

## Major Cardiovascular Risk Factors for Menopausal and Non-menopausal Women, Compared with Men of the Same Age, among Patients Admitted to the Cardiology Department of Imam Reza Hospital, Mashhad, Iran

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### ABSTRACT

**Background & aim:** Menopause refers to the cessation of menstruation due to hormonal changes and ovarian inactivity in women. These changes in hormone levels lead to various health consequences. This period of physiological change usually starts in women with 40-50 years of age, and is characterized by the reduction of estrogen level. The mortality rate of premenopausal women, due to cardiovascular diseases (CVDs), is one fifth of men, though it rapidly increases after the menopause. Therefore, this descriptive study was conducted in order to determine the cardiovascular risk factors for menopausal and non-menopausal women in comparison with men of the same age.

**Methods:** The study sample included patients referring to the cardiology department of Imam Reza Hospital, Mashhad, Iran. The subjects were divided into 4 groups: non-menopausal women (n=35), men of the same age (as the non-menopausal women, n=35), menopausal women (n=50), and men of the same age (as the menopausal women, n=50). All criteria related to major cardiovascular risk factors including systolic and diastolic blood pressure (SBP and DBP), cholesterol, triglyceride (TG), and low and high-density lipoprotein (LDL and HDL) were measured and compared in all four groups. In order to analyze the data, Fisher's exact test was carried out, using SPSS version 16.

**Results:** There was a significant difference between non-menopausal women and men of the same age with regard to high SBP and DBP, hypercholesterolemia, low HDL, and high LDL. However, no significant difference was observed among these groups, regarding high levels of TG. The menopausal women and men of the same age showed significant differences in terms of high SBP and low HDL. However, no differences were observed in DBP, hypercholesterolemia, hypertriglyceridemia, and high LDL.

**Conclusion:** Menopausal women, non-menopausal women, and men had significant differences in terms of high SBP and low HDL. However, regarding high DBP, hypercholesterolemia, and high LDL, there was a significant difference only between non-menopausal women and men of the same age.

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### Introduction

Menopause impacts 25 million women each year, worldwide. Based on the reports by World

Health Organization (WHO), the number of postmenopausal women is expected to increase to approximately 1.2 billion by ۲۰۳۰ (1).

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Menopause is a developmental occurrence during midlife, which marks the end of a woman's fertility (2). It is described as the women's transition from the reproductive to non-reproductive stage. Changes in hormone levels lead to many health consequences during the pre- and post-menopausal periods. Menopause refers to the cessation of menstruation due to ovarian inactivity. Consequently, several problems occur as the estrogen secretion completely stops in the body. The onset age of menopause is about 46 years of age, and approximately 95% of women enter the menopause stage by the age of 39 to 51 years (3).

This period starts in 40-50-year-old women, and is characterized by the reduction of estrogen levels. The hormonal conversion, especially lack of estrogens, leads to moderate/severe menopausal symptoms and climacteric disturbances in two thirds of women. These menopausal symptoms are not life-threatening, but may reduce the quality of life in these women.

The main related complaints include vasomotor and vaginal symptoms, depressive episodes, hot flashes, night sweats, dysphoric mood, sleep disturbance, cardiovascular conditions, depression, osteoporosis, osteoarthritis, dementia, and physical weakness (1, 4).

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality in menopausal women, in spite of the overall reduction in age-adjusted CVD mortality in the last few years. It has been shown that the mechanisms of CVD, while accelerating during midlife in menopausal women are similar to men (5). Menopause, independent of other CVD risk factors, incurred cardio-metabolic risks (6). The risk of CVD also increases after menopause, suggesting vascular benefits of endogenous estradiol (E2) (7).

Sex differences in cardiovascular pathophysiological mechanisms involved in cardiovascular functions and remodeling are partially regulated by steroid hormones. These mechanisms include: the synthesis and degradation of norepinephrine, the adrenergic receptor expression in vascular smooth muscle, the regulation of ion fluxes in cardiac and vascular smooth muscles, the production of endothelium-derived vasoactive factors which

affect total peripheral resistance, and cerebral blood flow (8).

Whether estrogen reduction happens naturally or surgically, the risk of developing hypertension, ischemic heart disease, myocardial infarction, and stroke increases in women after the onset of menopause (9). According to one hypothesis, estrogens have protective effects on atherosclerosis. The mortality rate of CVD in women prior to menopause is one fifth of men, though this rate rapidly increases after menopause. One underlying reason could be the presence of estrogens, which have a protective impact on women before menopause; however, this factor is not present after menopause (3, 10, 11, 12).

Herein, the main function of estrogen is decreasing the risk of CVD and the level of LDL, along with increasing HDL level. It is also believed that estrogen decreases the relative risk of CVD through blocking LDL oxidation, changing prostaglandin metabolism, and direct vasodilation effect (10).

In other words, women during the premenopausal age are protected against atherosclerosis compared with men of the same age; this is due to the low level of LDL and high HDL level. The increase in LDL level happens simultaneously with estrogen deficiency in menopausal women, and exceeds its normal level in comparison with men; in addition, the cholesterol level increases in these women (12, 13).

In the cardiovascular system, it is difficult to distinguish between normal changes associated with aging and pathological alterations. Some changes in the system are common and considered normal. Physiological changes include myocardial hypertrophy and calcification of heart valves, along with reduction of maximum oxygen absorption, and cardiac output. These events begin in the third decade of life and develop approximately one percent each year.

Atherosclerosis is probably one of the consequences of menopause, related to lack of estrogens. More than 500,000 women die from CVD each year, and hypercholesterolemia is one of the major risk factors for these diseases. Furthermore, the increase in LDL level leads to cholesterol accumulation and consequently

contributes to atherosclerosis formation (3,10,11).

In summary, CVD risk factors, particularly atherosclerosis and hypercholesterolemia, lead to several metabolic changes, such as:

- inappropriate changes in lipid and lipoprotein profiles of blood circulation,
- LDL oxidation,
- endothelial damage and dysfunction,
- macrophage immigration and function,
- vasoconstriction and thrombogenic events, and
- structural changes in coronary arteries.

One of the strongest preventive factors for CVD in women is HDL level. In fact, HDL level reduction by 10 mg/dl increases the risk of CVD up to 40-50% (3). Moreover, many changes during menopause may affect CVD. Various factors including inactivity, religious beliefs, social affairs, and misconception regarding nutrition (such as tendency toward fat-enriched foods) may influence the evaluation of CVD risk factors in different regions.

So far, there have been no studies on some aspects of CVD in menopausal women in Khorasan Razavi, Iran. Due to the importance of this issue and with the aim to promote the health of these women, this study was performed to determine cardiovascular risk factors in menopausal and non-menopausal women, and compare them with men of the same age in Khorasan Razavi Province.

## Materials and Methods

The present descriptive study was conducted from March 2009 to February 2011, on patients with chest pain, referring to cardiology department of Imam Reza Teaching Hospital, Mashhad, Iran. The sample size was calculated using similar research in this area. Afterwards, sample selection forms were collected from each patient.

The written consents were obtained from all the subjects, and the ethical criteria of Mashhad University of Medical Sciences were considered; moreover, the use of recorded data was in accordance with the written consents.

The blood samples were obtained from each patient, and then measured in one laboratory, using a single type of kit. Blood pressure

measurements of the participants were done with one calibrated sphygmomanometer, and the conditions were controlled by two nurses.

The subjects who met the following criteria were included in the study: 1) no previous history of CVD, 2) 30-40 years of age for non-menopausal women and 55-75 years for menopausal women, and 3) being married. The exclusion criteria were as follows: 1) current heart condition, 2) previous history of heart disease, 3) coagulopathy, 4) medical/surgical conditions, 5) drug abuse, and 6) psychological disorders.

The inclusion and exclusion criteria were assessed using a sample selection questionnaire. Out of 110 patients, thirty-five non-menopausal women and men of the same age were selected. Also, out of 150 patients, 50 menopausal women and men within the same age group were selected.

In the current study, 4 groups were compared, which are as follows: non-menopausal women (n=35), men of the same age (as the non-menopausal women, n=35), menopausal women (n=50), and men of the same age (as the menopausal women, n=50). However, fifteen subjects under the age of 50 were excluded due to early discharge in each group.

Lipid ratios were calculated by dividing the plasma levels of proatherogenic and antiatherogenic lipoproteins. The total cholesterol/HDL and the LDL/HDL ratios are the two commonly-used atherogenic lipid ratios, which are shown to be superior to total or LDL levels of cholesterol in predicting cardiovascular events (14). Cardiovascular risk factors including SBP and DBP (SBP more than 140 mmHg and DBP more than 90 mmHg), cholesterol level (more than 250 mg), TG level (more than 150 mg), LDL (more than 150mg) and HDL levels (less than 50 mg for women and less than 40 mg for men) were measured (13).

Study participants were matched with regard to factors such as body mass index (BMI), socioeconomic status, social class, and occupation, which might influence CVD risk factors. The measurements were compared in all the groups. After coding the data, statistical analysis was performed, using SPSS v16 and

Fisher's exact test.  $P$ -value $\leq 0.05$  was considered statistically significant.

**Table 1.** Comparison of cardiovascular risk factors between non-menopausal women and men of the same age

Variables	Non-menopausal women		Men (same age)		P-value
	No.	Percent (%)	No.	Percent (%)	
High SBP (>140mmHg)	1	2.8	8	22.8	0.01*
High DBP (>90mmHg)	3	8.5	10	28.5	0.02*
High TG (>150mg/dl)	10	28.5	12	34.2	0.58
High cholesterol (>250mg/dl)	4	11.4	12	34.2	0.01*
High LDL (>150mg/dl)	2	5.7	19	54.0	0.01*
Low HDL (<50mg/dl for women and < 40 mg/dl for men)	1	2.8	7	20.0	0.02*

\* Significant difference between the two groups

**Table 2.** Comparison of cardiovascular risk factors between menopausal women and men of the same age

Variables	Menopausal women		Men (same age)		P-value
	No.	Percent (%)	No.	Percent (%)	
High SBP (>140 mmHg)	8	16.0	16	32.0	0.01*
High DBP(>90 mmHg)	18	36.0	22	44.0	0.08
High TG(>150 mg/dl)	21	42.0	22	44.0	0.30
High cholesterol (>250mg/dl)	14	28.0	18	36.0	0.13
High LDL (>150 mg/dl)	13	26.0	17	34.0	0.32
Low HDL (<50 mg/dl for women and < 40 mg/dl for men)	22	44.0	14	28.0	0.03*

\* Significant difference between the two groups

## Results

In this study, the menopausal women and men of the same age were matched in terms of age; the same applied to non-menopausal women and men of the same age. The mean age of non-menopausal women and men of the same age was  $38.75 \pm 4$  and  $39.52 \pm 3.5$  years, respectively. Also, the mean age of menopausal women and men of the same age was  $63.17 \pm 5.1$  and  $65.25 \pm 4.3$  years, respectively. The mean BMI of non-menopausal women and men of the same age was  $24.2 \pm 1.5$  kg/m<sup>2</sup> and  $24.8 \pm 1.7$  kg/m<sup>2</sup>, respectively ( $P=0.2$ ). In addition, the mean BMI was calculated  $8 \pm 1.6$  kg/m<sup>2</sup> and  $25.2 \pm 1.5$  kg/m<sup>2</sup> in menopausal women and men of the same age, respectively.

There was no significant statistical relationship between the participants regarding educational level and occupation. All groups were also equal in terms of socioeconomic status.

The results obtained from Fisher's exact test for non-menopausal women and men of the same age showed that there was a significant statistical difference between the two groups concerning SBP. Both blood pressure variables were significantly higher in men compared with

women ( $P=0.01$  and  $0.02$ ). Additionally, there was a significant difference between the two groups in terms of hypercholesterolemia and cholesterol level, as they were higher in men in comparison with women ( $P=0.01$ ).

A significant statistical difference was observed for low HDL and high LDL. HDL was significantly higher ( $P=0.03$ ), and LDL was significantly lower in women compared with men ( $P=0.01$ ). However, there was no significant difference between the two groups regarding high TG level ( $P=0.58$ ) (Table 1).

The results obtained from Fisher's exact test for menopausal women and men of the same age showed that there was a significant statistical difference in terms of SBP between men and women, as it was higher in men ( $P=0.01$ ); however, no difference was observed for DBP ( $P=0.02$ ). Furthermore, there was no significant difference between the two groups regarding hypercholesterolemia ( $P=0.13$ ), high TG level ( $P=0.30$ ), and high LDL ( $P=0.32$ ). However, statistical results showed a significant difference between men and women in terms of HDL, as HDL was considerably lower in women ( $P=0.03$ ) (Table 2).

## Discussion

The results of the present study showed significant differences in total cholesterol between women before menopause and men within the same age group. Moreover, factors such as LDL and HDL levels showed a statistical difference between the two mentioned groups.

Except for SBP, LDL and HDL levels, no difference was observed between men and non-menopausal women. It should be mentioned that in all cases of this study, the TG levels were not significantly different.

Compared with age-matched men, women during their reproductive age have a low rate of cardiovascular diseases and also fewer cardiovascular risk factors (14). It is clear that women in reproductive age are at lower risk of cardiovascular events. However, this protective effect does not persist after menopause (16, 17).

Alexander (2006) stated that coronary artery disease is the main reason for mortality among postmenopausal women, and risk factors such as high TG and low HDL are potent factors for coronary heart disease in women (10). In the current study, regarding low HDL and high LDL, there was a significant difference between non-menopausal women and men of the same age, i.e. HDL was remarkably higher and LDL was lower in women. However, HDL was significantly lower in menopausal women compared to men of the same age.

Mathew et al. suggested that cessation of menstruation cycles may be closely associated with CVD. In their study, women with low estrogen levels had higher levels of TG (11). Van in an article entitled "menopause problems, estrogen, and risks of heart disease" denoted that hormone replacement therapy decreases the risk of cardiovascular diseases, hot flashes, and osteoporosis (18). Welti concluded that menopause simultaneously initiates with estrogen reduction and serum lipid increase (19).

However, in our study, there was no remarkable difference between the groups regarding high TG. It is evident that artificially-induced and natural menopause are associated with reduced ovarian function, resulting in an increase in cholesterol levels (14).

In the current study, there was a significant difference between non-menopausal women and men of the same age in terms of

hypercholesterolemia. In other words, cholesterol level was higher in men, while no relationship was detected in the other two groups.

Gretchen (2004) suggested that CVD is a major condition in menopausal women. Furthermore, since atherosclerosis begins during childhood, it might be a deteriorating factor for the occurrence of menopause. It was revealed that estrogen therapy in young women had a decreasing effect on the risk of atherosclerosis, though this was not definite for menopausal women (20).

Hodis et al. (2007) studied the relationship between hypertension, menopause, and risk factors for CVDs. They reported that systolic hypertension and any alteration in the pulse rate are potential risk factors for CVD in menopausal women (21).

Our findings revealed that there was a significant difference between non-menopausal women and men of the same age in terms of SBP and DBP, as they were considerably higher in men. A significant difference was also found between the menopausal group and men of the same age regarding SBP; SBP was significantly higher in men. However, there was no relationship between the two groups regarding DBP. Despite the evident differences between pre- and post-menopausal women regarding some risk factors, the aim of this study was not quantitative comparison of these discrepancies. If the researchers had access to patients' environment and behavioral habits (such as diet and daily activities), it would be possible to identify why TG in these subjects was not significantly different. However, the researchers searched through the patients' addresses and found that the majority were from the rural areas; therefore, they might be more physically active (specially walking) in comparison with people living in major cities.

Although this study was not powered to detect between-person differences, the statistical analysis revealed some aspects which may serve as potential targets for identifying factors that attenuate risks of CVD. These aspects should be pursued by further research.

## Conclusion

The comparison of the results showed that there are more CVD risk factors in men compared with non-menopausal women of the same age. However, the other 2 groups had the same number of risk factors. As the results indicated, two risk factors (high SBP and low HDL) increased in menopausal women. Further research can be conducted for assessing the differences between the mentioned risk factors and other factors such as socio-economic status between these groups.

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### Conflict of Interest

No conflict of interest exists.

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