UDK: 616.36-003.82-07-08

GENETIC AND METABOLIC DETERMINANTS OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Abstract:

The study evaluates the impact of genetic and metabolic disorders on the health-related quality of life in patients with non-alcoholic fatty liver disease. A comprehensive clinical, biochemical, and molecular genetic analysis was performed on one hundred and ten patients of Uzbek nationality. The presence of the pathological T allele of the ADIPOQ gene was significantly associated with progressive insulin resistance and severe lipid metabolism disorders. These metabolic alterations led to pronounced asthenic and dyspeptic symptoms, which significantly reduced the physical and psycho-emotional components of patients' quality of life. Personalization of therapeutic strategies considering genetic polymorphisms is essential to optimize clinical outcomes and patient well-being.

Keywords: non-alcoholic fatty liver disease, adiponectin gene, polymorphism, quality of life, insulin resistance.

Аннотация:

В исследовании оценивается влияние генетических и метаболических нарушений на качество жизни пациентов с неалкогольной жировой болезнью печени. Комплексный клинический, биохимический и молекулярно-генетический анализ был выполнен у ста десяти пациентов узбекской национальности. Наличие патологического Т-аллеля гена ADIPOQ было достоверно связано с прогрессирующей инсулинорезистентностью и тяжелыми нарушениями липидного обмена. Данные метаболические изменения приводили к выраженным астеническим и диспептическим

симптомам, существенно снижающим физический и психоэмоциональный компоненты качества жизни. Персонализация терапевтических стратегий с учетом генетического полиморфизма необходима для оптимизации клинических исходов и благополучия пациентов.

Ключевые слова: неалкогольная жировая болезнь печени, ген адипонектина, полиморфизм, качество жизни, инсулинорезистентность.

Introduction:

Non-alcoholic fatty liver disease has become one of the most pressing challenges in modern gastroenterology and internal medicine, affecting a substantial portion of the working-age population worldwide. The progression from simple steatosis to non-alcoholic steatohepatitis involves complex multifactorial mechanisms, where visceral obesity, insulin resistance, and systemic chronic inflammation play a central role. Recent clinical studies indicate that the clinical course of the disease and its impact on the daily functioning of patients are deeply influenced by individual genetic characteristics. Metabolic disturbances, such as severe dyslipidemia and severe tissue insulin resistance, often manifest clinically as chronic fatigue, general weakness, and abdominal discomfort. These somatic symptoms directly impair the daily activities, emotional state, and overall health-related quality of life of individuals suffering from hepatic steatosis. Understanding the intricate link between specific candidate genes, metabolic parameters, and the subjective well-being of patients is crucial for developing effective management algorithms. Although conventional hepatoprotective therapies address basic biochemical syndromes, they frequently fail to provide a sustainable improvement in patient-reported quality of life without long-term lifestyle modifications. Therefore, identifying early genetic predictors of disease progression can help clinicians implement personalized preventive measures and targeted dietary interventions before irreversible structural damage occurs in the liver tissue.

Aim of the study: To evaluate the relationships between the ADIPOQ +276G>T gene polymorphism, metabolic indicators, and health-related quality of life parameters in patients with non-alcoholic fatty liver disease.

Materials and methods:

The clinical trial involved one hundred and ten non-related patients of Uzbek nationality who received stationary treatment in the gastroenterology department, including sixty-five individuals at the stage of hepatic steatosis and forty-five patients diagnosed with non-alcoholic steatohepatitis. A control group consisted of forty-nine virtually healthy individuals with no prior history of liver diseases or metabolic disorders. Anthropometric parameters, including body mass index, waist circumference, and hip circumference, were thoroughly measured for all participants. Laboratory tests included a comprehensive assessment of cytolysis markers such as alanine aminotransferase and aspartate aminotransferase, cholestasis parameters including alkaline phosphatase and gamma-glutamyl transferase, and a full lipid profile. Insulin resistance was precisely determined using the homeostatic model assessment index based on fasting glucose and insulin levels measured via enzyme-linked immunosorbent assay. Molecular genetic testing was carried out by extracting genomic DNA from whole blood samples, followed by polymerase chain reaction and restriction fragment length polymorphism analysis using specific oligonucleotide primers and the restriction enzyme Pct I to identify the distribution of the ADIPOQ rs1501299 genotypes. Statistical data processing was executed using the Statistica 6.0 software package, applying analysis of variance, Student’s t-test, Mann-Whitney U-test, and Pearson correlation analysis to establish significance at a level of p less than 0.05.

Results:

The clinical evaluation demonstrated that asthenic and dyspeptic symptoms were highly prevalent among the cohort, with increased fatigue reported by 35.5% of patients and general weakness observed in 30.9% of cases, which directly degraded their functional well-being. Molecular genetic analysis revealed that the

distribution of ADIPOQ +276G>T genotypes among the patients was 22.3% for GG, 56.4% for GT, and 21.3% for TT, indicating a significant accumulation of the heterozygous GT state compared to the control group. The presence of the pathological T allele was associated with a 2.3-fold increase in the risk of disease progression. Correlation analysis established a strong positive relationship between the HOMA-IR index and serum triglycerides (r=0.6), as well as with alanine aminotransferase (r=0.5) and aspartate aminotransferase (r=0.5), confirming that severe insulin resistance directly influences functional liver impairment. Patients carrying the TT genotype exhibited significantly higher HOMA-IR values and larger waist circumferences compared to those with the GG genotype. Furthermore, the evaluation of treatment dynamics over a thirty-day period demonstrated that carriers of the protective G allele achieved a substantial reduction in transaminases and lipids, whereas patients with the pathological T allele exhibited persistent elevations of metabolic markers. This resistance to standard therapy underscores the negative impact of the pathological polymorphism on both biochemical recovery and health-related quality of life.

Conclusions:

Genetic factors play a key role in determining the severity and progression of non-alcoholic fatty liver disease among the Uzbek population. The pathological T allele of the ADIPOQ +276G>T gene is significantly associated with severe insulin resistance, abdominal obesity, and profound lipid disorders, which exacerbate somatic symptoms and reduce patient quality of life. Standard hepatoprotective therapy combined with general lifestyle modifications shows limited efficacy in individuals carrying this genetic risk marker. Implementing a personalized management algorithm that includes early molecular genetic screening and targeted low-calorie dietary interventions is required to optimize metabolic parameters, prevent hepatic progression, and sustainably improve long-term quality of life.

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