

# Postmenopause and metabolic syndrome

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## ABSTRACT

In this review, the causes and results of the metabolic syndrome and the relationship between vasomotor symptoms like hot flashes, night sweats, which started with the termination of ovarian activity in the postmenopausal period, were compared.

The pathophysiology of the postmenopausal and metabolic syndrome has been examined in parallel. Vasomotor symptoms have been shown to be more severe in postmenopausal women with metabolic syndrome.

**Key Words:** Postmenopause, metabolic syndrome, vasomotor symptoms

## Introduction

The postmenopausal period begins twelve months after the last menstruation. Despite being a physiological process, menopause-specific conditions put postmenopausal women in a delicate group. Menopause complication affects the quality of life. With the improvement in life expectancy and medicine, the elderly population is increasing especially in the developed countries. Thus, the number of women entering the menopause increased but the mean menopause age did not change (1). With the loss of function of the ovaries and a decrease in estrogen levels, it causes many symptoms that adversely affect quality of life, as hot flashes, mood swings, night sweats and irregular sleep patterns. Estrogen deficiency can lead to long-term life-threatening conditions like cardiovascular disease and osteoporosis. The incidence of vasomotor symptom at the level that would impair the quality of life in post-menopausal women is 60-80% (2). Metabolic syndrome is a metabolic disorder with increased risk of cardiovascular disease in which factors like dyslipidemia, abdominal fat accumulation, obesity, impaired glucose tolerance, insulin resistance, DM, and hypertension are clustered (3). The International Diabetes Federation (IDF) and the American Heart Association / National Heart Lung Blood Institute (AHA / NHLBI) have reached consensus on the description of metabolic syndrome (Table 1) (4). In a postmenopausal woman with metabolic syndrome, the conversion of adrenal steroid to estrogen in the abdominal fat tissue is the reason that FSH value is low and the estradiol value is high. (5). Therefore, when the testosterone aromatization to estrogen in

the fatty tissue of the body considered, multifactorial vasomotor symptoms may be less likely to occur in patients with metabolic syndrome (6). While postmenopausal women have decreased HDL levels compared to premenopausal women, total cholesterol, LDL, triglyceride levels and cardiovascular disease risk have increased (7). Metabolic syndrome prevalence increases with menopause (2). Jeenduang et al. (8) Have shown an increased prevalence of metabolic syndrome in postmenopausal women and reported that the prevalence was between 16% and 69% in different populations. The increased risk of cardiovascular disease with menopause is further increased by the metabolic syndrome (9). The prevalence of metabolic syndrome is reported to be 22% in adults. Prevalence increases with age, 6.7% in 20-29 age group and 43.5% in 60-69 age group (3). According to TEKHARF study, by 2000, 9.2 million people aged 30 years and over have metabolic syndrome, and 53% of people with cardiovascular disease also have metabolic syndrome (7). Our country has high prevalence of metabolic syndrome, 28% in males and 40% in females (10).

No genetic, infectious, or environmental factors have been found that may clarify the pathogenesis of all components of the metabolic syndrome. Metabolic syndrome is a heterogeneous endocrinopathy that develops on the basis of insulin resistance. Although polygenic susceptibility is a matter of concern, the sedentary lifestyle of modern urban life and high calorie diet exacerbate the course of this syndrome (11). Insulin resistance is biologically unresponsiveness to insulin. Genetic factors, fetal malnutrition, physical inactivity, obesity and age

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**Table 1.** Consensus (UDF+AHA/NHLBI) 2009 (4)

Three of the following diagnosed as metabolic syndrome
Increased waist circumference BMI>30kg/m <sup>2</sup>
TG≥150mg/dl
HDL<40(male), <50(female)
Blood pressure≥130/85mm/hg
Fasting Blood Glucose≥100mg/dl

progression are common causes. Due to this resistance, hyperinsulinemia develops in order to keep blood glucose at normal level. In practice, HOMA (fasting insulin ( $\mu$  / ml) x fasting plasma glucose (mg / dl) / 405) score is lower than 2.7 in normal individuals; Above 2.7, it reflects insulin resistance at different grades (12,13). It's not necessary that all type 2 DM patients have insulin resistance. However, if the patient has significant Diabetes Mellitus and impaired glucose tolerance is considered insulin resistance for diagnosis. The diagnosis of diabetes mellitus is based on fasting plasma glucose and oral glucose tolerance test (OGTT) values (Tables 2 and 3). The risk of developing type 2 DM in patients with metabolic syndrome is 5 times higher than healthy individuals (14). Thus, the risk of developing type 2 DM in the presence of both insulin resistance and metabolic syndrome is 6-7 times higher than in other people (15).

One of the causes of essential hypertension is insulin resistance (13). Insulin; Stimulates renal water and salt uptake by enhancing central sympathetic activity and it balances the effect on blood pressure by creating

**Table 2.** Classification of fasting plasma glucose levels (16).

Fasting plasma glucose level	Definition
<100 mg/dl	Normal
100-125 mg/dl	Impaired fasting glucose
≥126 mg/dl	Diabetes mellitus

**Table 3.** Classification of 2. Hour OGTT (75g) plasma glucose levels (16)

2. hour plasma glucose level (75g OGTT)	Definition
<140 mg/dl	Normal
140-199 mg/dl	Impaired glucose tolerance
≥ 200 mg/dl	Diabetes mellitus

peripheral vasodilatation. In the presence of insulin resistance, hypertension is caused by resistance to the effect of peripheral vasodilators (17). Hypertension in patients with metabolic syndrome is associated with high levels of resistin and low levels of adiponectin (18). The endothelium is an active endocrine organ that produces vasodilators (nitric oxide) and vasoconstrictors (angiotensin II) that balance each other under normal conditions. The loss of balance between these two effects on the endothelium is referred to as endothelial dysfunction (13,17). In the postmenopausal period, vascular endothelial dysfunction (deterioration of vascular tone regulatory function) and atherosclerosis associated with decreased estrogen develops cardiac artery diseases. Metabolic syndrome is accepted as a risk factor for early-onset atherosclerosis (17). Patients have a 2-3 times higher mortality risk associated with cardiovascular disease (24). Another study showed a 1.5-fold increase in stroke risk in patients with metabolic syndrome (25). In metabolic syndrome, triglycerides and VLDL are increased, HDL is low, but LDL is not usually elevated. As insulin resistance progresses, triglyceride levels increase and HDL levels decrease. Hypertriglyceridemia and low HDL increase cardiovascular disease risk (19). Abdominal obesity and low HDL increases the prevalence of metabolic syndrome in postmenopausal women (20).

Although abdominal obesity is the most important indicator of insulin resistance, some of the cases of insulin resistant metabolic syndrome may not have obesity. Adipose tissue is an active endocrine organ that secretes cytokines (TNF- $\alpha$ , IL-6, IL-8) and many hormones such as leptin, resistin, adiponectin (13). Approximately 50% of postmenopausal women have been shown to be obese (21). In postmenopausal period even though there is no weight gain, redistribution increases central obesity which can trigger metabolic syndrome. Gluteofemoral fat accumulation is decreased and metabolic active abdominal fat accumulation is increased (22). Abdominal obesity has been suggested to contribute to insulin resistance and to cause dyslipidemia, glucose intolerance and hypertension (23). Insulin resistance is followed by hepatosteatosis, steatohepatitis and even cirrhosis (19). Patients with metabolic syndrome are 4 to 11 times more likely to develop non-alcoholic fatty liver in the future. Insulin resistance is the key pathologic factor in both cases (26). Non-alcoholic fatty liver is strongly associated with cardiovascular disease (27). The prevalence in the general population is estimated around 20-30%. (28). Insulin resistance may result in chronic anovulation and infertility with hyperandrogenism (29). Metabolic syndrome is associated with

hypogonadism in both men and women. Hypogonadism is also a risk factor for metabolic syndrome and type 2 DM. Hormone Replacement Therapy (HRT) improves the characteristics of the metabolic syndrome for both sexes (30). In patients with metabolic syndrome, obesity is strongly associated with osteoarthritis and gut disease in the knees (31). Evidence suggests that the development or progression of colorectal, prostate, and breast cancers is due to obesity in patients with metabolic syndrome (32,33). Type 2 DM is also associated with increased risk of developing cancer (34). In the prevention of vasomotor symptoms in the postmenopausal period, as HRT is currently inadequately used and there is no effective treatment to relieve these symptoms, it seems to be the right way to find and remove symptoms that exacerbate the symptoms (35). Metabolic syndrome prophylaxis is provided with regular exercise and appropriate dietary habits in postmenopausal women. Organized, group-based exercise, followed by home training and self-guided physical activity, reduces cardiovascular disease risk, which continuously improves cardiometabolic parameters.

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