DISEASE OF THE FEMALE REPRODUCTIVE SYSTEM, WHICH MANIFESTS ITSELF WITH DIABETES MELLITUS TYPE 2

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KEY WORDS: diabetes mellitus; endometrial tumors; ovarian tumors; signaling pathways; neoplasm proteins

Relevance: Epidemiological studies have shown that cancer of the female reproductive system, including endometrial and ovarian cancers, is more common in people with diabetes. One of the meta-analyses showed a statistically significant association of DM2 with the risk of endometrial cancer (total relative risk (HR) 2.10; 95% confidence interval (CI) 1.75-2.53). This meta-analysis also talks about the relationship between DM1 and endometrial cancer (total HR 3.15; 95% CI 1.07-9.29). It should be noted that many studies provide evidence in favor of the fact that the incidence of cancer of the ovaries, esophagus, endometrium, vulva and vagina, thyroid gland is higher among women with DM1. On the other hand, patients with DM1 have a lower risk of developing breast cancer, melanoma and Hodgkin's lymphoma. Cells of most types of malignant neoplasms predominantly express the type 1 glucose transporter, which has a high affinity for glucose. It is also worth mentioning the Warburg effect, in which glucose in tumor cells follows an energetically inefficient glycolysis pathway with a high level of lactate production. Increased glycolysis in tumor cells provides the materials necessary for the synthesis of nucleotides, amino acids and lipids. In addition, hyperglycemia is responsible for DNA damage, which is the first stage of oncogenesis. For endometrial cancer, it has been suggested that in precancerous conditions or an existing tumor disease, endometrial cells, as well as microenvironment cells, can use excess glucose to stimulate anabolic pathways and disease progression. The genetic features of endometrial cancer indicate that most of these tumors already have a predisposition to increased glucose metabolism due to loss of expression. In DM2, insulin resistance leads to the development of compensatory hyperinsulinemia. High concentration of insulin in the blood plays one of the key roles in the pathogenesis of malignant neoplasms, which has been demonstrated in numerous studies both in vitro and in vivo. It is assumed that the metabolic effects of insulin, which include glucose transport into the cell, are mediated by activation of the PI3K/Akt signaling pathway, whereas the mitogenic effect is exerted on cells through the Ras/Raf/MAPK (Rat sarcoma virus/RAF proto-oncogene serine/threonine-protein kinase/Mitogen-Activated Protein Kinase) signaling pathway, in this pathway, the underlying kinases are MEK (Mitogen-Activated Kinase) and ERK (Extracellular

signal-Regulated Kinase). Pro-insulin and insulin have similar stimulating effects on MAPK activation, proliferation and migration of breast cancer cells. It is also necessary to note the importance of insulin-like growth factors (IGF) involved in the development of malignant tumors. Hyperinsulinemia accompanying peripheral insulin resistance leads to a decrease in the secretion of growth hormone, while the overall level of IGF-1 remains relatively unchanged due to increased sensitivity of the liver to growth hormone. IGF-binding protein (IGFBP-1) levels decrease due to increased insulin levels, which leads to increased bioavailability of IGF-1. There is also other evidence of normal or elevated IGF-1 levels in obese patients. . IGF promotes cell growth and survival, cell cycle progression, inhibits apoptosis, enhances angiogenesis and metastatic activity in various types of cancer. These factors directly regulate cellular functions by interacting with specific cell surface receptors and activating intracellular signaling pathways. A large body of data indicates that hyperglycemia is a factor contributing to the occurrence and progression of epithelial cancer through a number of mechanisms, including hyperinsulinemia, increased angiogenesis, inflammation, and DNA damage. Hyperglycemia is believed to have an important effect on both cancer cells and the progression of epithelial ovarian cancer.

Purpose:to study the risk factors and causes of cancer in women in the reproductive system and what is the connection between diabetes mellitus.

Material and methods: To study the complications of the disease, data were collected from patients of the Endocrinological Center of the Samarkand region for 2023. The data of 435 sick women were studied.

The results of the study: It is also worth noting that at present the relationship between diabetes and the risk of developing breast cancer is poorly understood. The most commonly assumed mechanisms underlying this relationship (as for other neoplasms discussed above) are insulin resistance, which leads to secondary hyperinsulinemia, the mitogenic effect of insulin exerted through the IGF receptor, as well as hyperglycemia, which enhances carcinogenesis by inducing oxidative stress. Studies have shown that diabetes is a negative prognostic factor for other cancers. Anyway, there was no direct link between the existing DM and the risk of developing breast cancer.

Conclusion: Tumors of the female reproductive system are still a serious problem for both patients and the health care system. The article provides a literary analysis of the assessment of the effects of chronic hyperglycemia, hyperinsulinemia, systemic inflammation and oxidative stress, as well as changes in the level of sex hormones observed in diabetes on the formation of tumors of the female reproductive system. Taking into account the fact that oncological diseases are the second cause of death in patients with DM1 and DM2, the research results presented in this review indicate in favor of the expediency of screening for oncological diseases of the

reproductive system in women with DM, a role in this should also be played by medical examination.

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