ORIGINAL ARTICLE

The relationship between C-reactive protein, anthropometric parameters and lipids in menopausal transition

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ABSTRACT

Aim To investigate the relationship between C-reactive protein, anthropometric parameters, and lipids in women in the menopausal transition.

Methods This cross-sectional study included 150 women divided into three groups: premenopausal (n=50), perimenopausal (n=50), and postmenopausal (n=50). All women were interviewed, body mass index (BMI) and waist-hip ratio (WHR) values were calculated, and a blood sample was taken for laboratory analysis. The values of the lipids were determined including triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol, while low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) cholesterol values were obtained through formulas. The concentration of CRP was determined by immunoturbidimetry on the Architect ci8200 device.

Results The BMI of postmenopausal women was significantly higher than that of premenopausal ($p=0.025$) and perimenopausal women ($p=0.010$). The ratio of the waist-hip circumference of postmenopausal women was significantly higher than the ratio of the waist-hip circumference of premenopausal women ($p<0.001$), as well as that of perimenopausal women ($p<0.001$). A significant difference in CRP concentration was found only between the postmenopausal and premenopausal groups ($p=0.009$). CRP significantly positively correlated with BMI in all three groups. A significant positive correlation was found between CRP and WHR in the perimenopause and in the postmenopause group. No significant correlation was found between CRP and lipid parameters in any group.

Conclusion An increase in body weight or obesity in the postmenopausal period, increase in CRP concentration, and positive correlation between these parameters suggest that entering menopause could mean a potential increase in the risk of developing cardiovascular and metabolic diseases.

Key words: body mass index, inflammation, lipids, menopause, waist-hip ratio

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INTRODUCTION

Menopause is a permanent cessation of menstruation due to the reduction of egg cells. The result is a sudden drop in endogenous estradiol. During the transition to menopause, women undergo phenotypic, metabolic, and biochemical changes that increase the risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Whether these changes are independent of aging itself is a matter of debate (1). Women gain weight during the transition to menopause. Although this may be influenced by age rather than menopause per se, the transition to menopause is independently associated with an increase in adipose tissue, particularly in the abdominal region (2). In perimenopausal women, there is a decrease in lean body mass and a significant decrease in energy consumption, mainly due to fat oxidation, which favours an increase in total body and visceral fat without significant changes in energy intake (3). Visceral adiposity increases the production of pro-inflammatory cytokines, increases circulating free fatty acids, and promotes the formation of reactive oxygen species, contributing to the development of insulin resistance and, consequently, CVD (4).

Adipose tissue dysfunction in obesity results in a shift from an anti-inflammatory to a pro-inflammatory profile (5). Obesity-related inflammation begins in the adipose tissue and liver with increased macrophage infiltration and expression of pro-inflammatory cytokines. The obesity-induced inflammatory response also results in increased circulating cytokines such as interleukin (IL)-6 and tumour necrosis factor-α (TNFα) and increased acute phase proteins, C-reactive protein, and serum amyloid A and causes systemic inflammation (6). Therefore, overloaded, dysfunctional adipose tissue is associated with the activation of immune cells and inflammatory mediators, both locally in the adipose tissue and systemically, resulting in a low degree of chronic inflammatory state (6,7).

Menopause, age and increased distribution of abdominal fat tissue are three independent and important factors that disrupt the lipoprotein profile from the beginning of the menopausal transition (8). Cardiovascular risk associated with menopause is primarily attributed to a change in the lipid profile towards atherogenesis, which is characterized by an increase in the concentration of total cholesterol (TC), low-density lipoprotein (LDL-C) and triglycerides, and a decrease in the concentration of high-density lipoprotein (HDL-C) (9,10). Some studies suggest a reversal in the protective association of HDL-C and cardiovascular disease during the menopausal transition, pointing to a decrease in estrogen during menopausal transition (MT) and an increase in C-reactive protein (CRP) as the leading causes (11). With the onset of menopause, the direction of the association between HDL cholesterol and the cardiovascular risk appears to change from protective to detrimental. Previous studies have shown increased values of total cholesterol, triglycerides, LDL, apo B and decreased values of HDL and apo A in postmenopause (10-13).

Similar studies have not been conducted in our region yet.

The aim of this study was to investigate the relationship between C-reactive protein, anthropometric parameters, and lipids in menopausal transition, as well as the relationship between components of the metabolic syndrome and the risk of developing cardiovascular diseases in menopausal transition.

PATIENTS AND METHODS

Patients and study design

This cross-sectional study included 150 women divided into three groups: premenopausal (n=50), perimenopausal (n=50), and postmenopausal (n=50). The first group was aged between 45-50 years, the second between 50-55 years, and the third over 55 years. The study was conducted in the period between April and July 2022. The women were processed at the Clinic for Gynaecology and Obstetrics and the Polyclinic for Laboratory Diagnostics of the University Hospital Tuzla, previously stratified according to the inclusion and exclusion criteria of the study. The inclusion criteria were as follows: do not take hormone replacement therapy or anticonvulsants, do not take medications that could affect the lipid profile, do not suffer from hyperthyroidism, hypogonadism, liver disease, and myxedema.

The Ethical Committee of University Clinical Centre Tuzla approved the study. All women signed an informed consent.

Methods

All women were interviewed, body mass index (BMI) and waist-hip ratio (WHR) values were calculated, and a blood sample was taken for laboratory analysis. A special question-form was created and it was conducted the interview with the examinees. Body mass, height, waist, and hip circumference were measured, and BMI and WHR were determined. The BMI was calculated according to the formula: BMI = body weight/ body height (kg/m2). Obesity was considered as BMI >30 kg/m2. The WHR was calculated as the ratio of waist circumference and hip circumference. Blood for laboratory analysis was taken by venipuncture from the cubital vein in the early morning hours on an empty stomach. From the blood sample, the lipid profile values were determined by a standard method, including triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol, while the low-density lipoprotein (LDL) - and very-low-density lipoprotein (VLDL) cholesterol were obtained through formulas. The concentration of C-reactive protein was determined by immunoturbidimetry on the Architect ci8200 device (Abbott Laboratories, Hercegovina lijek Mostar, Bosnia and Herzegovina).

Statistical analysis

Results are expressed as mean ($\bar{X}$) and standard error of the arithmetic mean (SEM), and as median and interquartile range (25-75 percentile). To test the significance of the difference in the deviation from the normal distribution, the Kolmogorov-Smirnov or Shapiro-Wilk test was used. Independent numerical variables were analysed by ANOVA test and t-test for those that met the conditions for application, i.e. by appropriate non-parametric tests (Kruskal-Wallis test and Mann-Whitney U test) for variables with an irregular distribution. The $\chi 2$ test was used to analyse categorical variables. The correlations between the variables were assessed by Spearman's test. A $p<0.05$ was taken as statistically significant.

RESULTS

The median age of premenopausal women was 47.0 (45.0-48.9), perimenopausal 52.0 (49.0-55.0), and postmenopausal 59.0 (57.0-61.0) years old ($p<0.001$). Menarche in the premenopausal group was at 13.0 (13.0-14.0) years, perimenopausal 14.0 (13.0-14.25) years, and postmenopausal at 14.0 (13.0-15) years ($p=0.371$).

Table 1. Values of anthropometric parameters, C-reactive protein and lipid profile parameters in women in the menopausal transition

Parameter	Premenopausal group (n=50)	Perimenopausal group (n=50)	Postmenopausal group (n=50)	p
BMI (kg/m^2)	25.59 (23.94-28.74)	25.37 (23.65-28.10)	27.72 (25.47-31.22)*†	<0.05
WHR	0.80±0.05	0.80±0.05	0.85±0.08*†	<0.001
Total cholesterol (mmol/L)	5.35 (4.93-6.41)	6.08 (5.44-6.82)*	6.01 (5.34-6.92)*	<0.05
Triglycerides (mmol/L)	1.47 (0.96-1.89)	1.54 (1.06-2.16)	1.53 (1.13-2.45)	0.247
LDL-cholesterol (mmol/L)	3.74±0.93	4.19±0.94*	4,13±0.95*	<0.05
HDL-cholesterol (mmol/L)	1.47±0.30	1.50±0.33	1.44±0.35	0.598
VLDL-cholesterol (mmol/L)	0.66 (0.43-0.85)	0.70 (0.48-0.98)	0.69 (0.51-1.11)	0.243
C-reactive protein (mg/dL)	1.0 (0.0-1.8)	1.0 (0.37-2.20)	1.0 (0.60-4.10)*	<0.05

Results are expressed as mean ($\bar{X}$) and standard error of the arithmetic mean (SEM), and as median and interquartile range (25-75 percentile).
*p<0.05 comparison to the premenopausal group; †p<0.05 comparison to the perimenopausal group
BMI, body mass index; WHR, waist-hip ratio; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very-low-density lipoprotein;

Body mass index in premenopausal women was 25.59 (23.94-28.74) kg/m2, in perimenopausal 25.37 (23.65-28.10) kg/m2, while 27.72 (25. 47-31.22) kg/m2 in postmenopausal women. The body mass index of postmenopausal women was significantly higher than that of premenopausal ($p=0.025$) and that of perimenopausal ($p=0.010$). The waist-hip ratio in premenopausal women was 0.80±0.05, in perimenopausal women 0.80±0.05, and in postmenopausal 0.85±0.08. The ratio of the waist-hip circumference of postmenopausal women was significantly higher than the ratio of the waist-hip circumference of premenopausal women ($p<0.001$), as well as that of perimenopausal women ($p<0.001$). Concentrations of total cholesterol in the perimenopausal and postmenopausal groups were significantly higher than in the premenopausal group ($p=0.020$). In contrast, the total cholesterol concentrations between women in perimenopause and postmenopause did not differ significantly ($p=0.865$). The concentrations of LDL-cholesterol in the perimenopausal ($p=0.019$) and the postmenopausal ($p=0.041$) group were significantly higher than

in the premenopausal group, 4.19±0.94 mmol/L, 4.13±0.95 mmol/L, and 3.74±0.93 mmol/L, respectively. The concentration of HDL-cholesterol, triglycerides, and VLDL-cholesterol between the groups was not significant. A significant difference in CRP concentration was found only between the postmenopausal and premenopausal groups, 1.0 (0.60-4.10) mg/dL and 1.0 (0.0-1.8) mg/dL, respectively (p=0.009). The median concentration of total cholesterol in the postmenopausal group was higher than in the other.

C-reactive protein significantly positively correlated with BMI in the premenopausal group (Rho=0.510; p<0.01), in the perimenopausal group (Rho=0.304; p<0.05), and in the postmenopausal group (Rho=0.418; p<0.01). A significant positive correlation was found between CRP and WHR in the perimenopause group (Rho=0.304; p<0.05) and in the postmenopause group (Rho=0.293; p<0.01). No significant correlation was found between CRP and lipid profile parameters in any studied groups (Table 2).

Table 2. Correlation of C-reactive protein, anthropometric parameters and lipid profile in the studied groups

Parameter	C-reactive protein correlation (Rho)		
	Premenopausal group (n=50)	Perimenopausal group (n=50)	Postmenopausal group (n=50)
BMI (kg/m^2)	0.510*	0.304†	0.418*
WHR	0.189	0.313†	0.293†
C-reactive protein (mg/dL)	0.114	-0.015	0.179
Total cholesterol (mmol/L)	0.161	0.054	0.174
Triglycerides (mmol/L)	-0.030	0.027	-0.157
LDL-cholesterol (mmol/L)	0.043	0.136	0.125
HDL-cholesterol (mmol/L)	0.017	-0.010	0.175

*p<0.001; †p<0.005;
BMI, body mass index; WHR, waist-hip ratio; LDL, low-density lipoprotein; HDL, high-density lipoprotein

DISCUSSION

The results of our research showed that the BMI of postmenopausal women was significantly higher than BMI of premenopausal, as well as that of perimenopausal women. Also the ratio of the waist-hip circumference of postmenopausal women was significantly higher than in the other two groups. A significant difference in the CRP concentration was found only between the postmenopausal and premenopausal groups. The concentrations of total cholesterol in the perimenopausal and postmenopausal groups were significantly higher than the concentrations of total cholesterol in the premenopausal group. In contrast, the total cholesterol concentrations between the subjects in perimenopause and postmenopause did not differ significantly. The concentrations of LDL-cholesterol in the perimenopausal group and the postmenopausal group were significantly higher than the concentration of LDL-cholesterol in the premenopausal group, and the concentrations of HDL-cholesterol, triglycerides, and VLDL-cholesterol between the examined groups did not differ significantly.

It was shown that the average BMI of postmenopausal women was higher than that of premenopausal women, even if they had better eating habits. An important result in Bhurosa et al. (14) study showed that the mean anthropometric values of waist circumference, WHR and BMI were significantly higher in postmenopausal women. In a study by Giannini et all. (15) the prevalence of obesity was higher in postmenopausal women than in premenopausal women. It results from a multifactorial process that includes reduced energy consumption due to physical inactivity, sometimes accompanied by depression, muscle atrophy, and lower basal metabolism. Some authors believe menopause is not associated with weight gain but leads to an increase in total body fat and a redistribution of body fat from the periphery to the trunk, resulting in visceral adiposity (16). In a study conducted by Hummadi et al. (17) it is commonly assumed that the volume of fat mass increases with age and results in a higher BMI recorded during aging. Higher levels of LDL-C, TC, and TG were detected in postmenopausal women than in the groups of premenopausal women. At the same time, HDL did not differ significantly between premenopausal and postmenopausal women, as shown in a meta-analysis conducted by Li et al. (18). A significant increase in TC, TG, and LDL-c with a significant decrease in the level of HDL-C was found in postmenopausal compared to premenopausal women in a study by Hamza et al. (19). Higher CRP values in postmenopause and significantly higher levels of CRP in perimenopause compared to premenopause were found in a study conducted by Ebong et al. (20). The authors conclude

that higher TNF-α characterizes postmenopausal status and that CRP may be associated with increased cardiovascular risk in postmenopausal women due to its association with higher intra-abdominal fat (21). Opposite results were presented by Sharma et al. (22), who proved that women with early menopause had higher CRP values than women in late menopause. Our research showed that C-reactive protein significantly positively correlated with BMI in all three experimental groups. A significant positive correlation was found between CRP and WHR in the perimenopause group and in the postmenopause group.

In a sample of 61 obese postmenopausal women, plasma CRP levels were found to be positively associated with dual X-ray absorptiometry-measured total body fat. Plasma CRP level was significantly reduced by weight loss. The authors concluded that obesity was a significant predictor of plasma CRP in postmenopausal women on a cross-sectional basis (23). In the study by Chitra et al. (24), a positive correlation was found between BMI and increased level of hs-CRP suggesting that underlying pathology of obesity was involved, as fat cells secrete several substances that have adverse effects on the body (such as increased inflammation, hardening of the arteries and blood clotting).

In conclusion, considering that our results showed a tendency to increase body weight or obesity in the postmenopausal period and an increase in CRP concentration, as well as positive correlation between these parameters, we believe that entering menopause can potentially increase the chances of developing cardiovascular and metabolic diseases.

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TRANSPARENCY DECLARATION

Conflict of interest: None to declare.

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