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The Association Between Body Mass Index, Lipid Profile and Serum Estradiol Levels in a Sample of Iraqi Diabetic Premenopausal Women

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Abstract

Objectives: To evaluate the association between body mass index (BMI), serum lipid profile and estradiol level in a sample of Iraqi diabetic premenopausal women at their pre ovulatory period.

Methods: A total of 155 diabetic female patients aged between 20-45 years, were enrolled in this study, which was conducted in Al Khademiyia Teaching Hospital from July 2008 to January 2010. Venous blood samples were taken, each serum sample was analyzed for total cholesterol, triglycerides, high density lipoprotein - cholesterol (HDL-C), low density lipoprotein - cholesterol (LDL-C), fasting glucose, insulin and estradiol. Body weight and height were measured for all patients included to calculate their Body Mass Index.

Results: The age of diabetic patients was 29.7 ± 4.3 years and BMI was 28.3 ±5.84 kg/m^2. Fifty patients had normal BMI, while 50 patients were overweight and 55 were obese. The study revealed a positive association between obesity, triglycerides and LDL-C and a negative association between serum estradiol, obesity and LDL-C.

Conclusion: Iraqi diabetic pre menopausal women at their pre ovulatory period exhibit a pro-atherogenic risk profile because of their abnormal BMI, higher LDL-C, lower HDL-cholesterol and estradiol level.

Keywords: BMI; Lipid Profile; Serum Estradiol; DM; Premenopausal women.

Introduction

Diabetes mellitus is a world health problem that affects all human society at various stages of development. It is more common amongst developed countries where affluent and overweight individuals live longer than in under developed countries. A worldwide epidemic exists with respect to diabetes mellitus, primarily because of increased rates of obesity. Obesity has become widespread in developed countries along with a corresponding increase in the prevalence of diabetes.[1]

Epidemiological studies have shown that, compared to lean individuals, very obese men and women (body mass index >35) have several folds increase in probability of developing Type 2 diabetes. Although the precise underlying mechanisms in the development of diabetes are yet unknown, the initial pathophysiological event is usually insulin resistance, which involves a genetic component that is exacerbated by obesity and a sedentary lifestyle.[2]

According to WHO 1997,[3] epidemiological studies have shown that South Asians are more likely to have central obesity measured in terms of waist circumference and increased body mass index (BMI). Increased body fats are related to increased insulin resistance and may account for the increased prevalence of diabetes mellitus in South Asians.[1]

Lipoprotein abnormalities are common in diabetes and contribute significantly to its complications. The misconception that such abnormalities are always secondary to poor glycemic control focuses most of the attention on the management of hyperglycemia. As a result, the treatment of dyslipidemia was often neglected, despite convincing evidence linking it to the development of atherosclerosis.[4] Lipoprotein abnormalities often precede the onset of diabetes mellitus by many years and persist despite achievement of euglycemia, particularly in type 2 diabetes. Estrogen-induced alterations in serum lipids account for only approximately one-third of the observed clinical benefits of estrogen. The atheroprotective effects of estrogen were principally attributed to the hormone's effects on serum lipid concentrations.[5]

Estradiol reduces the development of early lesions of atherosclerosis, through an improvement in the blood lipid profile, which reduces lipid deposits in the endothelium, with a decrease in total cholesterol and low-density lipoprotein cholesterol (LDL-C) and an increase in high-density lipoprotein cholesterol (HDL-C) in the plasma.[6] The physiological process of estrogen works by binding to estrogen receptors.[7]

In this study, we aimed to examine the correlation between BMI, lipid profile and estradiol in diabetic pre-ovulatory women as a sample of Iraqi Asian women.

Methods

A total of 155 diabetic female patients aged between 20-45 years, were enrolled in this study, which was conducted in Al Khadimiya

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Teaching Hospital from July 2008 to January 2010. Patients with previous history of cardiac, renal, hepatic, thyroid disease or hormonal disturbances were excluded. Other exclusion criteria included; pregnancy and breast feeding, acute infections and blood diseases. The participants were asked to fast for 12 hours prior to blood sampling for lipid profile and other parameters. The body weight and height were measured for all patients included. Body Mass Index was calculated by dividing the body weight over the square of the height (Kg/m^2).

Venous blood samples were taken; the sera were separated by centrifugation at (3000 rpm) for 15 minutes. Part of the serum was used to determine HDL-C and fasting serum glucose immediately while the rest of the serum was stored frozen at -20°C until assay. The blood samples were taken one day before ovulation, which was calculated by the "mean" of three consecutive menstrual cycles, with subtraction of 14 days to determine the date of ovulation.

Then each serum sample was analyzed for total cholesterol, triglycerides, and estradiol. All assays were obtained by running duplicates for the test and standard. Serum HDL-C, triglycerides and total cholesterol (TC) were measured by the enzymatic method using Biomaghreb, Tunisia Kits. Serum VLDL-C was calculated by: S.VLDL-C= (T.G/5) in mg/dl, while LDL-C was determined indirectly using Friedewald equation: [LDL-C = TC - (HDL-C + VLDL-C)].[8] Estradiol was estimated using miniVIDAS Estradiol Kit (Biomérieux, France). Patients were informed about the study and they accepted enrollment in the study.

Patients with hormonal disturbance, renal disease, thyroid disease, or using antidepressant drugs or contraceptive pills were excluded from the study. Ethical approval was obtained from the local ethics committee, together with informed patient consent.

It should be mentioned that all study patients were diagnosed with insulin resistance and their serum insulin mean ± standard deviation was 28.16± 4.43 µU/ml when the insulin normal reference range = 2-25 µIU/ml according to the American Medical Association.[9] Fasting serum insulin was measured using the insulin ELISA kit (biocompare, Catalog Number YK060).

The data of the research were saved in Microsoft Excel Spread sheet and analyzed on the computer using Microsoft Excel program (2010) and SPSS (v.17).

Results

One hundred fifty five diabetic pre menopausal women aged 20-45 years (mean ± Standard deviation; 29.7±4.3 years) were involved in this study. They were classified according to their BMI as shown in Table 1. Fifty patients had normal BMI; 50 patients were overweight, while 55 patients were obese. All patients were at their pre-ovulatory period (normal reference range for estradiol at this period = 93-575 pg/ml), their estradiol levels were within the normal range except for those with normal BMI, their estradiol levels were slightly increased. From Table 1, obese diabetics had lower mean HDL-C levels than the overweight patients who had lower mean HDL-C than normal diabetic patients. This means that their LDL-C levels were increasing in the opposite way which shows their ability to have cardiac problems. This finding can be confirmed by the positive significant correlations between BMI, triglycerides, and total cholesterol with LDL-C. (Table 2)

Table 1: Clinical presentation of study subjects (n=155) distributed according to their body mass index; normal (50), overweight (n=50) and obese (n=55).

Parameter	Mean±SD		
	Normal*	Overweight**	Obese***
FSG (mg/dl)	135.3±11.09	152.41±20.12	157.68±29.64
Body mass index (Kg/m^2)	21.9	28.7±0.6	34.5±4.5
Total cholesterol (mg/dl)	205	179±20.1	190±19.6
HDL-C(mg/dl)	41.6	39±3.1	36±2.8
Triglycerides (mg/dl)	74	204±36.2	197±31.4
LDL-C(mg/dl)	197	189±16.7	208±25.6
S. estradiol (pg/ml)	583	484±80.0	423±93.4

*N=number of study subjects, SD= standard deviation, FSG= fasting serum glucose, *normal BMI=18.5-24.9Kg/m^2, **Overweight BMI=25-29.9 Kg/m^2, ***Obese BMI=30-34.9 Kg/m^2*

Table 2: Correlation between different study variables (n=155).

Diabetic pre menopausal women		Body mass index	Total cholesterol	Triglycerides	HDL-C	LDL-C
Total cholesterol	r	-0.046				
	P	0.882				
Triglycerides	r	0.642(*)	0.202			
	p	0.018	0.508			
HDL-C	r	-0.240	0.121	-0.129		
	p	0.430	0.694	0.674		
LDL-C	r	0.162	.849(**)	0.274	-0.439	
	p	0.596	0.000	0.365	0.133	
S. estradiol	r	-0.689(*)	-0.602(*)	0.395	0.864(**)	-0.008
	p	0.189	0.508	0.182	0.779	0.979

*r= Pearson Correlation, p= Sig. (2-tailed), * Correlation considered significant when p<0.05 and ** Correlation considered highly significant when p<0.01*

Discussion

The present study revealed a proportional correlation between serum triglyceride level and BMI, with the highest triglyceride levels observed in overweight and obese patients. Many studies have shown an association between BMI and triglycerides, and the association between lipid profile and body fat distribution had been much discussed during the past decades. Both lipid profile and body fat have been shown to be the important predictors for metabolic disturbances including dyslipidemia, hypertension, diabetes, cardiovascular diseases, hyperinsulinaemia etc.[10,11]

In addition, the present data revealed an inverse correlation between serum estradiol level and BMI. Tworoger et al. (2006) suggested two hypotheses to prove the inverse correlation between BMI and estradiol level. First, a high BMI may be associated with ovulatory insufficiency beyond its known role in increasing ovulatory cycles. The hypothesis is also supported by epidemiological data suggesting that a BMI as low as 24 kg/m^2 is associated with an increased risk of an ovulatory infertility. A second hypothesis may be through an indirect regulation by sex hormone binding globulin (SHBG). As SHBG declines, free estradiol should increase. Therefore, in response to decreased SHBG, follicle-stimulating hormone levels may decrease to lower total estradiol production by the ovaries, thus keeping free estradiol relatively constant. Additionally, the molecular clearance rate of estradiol is positively associated with weight, also potentially reducing total estradiol levels.[12,13]

Also, there was a strongly negative and significant association between serum estradiol level and total cholesterol. Furthermore, the associations between serum estradiol concentrations were found to be significantly positive with HDL-cholesterol. This explains why the premenopausal women are more protected against atherosclerosis and coronary heart diseases.

The study revealed that Obesity is a major risk factor for diabetes Mellitus; obesity is permanently associated with unhealthy lipid profile characterized by high triglycerides and LDL-C, and low HDL-C. In diabetic premenopausal patients; serum estradiol level is inversely correlated with BMI. In addition, there is a negative association between serum estradiol level and LDL-C, and a positive one in association with HDL-C.[14]

There are only a small number of studies on the differences in endogenous hormone levels between racial/ethnic groups in the United States. Also, most of the studies were in women during their ovulatory time and not pre-ovulatory period and the women were not diabetic.[15,16]

Even so, Stefania et al. (2005) studied the differences in serum sex hormones and lipid levels in Caucasian and African-American premenopausal women and concluded that race is an important determinant of plasma triglycerides and sex hormone levels, even after adjustment for differences in body size. A significant association between endogenous estradiol and HDL-C levels exists in premenopausal women, independent of their race.[17]

In 2007, Ausmanas et al.[18] studied estradiol, FSH and LH profiles in nine ethnic groups of postmenopausal Asian women and concluded that the levels of FSH, LH and particularly of estradiol differed substantially among ethnic groups of postmenopausal Asian women, but the clinical significance (if any) of these differences remains to be investigated.

Conclusion

From this study, it can be concluded that Iraqi diabetic pre menopausal women at their pre ovulatory period exhibit a pro-atherogenic risk profile because of their abnormal BMI, higher LDL-C, lower HDL-C and estradiol levels.

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