

## MENOPAUSAL SYNDROME IN WOMEN WITH DIABETES MELLITUS

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### ANNOTATION

Data on the prevalence of various disorders of carbohydrate metabolism in the world are given. The pathogenesis of metabolic syndrome in women during menopause (menopausal metabolic syndrome) is considered. Its clinical and laboratory manifestations are described

**Keywords:** diabetes2, menopausal metabolic syndrome, laboratory manifestations.

### INTRODUCTION

Currently, the number of patients with diabetes in the world is more than 371 million people, and 50% do not know about their disease, in all countries of the world, high rates of increase in the incidence of diabetes remain, mainly due to patients with type 2 diabetes.

According to the State Register of Patients with Diabetes, over the past 10 years, the number of patients with type 2 diabetes mellitus has doubled and amounted to more than 3 million people (January 2009). At the same time, the results of control and epidemiological studies conducted by the Endocrinological Research Center in the period from 2002 to 2009 showed that approximately 6 million more have diabetes mellitus 2, but do not know about it and, therefore, do not receive treatment. It should be noted that women over 45 suffer from diabetes 2 times more often than men.

Thus, diabetes can be called an epidemic of the 21st century. The prevalence of overweight and obesity in the world is steadily increasing. According to the World Health Organization (WHO), in 2008 more than 1.4 billion adults aged twenty years and over were overweight, of which over 200 million were men and about 300 million women were obese. According to WHO experts, by 2025 the number of people with obesity will almost double, and the high growth rates and widespread prevalence of this disease have made it possible to call it a new "non-communicable epidemic". According to a survey of a national sample of the adult population of Russia, the prevalence of overweight and obesity varies from 45 to 56% in men and from 56 to 62% in women.

Menopause is a natural biological process of transition from a woman's reproductive period to old age, which is characterized by a gradual fading ovarian function, decreased estrogen levels, cessation of menstrual and reproductive function. The average age of menopause for women in the European Region is 50–51 years. At the same time, in the condition of estrogen deficiency, women live almost 1/3 of their lives [6]. Climacteric syndrome (CS), which develops under conditions of estrogen deficiency, is accompanied by a complex of pathological symptoms that occur depending on the phase and duration of this period.

The earliest signs of CS in women without endocrinopathies are neurovegetative disorders (hot flashes, sweating, blood pressure lability, palpitations, tachycardia, extrasystole, dizziness) and psycho-emotional disorders (mood instability, depression, irritability, fatigue, sleep disturbances), which in 25 -30% of patients persist for more than 5 years.

Retrospective analyzes show that women with type 1 diabetes go through menopause earlier than women in the general population. For example, Dorman J.S. et al. found that menopause in women with diabetes mellitus 1 occurred at an earlier age than in women without this disease (41.6 and 48.0 years, respectively) [8]. At the same time, in a study conducted in Finland a decade later, the age of menopause in women with diabetes mellitus 1 did not significantly differ from that in the general population.

Significantly significant factors independently associated with earlier menopause were microvascular complications of the underlying disease, such as end-stage diabetic nephropathy and proliferative retinopathy. Soto N. et al. found that the level of anti-Müllerian hormone, which accurately reflects the follicular reserve, begins to decline at the age of 33 in both healthy women and patients with diabetes mellitus.

However, in the latter, who have crossed this age limit, its levels are significantly significantly lower in comparison with their peers without carbohydrate metabolism disorders. It is assumed that in the cause of the development of early depletion of the ovarian follicular apparatus in women with diabetes mellitus 1, great importance is attached to the direct toxic effect of persistent hyperglycemia on the viability of the oocyte and autoimmune reactions (formation of autoantibodies to the ovaries and adrenal glands).

After unilateral adnexectomy in women with diabetes mellitus 1, the risk of early menopause is 10 times higher compared with preserved bilateral ovarian function. With regard to diabetes mellitus 2, one study showed that women with this disease go through menopause earlier than healthy women (46 and 48 years, respectively). At the same time, in another study, diabetes mellitus 2 was not associated with a change in the age of menopause.

The level of leptin with aging changes according to the principle of *pari passu* (decrease in parallel with increasing age). In menopausal women, skipping a scheduled meal suppresses leptin secretion and stimulates the release of hypothalamic neuropeptide Y less actively than in women of reproductive age. It has also been shown that the administration of leptin to women over 50 does not lead to an increase in energy expenditure, which suggests the presence of a "defect" both in the receptor function of leptin and in its action. Moreover, during menopause, a change in the functional state of the hypothalamic-pituitary adrenal system, leading to an increase in the production of glucocorticoids. This promotes an increase in the size of abdominal adipocytes and an abdominal redistribution of fat. The effect of estrogens on the sympathetic nervous system is realized through the suppression of the activity of tyrosine hydroxylase, an enzyme involved in the synthesis of catecholamines. It has been shown that in women during the menopause, compared with women of reproductive age, elevated, both basal and stress-induced, levels of norepinephrine in the blood are determined, which are leveled against the background of estradiol treatment.

Almost all metabolic disorders that occur after menopause are interrelated and further exacerbate the adverse effects of sex steroid deficiency on the cardiovascular system. This is especially true for insulin resistance, which is a key feature of MMS and almost always associated with abdominal obesity. Compensatory hyperinsulinemia is an independent risk factor for coronary artery disease. According to statistics, in menopausal women, the relative risk of CHD is almost 2.7 times higher than in women of the same age, but with preserved ovarian function. It is known, for example, that normally insulin inhibits lipolysis in adipose

tissue; with insulin resistance, the implementation of these effects is impaired, the level of free fatty acids increases, the synthesis of triglycerides increases, and the content of antiatherogenic lipoprotein fractions decreases. Normal insulin-stimulated vasodilation is impaired in insulin resistance, suggesting a link between hyperinsulinemia and hypertension.

Thus, menopause is an insulin-resistant state, and menopause is associated with a significant increase in the risk of developing coronary artery disease and other macroangiopathies, contributing to a decrease in a woman's life expectancy.

The main clinical manifestation of MMS is an increase in body weight with the formation of abdominal-visceral obesity (with normal body weight during the reproductive period). The main clinical and laboratory indicators of MMS include: the presence of a waist circumference ( $> 80$  cm), triglyceride levels ( $\geq 1.7$  mmol / l), high-density lipoprotein cholesterol ( $< 1.29$  mmol / l), increased blood pressure ( $> 130/85$  mm Hg), fasting plasma glucose ( $\geq 5.6$  mmol/l).

In 30-40% of women with MMS, a characteristic sign associated with insulin resistance is revealed - rough patches of skin of various shades of brown on the elbows, under the mammary glands and in the groin - the so-called acanthosis nigricans.

In women with disorders of carbohydrate metabolism, vegetovascular (hot flashes, sweating, palpitations, etc.) and emotional and mental disorders (in 90% and 99% of women, respectively) predominate in the structure of manifestations of the climacteric syndrome.

#### LITERATURE

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