Iraqi JMS

Published by Al-Nahrain College of Medicine
ISSN 1681-6579
Email: iraqijms@colmed-alnahrain.edu.iq
http://www.colmed-nahrain.edu.iq

Postprandial Triglyceride and Testosterone in Women with Cardiovascular Diseases

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Abstract

Background High androgen levels may increase cardiovascular disease (CVD) risk in women through adverse effects on lipids, blood pressure, and glucose metabolism. Lipid abnormalitiesare often found in women with CVD.

Objective To study the relationship between postprandial triglycerides (TG) as a risk factor for cardiac disease and the androgenic activity in postmenopausal women with CVD.

Methods Postprandial lipid profile and sex hormone levels were measured in 30 patients with CVD and 25 postmenopausal women age and body mass Index (BMI) matched served as control group.Testosterone and sex hormone binding globulin (SHBG), Estradiol (E2), follicular stimulating hormone (FSH) and luteinizing hormone (LH) were estimated.

Results Postprandial TG, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and atherogenic index (AI) were different between the two groups ($P \leq 0.001$). The SHBG and Free Androgenic Index (FAI) were significantly higher in the CVD postmenopausal women ($P \leq 0.001$) while no differences in testosterone, LH, FSH, and E2 levels noticed between CVD patients and the control group. Serum testosterone levels correlated positively with the postprandial TG and the atherogenic index, and negatively with HDL-C in the CVD patients.

Conclusion Elevation in androgenic activity could be a cause of higher elevation in postprandial serum TG which may increase the risk of CVD in women.

Key Words postmenopausal women, cardiovascular disease, postprandial lipid profile, testosterone, sex hormone binding globulin, free androgenic index

Introduction

Cardiovascular disease (CVD) is the leading cause of death in women [1,2]. Postprandial triglyceride (TG) concentrations areoften elevated throughout the day,a point which makes postprandial TG concentration a better predictor of cardiovascular events than fasting triglycerides [3-5]. The adverse effect of postprandial TG is thought to be mediated by the pro-atherogenic lipolysis products of nascent triglyceride-rich lipoproteins, which may worsen vascular function [3-5].

In subsequent analysis of a larger number of men and women, non-fasting TG was not associated with coronary death in men but showed a 5-fold risk of death from coronary heart disease in women when its concentration was 3.5 mmol/L,or more, as compared to those with a level of less than 1.5 mmol/L, even after adjustment for traditional coronary risk factors [6].

The aim of the present study was to emphasize the association of postprandial rise in serum TG with changes in sex hormones in women with CVD and their role in increasing the risk of CVD.

Methods

Thirty patients with CVD aged between 48-63 years (55±8.9, mean±SD) were recruited from Al-Imamain Al-Kadhimyian Medical City during the period from January to April2012. Another 25 apparently healthypostmenopausal women were involved as a control group with matching age and body mass index (BMI) to the patient group (53.3±6.7years, mean±SD). None of them had a history of thyroid disease, polycystic ovary syndrome (PCOS), diabetes mellitus, renal impairment, or any other severe illness or infection, and not taking any drug (including hormone replacement and any estrogenic, anti hypertensive or lipid lowering medication) or had any operation in the ovary. Ten mls of blood were collected in a plain tube in postprandial state (2-3 hours after breakfast). The serum was obtained after centrifugation at 3200 rpm for 10 min. and divided into small aliquots.

a- Immediate measurements of serum glucose, lipid profile, were done using the enzymatic colorimetric methods.

b- The rest was stored at - 20^{o}C until assayed for hormones analysis (luteinizing hormone (LH), follicular stimulating hormone (FSH), and estradiol (E2)) by mini VIDAS Kit (Biomerieux, France), while testosterone and sex hormone binding globulin (SHBG) wereestimated by manual Eliza kit.

c- Free Androgen Index (FAI) was calculated by using the formula total testosterone (mmol/ L) / SHBG (mmol/L).

d- Body mass index (BMI) was calculated by weight (Kg)/sq height (m)

e- The atherogenic index = LDL.C / HDL.C

Results

The results show highly significant elevations in the postprandial TG, TC LDL-C, and atherogenic index, with a highly significant reduction in HDL-C (p-value = 0.0001) in the postmenopausal women with CVD as shown in table 1 when compared to their healthy controls.

Table 1. Demographic features of postmenopausal women with cardiovascular disease and the control group

Parameters	Women with CVD N = 30	Control group N = 25
Age (year)	55±8.9	53.3±6.7
BMI (kg/m^2)	30.9±2.4	29±3.1
Triglyceride	3.82±0.85*	2.45±0.34
Total cholesterol	6.41±0.48*	5.17±0.11
HDL-C	0.65±0.26*	0.93±0.06
LDL-C	3.82±0.44*	3.13± 0.14
Atherogenic index	4.93±1.48*	3.37±0.68

* $P \leq 0.0001$, CVD = cardiovascular disease BMI = body mass index, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol.

As shown in table 2 there was no significant differences in testosterone, LH, FSH and E2 levels in postmenopausal women with CVD and postmenopausal women without CVD (p = 0.62, 0.78, 0.27 and 0.057 respectively), with a highly significant reduction in SHBG levels (P = 0.0001), however, the free androgenic index was significantly higher inthe postmenopausal women with CVD than their controls (menopausal women without CVD, P = 0.001).

Table 2. Sex hormones & Free Androgenic Indexin thepostmenopausal women with CVD and control group

Parameters	Women with CVD N = 30	Control group N = 25
LH (mIU/ml)	41.44±4.08	38.46±5.42
FSH (mIU/ml)	45.39±3.19	41.74±6.31
E2(pg/ml)	59.73±15.99	50.32±4.11
Testosterone (nmol/l)	2.92±0.54	2.43±0.27
SHBG (nmol/l)	61.23±10.54*	71.61±5.41
FAI	5.66±1.67*	3.38±0.35

*P ≤ 0.0001, CVD = cardiovascular disease, LH = luteinizing hormone, FSH = follicular stimulating hormone,E2 = estradiol, SHBG =sex hormone binding globulin, FAI = free androgenic index.

Discussion

The significant increase in postprandialserum TG, total and LDL cholesterols and atherogenic index with a significant reduction in HDL-C seen in this study contributes to the irregular lipid metabolism in postmenopausal women with CVD when compared to the healthy postmenopausal women.

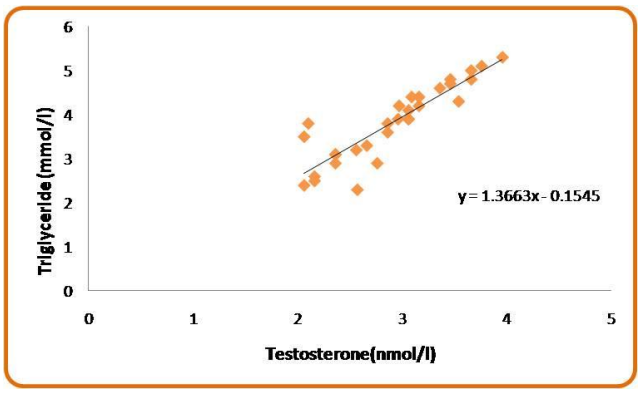

Fig. 1. The correlation between testosterone level and postprandial triglyceride in the postmenopausal women with cardiovascular disease

Studies had related these abnormalities in lipid profile to insulin resistance, which may cause elevation in LH and testosterone and reduction in FSH, E2 and SHBG [7,8]. The LH stimulates theca cells resulting in production of testosterone and androstenedione, whereas the FSH stimulates aromatase in the granulose cells, resulting in aromatization of androgens to estrogens [9-11]. The reduction in SHBG is related to hyper-insulinemia due to the ability of insulin to inhibit hepatic SHBG synthesis [12]. From the calculated value of FAI, whichdetects free testosterone, it could be said that the loss in circulating SHBG leads to greater bioactivity of circulating testosterone.

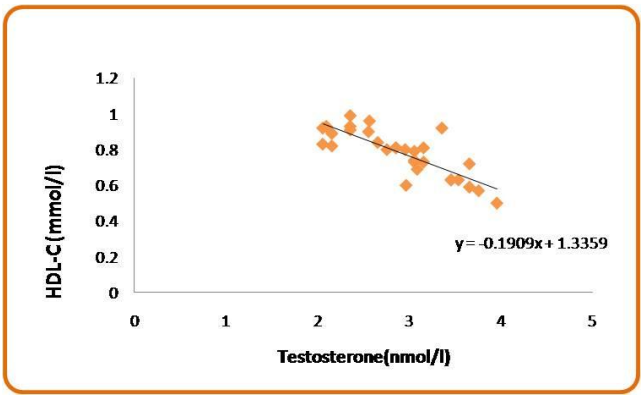

Fig. 2. The correlation between serum testosterone level and postprandial high density lipoprotein cholesterol in the postmenopausal women with cardiovascular disease

Measurement of postprandial serum lipids has been recommended as a better marker than fasting serum lipids for many diseases including the CVD, as it would catch the peak of serum TG during the 2-4 hours after meals which is believed to play an important role in the preparation for the process of atherosclerosis [13,14].

Previous studies showed that SHBG may mediate its positive effect on the lipid profile by regulating bioavailable androgen levels. SHBG binds testosterone with high affinity and regulating its free concentration [15,16].

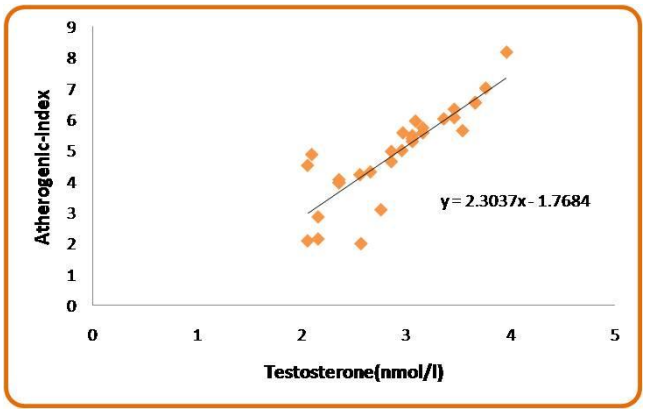

Fig. 3. The correlation between serum testosterone level and atherogenic index in the postmenopausal women with cardiovascular disease

Reports on the relationship between SHBG and CVD were controversial: Low SHBG levels, sometimes wereconsidered androgenic marker in women, demonstrating a positive correlation between SHBG and HDL-C and a negative correlation with more atherogenic lipid profile total and LDL cholesterols [17-18] while another study failed to find such an association [19].

In this study the significant correlations between testosterone and various postprandial serum lipids in the postmenopausal women with CVD (Fig.1-3) emphasize the association between the two parameters and may lead to the suggestion that the increase in androgenic activity (or free testosterone) may increase the elevation in postprandial TG which is believed to be a cause of increased risk of CVD in women [13,14].

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Received 29th Jan.2013: Accepted 18th Jun. 2013