THE COINCIDENCE OF THYROID GLAND DISORDERS AND DYSLIPIDEMIA DURING A CLIMACTERIC PERIOD: A HOSPITAL-BASED STUDY AT AL-BASHEER AND IBN-ALHYTHAM HOSPITALS

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ABSTRACT

Objective: To examine the complex triple inter-relationship between dyslipidemia, menopause, and thyroid abnormalities in a group of Jordanian women during climacteric period.

Methods: This is a preliminary descriptive pilot study of premenopausal, perimenopausal, and postmenopausal women who were visiting various clinics at Al-Basheer hospital and Ibn-Alhytham hospital over a period of two years (August 1999 to August 2001). A total of 149 women were actually included in the study. The sampling method was randomized and on expedient basis. Lipid profile, fasting blood sugar, thyroid stimulating hormone, free thyroxine, and follicle-stimulating hormone were determined in the obtained blood samples. Other demographic, social, lifestyle, and clinical data were evaluated during a 4-hour interview/examination in a health clinic.

Results: The prevalence of dyslipidemia was 60% of which 20% were not previously diagnosed, and with similar rates in peri-and postmenopause. When further multiple comparisons were performed, postmenopausal women had significantly higher FBS than pre and perimenopausal subjects (P= 0.05), while their total cholesterol and low-density lipoprotein (LDL) were only significantly elevated from premenopausal females (P= 0.01, P= 0.03, respectively). Although the triglyceride levels were higher in postmenopause as contrasted to pre-and perimenopause categories, the final results did not reach the level of statistical significance (P=0.7). The total prevalence of thyropathy based on TSH and free thyroxine levels in addition to past medical history was 29.5% of the study sample. However, no marked association was found between thyropathy and either menopausal status (OR=1.75, 95% CI, 0.6 to 5; P=0.3), or dyslipidemia (OR=0.7; 95% CI, 0.3 to 2; P=0.56).

Conclusion: In general, the high prevalence of thyroid disease in our female population was independent on age or the menopausal condition. Although dyslipidemia was strongly associated with postmenopause, it occurred at equal probabilities in both euthyroid as well as thyropathic postmenopausal women.

Key words: Menopause, Dyslipidemia, Jordan, Thyroid Function.

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Introduction

Several epidemiological studies indicated increased incidence of coronary heart disease (CHD) in postmenopausal women compared to men of a similar age [1,2], which is basically related to estrogen deprivation [3,4]. In addition, hypothyroidism, being a common disorder in elderly women more than old men [5,6], is declared to induce atherosclerosis with an extent comparable to that for known classic risk factors of CHD [7-10]. However, considerable controversy surrounds this association and its mediated physiological mechanisms [11-14].

The major aim of the study was to test the association between hypothyroidism, and plasma lipids in a group of Jordanian women during the climacteric period, that is a span of about five years before and after menopause. Specific objectives were:

- To describe various levels of lipid components [total-cholesterol, triglycerides (TG), high density lipoprotein (HDL) cholesterol, low density

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lipoprotein cholesterol (LDL) and fasting blood sugar (FBS)] in premenopausal, perimenopausal and postmenopausal women.

- To express the range of lipid components at different stages of thyroid function disorders.

Design And Setting

This is a hospital-based study of premenopausal, perimenopausal and postmenopausal women who were visiting various primary health clinics in Al-Basheer hospital, and Ibn-Alhytham hospital over a period of two years. The sampling method was a randomized one and on convenient basis. After obtainment of individuals' informed consent, selected subjects were recruited for a 4-hour interview/examination in a senior health clinic.

Methods

Examination Procedure

During interview, the principal investigator assembled information on current and past health, medication, reproductive status, lifestyle, physical activity level, and other classic risk factors for coronary heart disease (including hypertension, diabetes mellitus, and smoking status 'never, former, or current'). For patients who reported positive cardiac history, we contacted their experienced cardiologist to confirm the diagnosis. A qualified research assistant and two nurses measured sitting systolic and diastolic blood pressure (SBP, DBP) with a standard sphygmonanometer.

Women were defined as premenopausal if they had regular menstrual periods; and perimenopausal if they had irregular periods but amenorrhoea for less than 12 months and an age > 45 years (serum follicle-stimulating hormone (FSH) is generally increased). Postmenopausal status was defined as the presence of one of the following conditions: an age of at least 55 years without natural menses for at least five years; no natural menses for at least one year and serum FSH level of more than 40 IU/ L; documented bilateral oophorectomy; or self-reported bilateral oophorectomy; FSH level of more than 40 IU/ L, and a serum estradiol level of less than 25 pg/ ml [(15)].

Patients were then further subdivided into subgroups on the basis of thyroid stimulating hormone (TSH) and free thyroxine (FT4) levels:

- Euthyroidism if TSH and FT4 were within the normal limits according to the reference ranges (provided by the applied commercial kits), which were 0.4-5.4 mU/ L and 0.8 -2 ng/ dL respectively.
- Subclinical hypothyroidism was diagnosed if patients had high TSH and normal FT4.
- Clinical hypothyroidism was diagnosed if TSH was high and FT4 low.
- Hyperthyroidism was diagnosed if TSH was low and FT4 high.

Body-mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

Data Analysis

Differences among groups were analyzed by the Chi-square test for categorical variables or the analysis of the variance (ANOVA) for continuous variables, using SPSS statistical software (version 10). Subsequently, multiple logistic regression analysis was employed to evaluate the interactive association between the menopausal status and thyroid function categories in dyslipidemia.

Analytical Assays

After obtainment of participants' informed consent, they were asked to fast overnight for 12-14 hrs, and venous blood was drawn into vacutainer tubes. The samples were centrifuged immediately, separated, and stored at -20^{o} C until analysis.

Glucose, total cholesterol, triglycerides (TG), and HDL were determined in the fasting blood samples by standard enzymatic-colorimetric methods, while (LDL) was estimated by calculation using the Friedewald formula [(16)]. TSH, FSH, FT4 were assayed by using standard enzyme immunoassay commercial kits.

Results

Dyslipidemia and Menopause

Table I illustrates the distribution of lipid measurements and fasting blood sugar according to menopausal status. Fundamentally, significant mean differences were demonstrated between the menopausal conditions in serum total cholesterol (P= 0.02), LDL (P=0.05), and FBS (P= 0.01). When further multiple comparisons by using Tukey HDS test were performed, postmenopausal women revealed to have a significantly higher FBS than pre and perimenopausal subjects (P= 0.05), while their total cholesterol and LDL were only significantly elevated from premenopausal women (P= 0.01, P= 0.03, respectively). The latter finding was considerably substantial for postmenopausal women who had never been exposed to hormone replacement therapy (HRT) (P=0.01). Although, the triglyceride TG levels were higher in postmenopause as contrasted to pre and perimenopause categories, the final results did not reach the level of statistical significance (P=0.7). Moreover, with further scrutinizing, lower TG and FBS were identified in postmenopausal group on HRT (n=20) as related to those who had never used HRT (124±56.8 vs 160.5±59.5 mg/dl).

With regard to HDL, the highest level was associated with postmenopause on HRT group (47.9±12.5 mg/dL). Interestingly, higher levels were also noted in the peri and postmenopausal women who did not have HRT as compared to premenopause group, but these increments were either small or insignificant relative to the increase in total cholesterol and LDL levels. Indeed, it is the total cholesterol/ HDL and/ or LDL/ HDL ratio that may have the greatest influence on the risk index of heart disease. Globally, the ratio was raised in all our subjects with a mean of 5.3 and 3.6, respectively (normal < 4, and < 2.5,

respectively). Therefore, it was assumed that variables other than the menopausal condition such as lack of exercise, fat-rich diet, obesity, smoking, and stress could be additionally contributing to the observed abnormality in either lipid ratios.

Overall, the prevalence of dyslipidemia was significantly higher in the post and peri as compared to the premenopause group (Table II). The predominant type was isolated hypercholesterolemia with the highest incidence rate in the perimenopausal subjects (57.9%). The distribution of other types of hyperlipidemia did not reveal consequential correlation between a particular class and a menopausal situation (P=0.17). Noteworthy, a total of 20 (13.4%) dyslipidemia cases were not previously diagnosed and had never received a physician's or dietitian's consultation. This has raised the total prevalence of dyslipidemia among women in this study to 60%, of whom only 3.4% were receiving lipid-lowering agents at the time of enrollment, in spite of previous diagnosis.

Table II represents the distribution of risk markers for CHD and dyslipidemia according to menopausal condition. As shown, documented diagnosis of myocardial infarction (MI), angina, previous history of angioplasty/Stent operation, low physical activity, and body mass index did not differ within the three reproductive conditions. However, further comparisons conferred a high prevalence of diabetes, hypertension, family history of CHD, age $\geq$ 55 years old, and current smoking in the postmenopausal group ($P<0.05$). Therefore, to rule out the confounding bias in quantifying the impact of postmenopause on lipid abnormality, adjustment for these covariates, in addition to thyroid status was thought to be mandatory.

Menopause and Thyroid Function Abnormalities

The total prevalence of thyropathy based on TSH and free thyroxine levels in addition to past medical history was 29.5% of the study sample. The subclassification of thyroid disorders was as follows: 3.4% of the women had subclinical hypothyroidism, 12.8% had clinical hypothyroidism, 0.7% had subclinical hyperthyroidism, and 12.8% had clinical hyperthyroidism. Twenty three of the analyzed subjects had thyroid function disorders that had not been previously detected by laboratory tests or diagnosed by clinical assessment; of whom 9 (6%) women were identified to have hypothyroidism and 14 (9.4%) were found to have hyperthyroidism. There was no significant difference in mean age between euthyroid or between hypothyroidism and hyperthyroidism cases (P=0.9). The average mean age in all the four thyroid abnormal function subgroups was 55.5 years.

Table III shows the distribution of lipid profile, FBS, FSH, TSH, and FT4 measurements by the thyroid conditions. Systolic BP and diastolic BP as well as total cholesterol, triglycerides, LDL, and FBS did not differ significantly among the specific thyroid function categories ($P>0.05$). Unexpectedly, women who had normal thyroid function had less HDL levels than women who had thyroid dysfunction findings. In particular, a significant elevation in HDL level was distinguished in the clinical hypothyroidism patients compared to subjects in the euthyroid group (P=0.04).

Moreover, no marked difference in the prevalence of thyroid abnormalities with respect to the three reproductive conditions presented in our study (P=0.7). The prevalence of Euthyroid was 78.3%, 78.9%, and 67.3%, while the frequency of subclinical hypothyroidism was 4.3%, 5.3%, and 2.8% in pre, peri, and postmenopausal women, respectively. With regard to other thyroid classes, although the incidence of overt clinical hypothyroidism and hyperthyroidism (15% and 15%, respectively) was higher in postmenopausal women as compared to those in the premenopausal (4.3% and 13%, respectively) and perimenopausal class (10.5% and 5.3%, respectively), the overall distribution difference did not attain the level of statistical significance in our population.

In addition, when we examined the effect of HRT on thyroid dysfunction, a nonsignificant reduction in the incidence of all types of thyroid problems was observed for HRT users (P-Chi-Square= 0.7).

It was concluded from this section of results that the prevalence of any thyroid abnormality in women was independent of menopausal status and HRT use. Moreover, the impact of hypothyroidism and hyperthyroidism on alteration of FBS and lipid parameters was not evidently validated in the current study, except for HDL, which was significantly elevated in patients with clinical hypothyroidism.

Menopause, Thyroid Function Abnormalities, and Dyslipidemia: Multiple Logistic Regression Analysis

To study the interactive effect of menopause and thyroid abnormality on the lipid metabolism and glucose tolerance, a logistic regression model was fitted to our data. The unadjusted odds ratio of postmenopausal female to develop hyperlipidemia was 2.8 times more than premenopausal female (95% CI, 1.1 to 7; P=0.03). While the unadjusted odds ratio for perimenopausal women was 2.8, which was insignificant due to its wide confidence interval (95% CI, 0.7 to 10, P=0.11).

Fitting a reduced model for prevalence of hyperlipidemia with abnormal thyroid function situations revealed a negative association with an odds ratio of less than 1 for subclinical (SCH) and clinical hypothyroidism (CH) [OR_{SCH}=0.8; 95% CI, 0.13 to 5; P=0.8 and OR_{CH}=0.7; 95%CI, 0.3 to 2; P=0.56], and a positive association with hyperthyroidism [OR=1.3; 95% CI, 0.45 to 3.6; P=0.6]. However, the results did not approach statistical significance since the 95% confidence interval of odds ratio were broad and included 1.

To test the coexistent effect of menopause and hypothyroidism on lipid disturbance, a third model was fitted to 149 cases that included a complete data set of the two covariates (thyroid function status and menopausal condition). Again, the association of

various levels of thyroid function status (subclinical and clinical hypothyroidism, as well as hyperthyroidism) with pre, peri, and postmenopause condition did not have an impressive effect on odds ratio for incidence of dyslipidemia in any of the menopausal category.

Women of age greater than 55 years old were less likely to have hyperlipidemia as compared to those of an age less than 55 years old (OR=0.3; 95%CI, 0.1 to 0.99; P=0.04). Interestingly, the current or ever use of HRT did not reduce the odds ratio for abnormal lipid estimation in the peri and postmenopausal women compared to pre, peri, and postmenopausal subjects who had never used HRT (OR=2.15; 95%CI, 0.81 to 5.7, P=0.13).

Discussion

In an attempt to provide a preliminary description of the postmenopausal situation in Jordan, we have undertaken this pilot study. The main argument in this paper is whether coexistence of thyroid abnormality and estrogen-deprivation in the postmenopausal period are detrimental for increased cardiovascular morbidity and mortality, since both factors were claimed to induce lipid disorders independently. The total prevalence of dyslipidemia in our population was 60%, of which 20 (13.4%) were undiagnosed. This ratio was considered extremely high compared to previous universal surveys, indicating that the size of this epidemiological problem in Jordan is expected to be huge which is most probably related to diet rich in saturated fats. However, the issue of extraordinarily high BMI among the subjects in this study could disagree with representativeness. Yet, further large-scale surveys support this finding. Interestingly, the prevalence of lipid abnormality was equal in the peri-and postmenopause period, but much less in premenopause lifetime. The chiefly expressed type was hypercholesterolemia, which was also detected at close rates in the peri-and postmenopausal groups. In accordance with previous studies [1,2,17] the mean levels of total cholesterol and LDL, the most atherogenic lipid components, were significantly elevated in peri-and postmenopausal women compared to premenopausal women. Similar findings were obtained after stratification of the postmenopausal group according to etiology into: Spontaneous, surgical (hysterectomy), and premature ovarian failure, suggesting no age consequence. The similarity of LDL levels in the peri and postmenopausal women (143.2 and 145.6 mg/dL, respectively) could be explained by similar linear decline in their estrogen levels, despite difference in the time of menstrual cycle cessation. However, esterone and estradiol were not measured in the current study. Therefore, their linear relationship with various lipid parameters could not be quantified. Moreover, the association of dyslipidemia of any type with perimenopause lost its statistical significance on multivariate regression analysis when other covariates such as age, hypertension, diabetes, and smoking were considered. The association of dyslipidemia with postmenopause endured highly significant, even after adjustment with other clinical variables.

The total prevalence of thyroid disease in our sample was considered very high as compared to previous reports [18,19]. However, we must not forget that the majority of our candidates were old women, who are known to be more exposed to thyroid defect than men [5,6]. The fractional proportions of thyroid subclassifications in the current study were comparable to previous surveys [10,20] and screening guidelines reports [21] based on meta-analyses, except for clinical hyperthyroidism, which was abnormally expressed in our series. However, our sample is still believed to be representative of the general women population in Jordan due to its random nature, particularly with regard to overt hypothyroidism prevalence [18,19]. Moreover, taken into account that TSH may be falsely elevated in nonthyroid illnesses [22] of varying severity, we ascertained that all our population had normal kidney function tests, serum albumin, and total protein.

As for estrogen deficiency, thyroid scarcity may lead to myocardial infarction and atherosclerosis by several mechanisms. A well-established etiology is immune-complex associated with elderly women thyroiditis with a consequent extensive vascular damage [10] and therefore coronary artery disease [7,8,12,14]. Nevertheless, measurement of antibodies to thyroid peroxidase was not an endpoint in the contemporary study. Thus, no firm deduction concerning pathogenesis of clinical hypothyroidism in postmenopausal women can be drawn from our data. Another mechanism, which was postulated in previous cross-sectional and case control studies, is the impact of hypothyroidism and hyperthyroidism on alteration of serum lipids [23-25,27]. However, considerable uncertainty surrounds this association. In agreement with a number of the previous studies [24-26], we did not find significant differences in total cholesterol, TG, HDL, and LDL levels between the thyroid illness group and euthyroid group. Noteworthy, the elevation in TSH levels among our subjects had a mean of 14.5 mU/L (±6.7) and ranged between 8.6 to 23 mU/L. Markedly elevated TSH (≥ 10 mU/L) was identified in only four of our patients (2.7%), whereas the rest of our patients had mildly elevated TSH levels (6 to 9 mU/L). Therefore, our pooled estimates showing no significant modification in lipids through the majority of the thyropathy group would also be consistent with results obtained from a more recent American survey [27] including 883 elderly men and women. In that study no pronounced effect on health measures including lipid components was observed till serum TSH exceeded a level of 10 mU/L. Moreover, when we inspected the lipid profile in our four cases who had marked TSH levels (≥ 10 mU/L), normal lipid measures were verified, except in one woman of 48 years of age who had a total cholesterol level of 248 mg/dL coupled with a TSH level of 23 mU/L. Therefore, we could not btain reliable inference and more data are needed to clarify this issue.

In general, the prevalence of thyroid disease in our population was independent of age or menopausal condition, and although dyslipidemia was strongly associated with postmenopause, it occurred at equal probabilities in both euthyroid as well as thyropathic postmenopausal women. Future studies should focus on determination of other potential non-lipid-thyropathy-mediated mechanisms contributing to increased cardiac mortality in elderly women. Until then, careful screening and early detection of thyroid defects in aged women is deemed critical to prevent subsequent vascular complications including stroke, peripheral vascular disease, and coronary artery disease [21].

Table I. The distribution of lipid profile measurement and FBS by the reproductive status (menopausal condition)

Measurements (mean, SD)	**Pre-menopause**	**Peri-menopause**	**Post-menopause**	**Post-menopause on HRT**	**Post-menopause without HRT**	**P-value Pre vs. Peri**	**P-value Pre vs. post**	**P-value Peri vs. Post**	**Total**
No. of subjects	22	18	103	20	83				246
Total cholesterol (mg/ dL)	188.5 (44.8)	215.5 (37.8)	219.9 (50.6)	218 (48.8)	220.3 (51.3)	0.18	0.01*****	0.93	
F (sig)¶			3.9 (0.02)*****		3.4 (0.02)*****				
P-value#				0.99					
Triglycerides (mg/ dL)	148.7 (93.9)	135.8 (110.6)	153.7 (90.4)	124.9 (56.8)	160.5 (95.7)	0.9	0.97	0.73	
F (sig)			0.29 (0.75)		0.9 (0.4)				
P-value#				0.4					
LDL cholesterol (mg/ dL)	120.7 (37.9)	143.2 (34.2)	145.6 (45.2)	145.2 (45.6)	145.6 (45.4)	0.2	0.03*****	0.9	
F (sig)			3 (0.05)*****		2.4 (0.07)				
P-value#				1					
HDL cholesterol (mg/ dL)	38.9 (12.3)	46.5 (12)	44.5 (12.6)	47.9 (12.5)	43.6 (12.6)	0.14	0.13	0.8	
F (sig)			2.26 (0.1)		2.4 (0.07)				
P-value#				0.5					
Total cholesterol/ HDL ratio	5.4 (2)	4.9 (1.7)	5.4 (2)	4.8 (1.6)	5.5 (2.2)	0.8	0.99	0.72	
F (sig)			0.3 (0.74)		0.8 (0.5)				
P-value#				0.5					
LDL cholesterol/ HDL ratio	3.5 (1.6)	3.4 (1.4)	3.6 (1.7)	3.3 (1.4)	3.7 (1.8)	0.9	0.9	0.8	
F (sig)			0.2 (0.8)		0.5 (0.6)				
P-value#				0.7					
Fasting blood sugar (mg/ dL)	92.8 (28.4)	89.3 (16.9)	118.9 (56.9)	111.9 (42.9)	120.7 (59.9)	0.97	0.068	0.05*****	
F (sig)			4.4 (0.014)*****		3.1 (0.02)*****				
P-value#				0.89					

¶: ANOVA TEST for the difference among subgroups means *: The mean difference is significant at the 0.05 level

#: P-value for the mean difference between Postmenopause on HRT vs. Postmenopause without HRT

For legend abbreviations see text

Table II. The distribution of risk factors for coronary heart disease by the reproductive status (menopausal condition)

RR	Premenopause	Perimenopause	Postmenopause	P-value¶
Age (mean, SD) < 55 years ≥ 55 years	 23 (100) 0 (0)	 19 (100) 0 (0)	 32 (29.9) 75 (70.1)	 0.00 0.00
Diabetes ***no (%)***	0 (0)	1 (5.2)	25 (23.4)	0.01
Hypertension ***no (%)***	1 (4.5)	1 (5.2)	39 (36.4)	0.00
Systolic BP (mean, SD) mmHg	120 (10.4)	123.7 (11.3)	132.1 (18.3)	0.005¥
Diastolic BP (mean, SD) mmHg	76.4 (7.4)	80.9 (6.5)	82.2 (10)	0.031¥
Dyslipidemia ***no (%)***	10 (43.5)	13 (68.4)	73 (68.2)	0.042
Isolated hypercholesterolemia	5 (21.7)	11 (57.9)	42 (39.3)	0.17
Isolated hypertriglyceridemia	2 (8.7)	0 (0)	4 (3.7)	invalid
Isolated HDL < 35 mg/dL	5 (21.7)	0 (0)	10 (9.3)	invalid
Combined hyperlipidemia	1 (4.3)	2 (10.5)	8 (7.5)	
Family history of CHD ***no (%)***	4 (18.2)	3 (15.8)	41 (38.3)	0.047
Current smoking ***no (%)***	5 (23.8)	2 (10.5)	12 (11.3)	0.39
BMI > 27.5 ***no (%)*** kg/m^2	22 (15)	19 (12.9)	106 (72.1)	NS
Physical activity‡ ***no (%)***	15 (71)	15 (78.9)	74 (69.8)	0.5
Cardiac history- no (%)				
MI ***no (%)***	1 (4.5)	2 (10.5)	4 (3.7)	0.496
Angina ***no (%)***	0 (0)	0 (0)	2 (1.8)	invalid
PTCA/ Stent ***no (%)***	0 (0)	0 (0)	1 (0.9)	invalid

‡: Classification was based on whether candidates walked "some or often", as contrasted to "hardly or none".
¶: Asymp. Sig. (2-sided) for Pearson Chi-Square test NS: nonsignificant difference
¥: by using ANOVA, a significant mean difference was found in SBP and DPB between premenopause and postmenopause groups (P= 0.01, 0.02 respectively)

Table III. The distribution of lipid profile, FBS, FSH, TSH, and FT4 measurements by the thyroid conditions

Measurements (mean, SD)	Euthyroid (a)	Subclinical Hypothyroidism (b)	Clinical Hypothyroidism (c)	Clinical Hyperthyroidism (d)	P-value (a) vs. (b)	P-value (a) vs. (c)	P-value (a) vs. (d)	P-value (c) vs. (d)
No. of subjects (%)	105 (70.5)	5 (3.4)	19 (12.8)	19 (12.8)				
Subject Age (years) F (sig)¶	55.5 (9.9)	53.6 (6.2)	55.6 (7.7)	57.2 (9.5) 0.26 (0.9)	0.9	1	0.88	0.9
Systolic BP F (sig)¶	128 (17.3)	138 (13)	133.4 (20.7)	129 (12.6) 0.95 (0.4)	0.6	0.6	0.99	0.85
Diastolic BP F (sig)¶	80.4 (9.7)	85 (5)	84.7 (9)	80.3 (8.7) 1.5 (0.23)	0.7	0.26	1	0.44
Total cholesterol (mg/ dL) F (sig)¶	210.7 (48)	233 (58)	213.4 (42.8)	229.6 (59.3) 1.04 (0.4)	0.76	0.99	0.4	0.75
Triglycerides (mg/ dL) F (sig)	153.6 (99)	162.4 (93.7)	146.6 (77.4)	135.3 (74.8) 0.24 (0.87)	0.9	0.9	0.86	0.98
LDL cholesterol (mg/ dL) F (sig)	139 (41.3)	151.6 (51.5)	133.4 (42.8)	158.5 (52.4) 1.4 (0.3)	0.9	0.9	0.28	0.29
HDL cholesterol (mg/ dL) F (sig)	42.3 (11.5)	48.9 (10.9)	50.7 (16)	44 (13.8) 2.6 (0.04)*****	0.65	0.04*****	0.94	0.39
Total cholesterol/ HDL ratio F (sig)	5.4 (1.9)	5.2 (2.8)	4.7 (1.9)	5.8 (2.5) 0.9 (0.44)	0.9	0.54	0.88	0.38
LDL cholesterol/ HDL ratio F (sig)	3.6 (1.6)	3.5 (2.2)	3 (1.8)	4 (2) 1.1 (0.3)	0.99	0.59	0.68	0.26
Fasting blood sugar (mg/ dL) F (sig)	109 (49.4)	107.2 (43.2)	111.4 (37.9)	123.7 (72.6) 0.44 (0.7)	1	0.99	0.67	0.88
FSH (IU/ L) F (sig)	53.3 (34.6)	70 (40.5)	65.9 (42.6)	56.9 (34) 0.89 (0.44)	0.73	0.52	0.98	0.87

¶: ANOVA TEST for the difference among subgroups means *: The mean difference is significant at the 0.05 level

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