantly higher in diabetic smokers which may play a role in this hypoadiponectenemia[18]., the hypoadiponectemia associated with smoking is in agreement with other studies [19,20] Serum leptin level was lower in DM smokers compared to nonsmokers; the effect of smoking on plasma leptin has been divergent in clinical trials. some studies have mentioned decreased serum leptin in smokers[21,22] while others found no difference between smokers and non-smokers regarding circulating leptin level [23] Possible mechanisms for the lower leptin in smokers could be related to the fact that smoking increases plasma catecholamines , cortisol, adrenocorticotrophic hormone ,these effects may be responsible for the decrement of insulin-mediated glucose uptake in smokers [24],in addition the nicotinic effect of smoking may alter the sensitivity of hypothalamic leptin receptors and modulate leptin synthesis[25], The low leptin had been shown to be a predictor of cardiovascular mortality which add to the burden of both diabetes and smoking related complications [26].Adiponectin correlate negatively with BMI and positively with age similar to the results of previous studies [27]. The study revealed that insulin resistance in diabetics was worsened by concomitant cigarette smoking, however the fasting glucose and glycated hemoglobin concentrations didn't differ significantly between smokers and nonsmokers; Over a long-term period, the mildly higher glucose levels might result in a greater propensity to develop chronic diabetic complications, as recently demonstrated by results from the Diabetes Control and Complications Trial [28].The main finding of this study is the low serum level of both adiponectin and leptin, this has many adverse clinical consequences as adiponectin has anti-atherogenic and anti-inflammatory properties [7, 8] and low leptin had been shown to be a predictor of cardiovascular mortality .Therefore, further focus on public health and clinical interventions is needed to prevent tobacco use and promote smoking cessation [28] .

Conclusion: the level of serum leptin and adiponectin were lower in diabetics who were cigarette smokers.

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