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UDC 616-089-053:610.08

CLINICAL AND DYNAMIC FEATURES OF DEPRESSIVE DISORDERS IN PATIENTS WITH TYPE II DIABETES MELLITUS AND THEIR IMPACT ON THE DEVELOPMENT OF DIABETIC POLYNEUROPATHY

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Abstract. This review article focuses on the clinical, psychiatric, and pathogenetic analysis of depressive disorders in patients with type 2 diabetes mellitus (T2DM) and their impact on the development of diabetic polyneuropathy (DPN). Current clinical, neurobiological, and psychosocial aspects of this problem are considered, including the role of inflammatory and neuroendocrine mechanisms, cognitive impairment, and emotional distress. The importance of psychiatrists in interdisciplinary therapy and complication prevention is emphasized. The relevance of this topic is due to the increasing prevalence of T2DM and the high incidence of mental disorders in patients in the Republic of Uzbekistan.

Key words: type II diabetes mellitus , depression, diabetic polyneuropathy, psychiatry, cognitive impairment, HPA axis, Uzbekistan.

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КЛИНИЧЕСКИЕ И ДИНАМИЧЕСКИЕ ОСОБЕННОСТИ ДЕПРЕССИВНЫХ РАССТРОЙСТВ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ II ТИПА И ИХ ВЛИЯНИЕ НА РАЗВИТИЕ ДИАБЕТИЧЕСКОЙ ПОЛИНЕВРОПАТИИ

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Аннотация. Данная обзорная статья посвящена клиническому, психиатрическому и патогенетическому анализу депрессивных расстройств у пациентов с сахарным диабетом 2 типа (СД2) и их влиянию на развитие диабетической полинейропатии (ДПН). Рассматриваются современные клинические, нейробиологические и психосоциальные аспекты этой проблемы, включая роль воспалительных и нейроэндокринных механизмов, когнитивных нарушений и эмоционального дистресса. Подчеркивается важность психиатров в междисциплинарной терапии и профилактике осложнений. Актуальность данной темы обусловлена растущей распространенностью СД2 и высокой частотой психических расстройств среди пациентов в Республике Узбекистан.

Ключевые слова*:* сахарный диабет 2 типа, депрессия, диабетическая полинейропатия, психиатрия, когнитивные нарушения, гипоталамо-гипофизарно-надпочечниковая ось, Узбекистан.

Relevance. Type 2 diabetes mellitus is one of the leading diseases of the 21st century, significantly impacting the physical and mental health of the population [1]. According to the World Health Organization, the prevalence of type 2 diabetes mellitus is steadily increasing and will exceed 500 million people by 2025 [2]. Mental disorders, among which depression occupies a central place, are increasingly becoming a major contributor to the complications of the disease.

According to various data, depressive disorders in patients with type 2 diabetes occur in 25–45% of patients, which is 2–3 times higher than in the general population [3]. Depression has a significant impact on the course of diabetes, complicating glycemic control, worsening the prognosis, and increasing the risk of developing vascular and neuropathic complications [4]. Furthermore, in patients with type 2 diabetes, depression is associated with higher mortality, increased hospitalization rates, and decreased quality of life [5]. In recent years, there has been a trend toward integrating a psychiatric approach into endocrinological practice, which is associated with the accumulation of evidence on the role of mental factors in the pathogenesis and course of diabetes [6]. The presence of depression is considered one of the independent risk factors for deterioration of metabolic control and the progression of chronic complications, including diabetic polyneuropathy (DPN) [7]. DPN is one of the most common and disabling complications of type 2 diabetes, affecting up to 70% of patients with long-term disease [8]. It manifests as pain, sensory, and motor disturbances that significantly impair quality of life. Chronic neuropathic pain, paresthesia, and insomnia contribute to the development of emotional instability and depression [9]. In turn, depression increases the subjective perception of pain and lowers the pain threshold [10]. Thus, a bidirectional pathogenetic relationship develops between depression and DPN, increasing the severity of both conditions [11]. Psychopathological features of depression in type 2 diabetes. The clinical structure of depression in patients with type 2 diabetes has specific features. Asthenodepressive and anxiety-depressive syndromes predominate, characterized by increased fatigue, sleep disturbances, decreased activity and motivation, irritability, and anxiety [12]. Somatized forms of depression are

often observed, when emotional disorders are masked by somatic complaints—pain, weakness, dizziness, paresthesia [13].

These symptoms are often mistakenly interpreted by doctors as manifestations of diabetic neuropathy or vascular disorders, which leads to a late diagnosis of depression [14]. However, differential diagnosis requires the attention of a psychiatrist: depression is characterized by anhedonia, a feeling of hopelessness, internal tension, emotional lability, and pronounced cognitive impairment [15]. and thinking speed) is found in 40–60% of patients with type 2 diabetes and depression [16]. They exacerbate self-control difficulties, leading to inadequate adherence to treatment regimens and decreased compliance [17]. Studies show that HbA1c levels positively correlate with the severity of cognitive impairment and the severity of depression [18].

II diabetes mellitus has a complex, multifactorial pathogenesis, including the interaction of biological, neuroendocrine, and psychosocial mechanisms [19]. Modern research shows that the key links in this relationship are inflammation, oxidative stress, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, and decreased levels of neurotrophic factors, primarily brain-derived neurotrophic factor (BDNF) [20].

Elevated levels of proinflammatory cytokines—interleukin-6 (IL -6), tumor necrosis factor -α (TNF - α), and C-reactive protein (CRP)—are found in both depression and T2DM [21]. These mediators contribute to vascular endothelial damage, impaired microcirculation, and demyelination of peripheral nerves [22]. This results in neuropathic pain, which, in turn, intensifies depressive symptoms [23].

Oxidative stress caused by chronic hyperglycemia plays a key role in the development of diabetic complications. Increased production of reactive oxygen species causes mitochondrial dysfunction, neuronal apoptosis, and

impaired nerve impulse transmission [24]. These processes lead to decreased neuroplasticity and worsening depression [25].

Hyperactivation of the HPA axis is accompanied by increased cortisol levels, which contribute to insulin resistance, increase blood glucose levels, and have a catabolic effect on brain tissue [26]. Patients with depression and type 2 diabetes often experience chronic hypercortisolemia associated with impaired feedback between the hypothalamus and pituitary gland [27]. Elevated cortisol levels correlate with the severity of depression and the severity of diabetic neuropathy [28].

Decreased BDNF levels observed during chronic stress and hyperglycemia lead to impaired growth and regeneration of nerve fibers, which contributes to the development of DPN [29]. This same mechanism is involved in the pathogenesis of depression, which explains the frequent combination of the two conditions [30].

In addition to biological factors, psychosocial factors are also important. Patients with chronic diseases often experience anxiety, feelings of helplessness, and social isolation [31]. These experiences lead to increased stress levels, decreased motivation for treatment, and the development of chronic depression [32]. Psychological maladjustment exacerbates somatic symptoms, creating a vicious cycle in which depression worsens the course of diabetes, and diabetes provokes further depression [33].

Cognitive-emotional aspects and neuropsychiatric manifestations. Cognitive impairment in type 2 diabetes and depression is primarily circulatory - metabolic in nature. Impairments in memory, attention, and executive functions are associated with hypoperfusion of the prefrontal cortex and hippocampus [34]. This is accompanied by a decrease in the ability to self-

control, plan, and follow treatment recommendations [35]. Such patients are more likely to exhibit emotional lability, irritability, guilt, and despair.

An important clinical observation is that the severity of cognitive deficits and depression often precedes the clinical signs of DPN, making psychiatric examination a valuable tool for early diagnosis [36]. In patients with severe depression, the incidence of neuropathic disorders is 1.5–2 times higher [37].

Diagnosis and clinical examination. Psychiatric examination of patients with type 2 diabetes should include an assessment of emotional state, anxiety level, and cognitive functioning . standardized instruments : PHQ-9 (Patient Health Questionnaire), HADS (Hospital Anxiety and Depression Scale), Beck Depression Inventory (BDI-II) [38].

For an objective assessment of cognitive functions, the MMSE (Mini-Mental State Examination) and MoCA (Montreal Cognitive Assessment) tests are used to determine the degree of impairment of memory, attention, and thinking [39]. Neuropathic symptoms are assessed using the DN 4, LANSS , and Neuropathic scales. Pain Scale [40].

It is important for the clinician to consider that somatic complaints (fatigue, insomnia, pain, loss of appetite) may be manifestations of depression, especially if they are accompanied by anhedonia and decreased interest in usual activities [41]. Psychiatric diagnosis should be aimed not only at identifying depression, but also at determining its degree, duration, and relationship to the somatic condition [42].

2 diabetes mellitus and diabetic polyneuropathy. Current principles of treating depressive disorders in type 2 diabetes mellitus suggest a comprehensive approach, including psychopharmacological, psychotherapeutic, and non-pharmacological interventions [43]. Given that patients with diabetes often experience metabolic disorders and a high risk of drug interactions, the choice

of antidepressant should consider not only efficacy but also safety in the context of somatic pathology [44].

The most preferred drugs are selective serotonin reuptake inhibitors (SSRIs)—sertraline, escitalopram , and paroxetine. They are highly effective and have minimal impact on carbohydrate metabolism [45]. Selective serotonin and norepinephrine reuptake inhibitors (SNRIs) —venlafaxine and duloxetine —are also widely used in patients with diabetes, especially in the presence of neuropathic pain [46].

Duloxetine has a dual antidepressant and analgesic effect, making it the drug of choice for the combination of depression and DPN [47]. Randomized trials have shown that duloxetine therapy leads to a 40–60% reduction in pain severity and a significant improvement in scores on the Beck Depression Inventory [48].

In addition to pharmacotherapy, psychotherapeutic methods play a significant role. Cognitive behavioral therapy (CBT) is the most proven non-drug method for treating depression in patients with somatic illnesses [49]. It promotes the development of adaptation skills, changes destructive cognitive patterns, and increases motivation for treatment.

Additionally, motivational counseling, psychoeducational programs and group therapy are used, aimed at increasing compliance and social support [50].

Physical activity has an independent antidepressant effect. Aerobic exercise (walking, swimming, yoga) in combination with drug therapy reduces the severity of depressive symptoms by 30–40%, improves metabolic parameters , and lowers HbA1c levels [51].

Diet also influences mental health. Deficiencies in B vitamins , omega-3 fatty acids, and magnesium are associated with an increased risk of depression in

patients with diabetes. Dietary modification and the use of antioxidants (alpha-lipoic acid, coenzyme Q10) improve neuroplasticity and reduce the severity of neuropathic symptoms [52].

A multidisciplinary approach. Optimal management of patients with type 2 diabetes and depression is only possible with close collaboration between an endocrinologist, psychiatrist, neurologist, and psychologist [53]. A psychiatrist plays a key role in diagnosing depression, selecting therapy, and monitoring side effects. An endocrinologist ensures glycemic and metabolic control, and a neurologist assesses the extent of peripheral nervous system damage.

Joint work of specialists allows for the development of individual treatment regimens, increasing the effectiveness of treatment and reducing the risk of complications [54]. In international studies (Fanelli et al ., 2025; Brooks , 2024) have been shown to reduce depression severity by 50% and improve HbA1c levels compared to the traditional approach [55].

The clinical significance and role of a psychiatrist. A psychiatrist not only diagnoses and treats depressive disorders but also participates in the psychoeducation of patients, helping them understand the relationship between their mental state and the course of diabetes [56]. In Uzbekistan, the creation of specialized interdisciplinary departments or offices within endocrinology clinics, where psychiatric examinations will become a mandatory part of comprehensive care, is relevant [57].

Psychiatric support facilitates the early detection of not only depression, but also anxiety, hypochondriacal and adaptation disorders, which often precede diabetic decompensation [58].

Thus, depression in type 2 diabetes is not a secondary phenomenon, but an independent pathogenetic factor influencing the course of the disease,

glycemic control, and the development of complications, including diabetic polyneuropathy [59,60]. Comprehensive diagnosis and treatment, taking into account the mental characteristics of patients, are essential for improving disease outcomes and enhancing quality of life.

Conclusion. Depression in patients with type 2 diabetes mellitus is not simply a comorbid mental disorder but a significant pathogenetic factor influencing the course of the disease, metabolic control, and the development of diabetic complications, particularly polyneuropathy. The relationship between depression and DPN is two-way: chronic pain, insomnia, and functional limitations exacerbate affective disturbances, while depression reduces treatment adherence and accelerates the progression of neuropathic impairments. Psychiatric assessment and early diagnosis of depression in patients with type 2 diabetes mellitus can prevent deterioration of metabolic control, improve treatment effectiveness, and reduce the risk of complications. Comprehensive therapy, including psychopharmacological agents, psychotherapy, physical activity, and social support, should become the standard of care for this patient population.

The implementation of an interdisciplinary approach in endocrinology clinics in Uzbekistan, where psychiatrists play an active role in diagnosis and treatment, will significantly improve treatment outcomes and patient quality of life. Conducting dissertation and clinical-epidemiological research in this area is of high scientific and practical significance, facilitating the integration of psychiatry and endocrinology into a unified clinical model.

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