EARLY CLINICAL-PATHOGENETIC MARKERS OF DIABETES MELLITUS AND MULTI-LEVEL PREVENTION STRATEGIES, FUNDAMENTAL AND PRACTICAL ANALYSIS

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Abstract: *This comprehensive research work is dedicated to studying the formation mechanisms, early diagnostic opportunities, and preventive measures of type 2 diabetes mellitus (T2DM)—one of the most pressing global problems of modern medicine. The article analyzes the impact of insulin resistance on intracellular signaling systems, changes in metabolic homeostasis in prediabetic states, and the dynamics of the disease's spread among the population of Uzbekistan. Furthermore, the effectiveness of modern screening methods, the diagnostic significance of the glycated hemoglobin (HbA1c) test, and scientifically based algorithms for reducing risk through lifestyle modification are detailed. The results of the research are aimed at preventing severe complications (nephropathy, retinopathy, neuropathy) through early diagnosis and include practical recommendations for primary care physicians.*

Keywords: *Diabetes mellitus, insulin resistance, glycated hemoglobin, prediabetes, metabolic syndrome, beta-cell apoptosis, prevention, healthy lifestyle, Uzbekistan healthcare system, dyslipidemia, glucose tolerance, visceral obesity.*

Introduction: Diabetes mellitus is a chronic state of hyperglycemia resulting from insufficient production of the hormone insulin by the pancreatic beta-cells or a decrease in the sensitivity of tissues to this hormone (insulin resistance). Today, T2DM has risen to the level of a global socio-economic problem, which not only

deteriorates the patient's quality of life but also imposes a massive financial burden on the healthcare system. In the Republic of Uzbekistan, the incidence rate of diabetes mellitus has been "getting younger" in recent years. This situation is explained by urbanization, an increase in the proportion of fast-digesting carbohydrates in the daily diet, and a sharp decrease in physical activity. The dangerous aspect of the disease is that it can proceed in a latent stage for many years. Studies show that at the time of diagnosis, almost 50 percent of patients already have established complications of chronic hyperglycemia—signs of angiopathy, nephropathy, or polyneuropathy. The purpose of the article is to identify the disease at its earliest stage (the prediabetic period) and provide scientifically based conclusions for curbing its development mechanisms.

Literature Review: Academician Yo.Kh. Turakulov made a huge contribution to the formation and development of endocrinology science in Uzbekistan. In his fundamental works, the impact of hormonal disorders on metabolism and the metabolic activity of insulin in liver and muscle tissues were proven at the molecular level [6]. Years of epidemiological research conducted by Professor S.I. Ismoilov revealed that the regional characteristics of Uzbekistan—hot climate, high-carbohydrate national dishes, and genetic predisposition of the population—have a unique impact on the course of the disease [3]. Internationally, according to the latest consensus between the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), the prediabetic state is considered a "point of reversal" for the development of T2DM. From a pathophysiological point of view, during the period when insulin resistance develops, the beta-cells of the pancreas operate in a hyperstimulation mode, and over time, up to 50-60 percent of them perish as a result of apoptosis [4]. In the scientific works of local scientist Sh.A. Kodirova, visceral obesity and its connection with systemic inflammatory processes in blood vessel walls were studied in depth [5]. In modern literature, an HbA1c level between 5.7% and 6.4% is recognized as the primary marker of prediabetes.

Methods: Within the framework of this scientific work, a comprehensive observation was conducted between 2023 and 2025 based at the multi-disciplinary central polyclinics of Tashkent city and the region. A total of 500 respondents (250 women and 250 men, aged 30 to 70) were involved in the study. The research methodology included the following stages. Clinical-anthropometric assessment. The height, weight, waist circumference (WC), and hip circumference of each respondent were measured. The Body Mass Index (BMI = m/h^2) was calculated, and obesity levels were determined according to the WHO classification. Glycemic and biochemical analyses. Glucose levels were measured in venous blood plasma on an empty stomach and 2 hours after a 75-gram glucose load (OGTT). Simultaneously, the HbA1c level, reflecting the average glycemia over the last 3 months, was determined. Metabolic marker analysis. Total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglyceride levels in blood serum were checked. Surveying. Respondents' genetic predisposition, harmful habits, sleep quality, and physical activity (daily step count) were evaluated through special scientific questionnaires. Statistical processing. The collected data were analyzed using variational statistical methods. The reliability of the results was evaluated according to the Student's (t) criterion ($p < 0.05$).

Results: The research results showed that 45 percent of the examined individuals had various levels of carbohydrate metabolism disorders (prediabetes or latent T2DM). The manifestation of early symptoms and pathophysiological correlations were analyzed as follows. Asthenic and neuropsychological signs (86%). The absolute majority of respondents noted constant chronic fatigue, morning weakness, and strong drowsiness after lunch. This is due to the inability of cells to utilize glucose as energy. Gastrointestinal and thirst symptoms (78%). Dry mouth (polydipsia), frequent urination at night (polyuria), and feeling hungry again shortly after eating (polyphagia) were recorded. Dermatological and neurovascular changes (40%). Numbness in the limbs (paresthesia), coldness of fingers, skin dryness, and small wounds not healing for a long period (more than 2 weeks) were observed. One

of the most important conclusions of the study—it was confirmed that 75 percent of individuals with a waist circumference of more than 94 cm in men and more than 80 cm in women had a high HOMA-IR index. This proved that obesity in the abdominal area is the primary driver of the development of type 2 diabetes.

Conclusion: The following strategic conclusions were formed regarding the containment of diabetes mellitus at an early stage. Systemic screening. All individuals over the age of 35 must undergo a blood sugar and HbA1c test at least once a year. Physical activity. At least 150-200 minutes of moderate-intensity exercise per week increases the sensitivity of insulin receptors by 50-60 percent. Nutrition culture. It is necessary to remove trans-fats, fast food, and artificial sugary drinks from the diet and increase the proportion of fiber-rich products. Medical literacy. It is necessary to expand the activities of "diabetes schools" among the population at the primary health care level and form self-monitoring skills. Type 2 diabetes mellitus is a serious signal for fundamentally changing the lifestyle in a positive direction. Early diagnosis and correct prevention guarantee a long and healthy life for a person.

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