ACADEMICIA: An International Multidisciplinary Research Journal
ISSN: 2249-7137 Vol. 12, Issue 01, January 2022 SJIF 2021 = 7.492
A peer reviewed journal

# ASSESSMENT OF THE ROLE OF THE LEU28PRO POLYMORPHIC MARKER OF THE APOE GENE IN DIABETIC NEPHROPATHY

**Jabbarov O.O*; Khujaniyazova N. K****

*Associate Professor,
Head of the Department of Faculty and Hospital Therapy,
UZBEKISTAN
Email id: dok_azim66@mail.ru

**Chilanzar College of Public Health named after Abu Ali ibn Sina,
UZBEKISTAN
Email id: teacher1201@mail.ru

**DOI: 10.5958/2249-7137.2022.00022.2**

## ABSTRACT

*The aim of this study was to study 129 patients with type 2 diabetes and 110 healthy people to determine whether the Leu28Pro polymorphic markers of the APOE gene are associated with the development of diabetic nephropathy (DN). Patients in the main group: 65 patients with a disease duration of up to 10 years, without diabetic nephropathy (33 patients) and with diabetic nephropathy (32 patients), 64 patients with diabetes lasting more than 10-20 years, with no diabetic nephropathy (31 patients ) and diabetic nephropathy (33 patients). Genotyping was carried out by polymerase chain reaction. The study showed that the association of the Pro allele and the Leu/Pro genotype of the ENOS3 gene play a role in the development of diabetic nephropathy in patients with type 2 diabetes mellitus in the studied Uzbek nation.*

**KEYWORDS:** *Diabetic Nephropathy, Diabetes Mellitus, Gene, Polymorphism, Allele, Genotype.*

## INTRODUCTION

Diabetic nephropathy (DN) is a microvascular complication of diabetes mellitus (DM), the development of which significantly worsens the course and further prognosis of the disease. In DN, damage to the small blood vessels of the filtering apparatus of the kidneys is observed, leading to a further increase in the amount of protein excreted in the urine (proteinuria) **[1, 2].** DN develops in 13-15% of individuals in the general population and much more often - up to 40-50% - in risk groups, which include patients with type 2 diabetes **[3,4].** According to the forecasts of the International Diabetes Federation, the number of patients with diabetes in the world by 2035 will increase to 587 million people, of which 95% are patients with type 2 diabetes **[5].**

In recent years, the risk of developing nephropathy has definitely been determined by genetic factors. Only about 40-50% of patients with both type 1 diabetes and type 2 diabetes subsequently develop DN **[6].** Genetic factors can directly influence the development of DN and / or act in conjunction with genes that influence cardiovascular disease. The search for genetic

markers of predisposition or, on the contrary, resistance to diseases is one of the most urgent tasks of medical science. **[7]**

Previous studies of the association of a large group of candidate genes have shown that only polymorphic markers of the gene for the enzyme that converts angiotensin I (ACE) and the gene for NO synthetize in vascular endothelial cells (NOS3) are associated with DN in patients with type 2 diabetes **[8].** The association of genes encoding lipoproteins has not previously been studied among the Uzbek nation, although it is believed that one of the risk factors for DN in type 2 diabetes is an increased plasma lipid concentration, since certain groups of lipoproteins have a strong affinity for the vascular wall and can contribute to it. damage. According to some reports, an altered lipid profile in the early stages may be the cause of the development of normoalbuminuric nephropathy in patients with type 2 diabetes. Therefore, the genes encoding apolipoproteins B and E, individual concentrations and properties of which largely determine lipid metabolism in a particular patient, are of undoubted interest for research as candidate genes that determine the predisposition to the development of vascular complications in type 2 diabetes.

**Purpose:** To study the distribution of allele and genotype frequencies and to identify the association of the Leu/Pro polymorphic markers of the APOE gene with the development of DN in type 2 diabetes patients of Uzbek nationality.

**Material and methods:** In the Republican Scientific and Practical Center of Nephrology on the basis of the III clinic of TMA, the main group of 129 patients with type 2 diabetes was examined and the control group consisted of 110 healthy individuals of the Uzbek nation, included on the basis of the "case-control" principle. Patients in the main group were distributed as follows: 65 patients with a disease duration of up to 10 years, without diabetic nephropathy (33 patients) and with diabetic nephropathy (32 patients), 64 patients with diabetes lasting more than 10-20 years, with no diabetic nephropathy (31 patients) and diabetic nephropathy (33 patients). We studied such indicators as the results of general blood and urine tests, lipid spectrum, glycaemic profile, glycosylated haemoglobin, microalbuminuria, glomerular filtration rate (GFR) according to the CKD-EPI formula, endothelin-1 level in blood plasma, echocardiography, ABPM and Doppler study of renal vessels.

Testing of the Leu/Pro polymorphism of the APOE gene was carried out on a programmable thermal cycler from Applied Biosystems 2720 (USA), using test systems from Litech (Russia), according to the manufacturer's instructions.

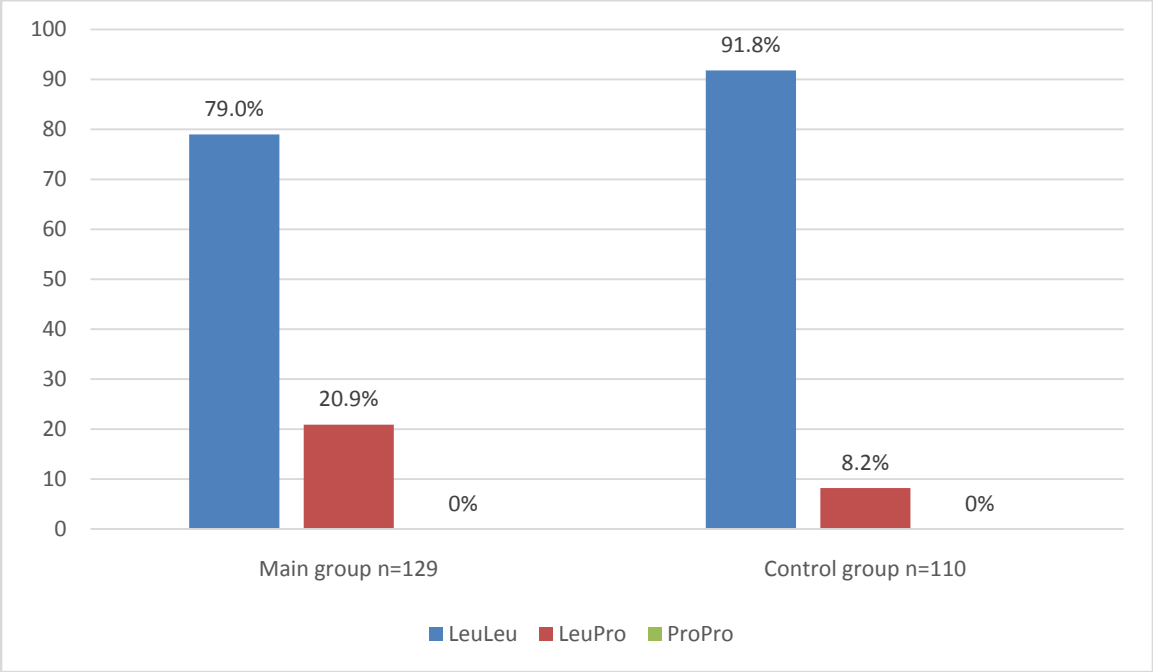
For statistical processing of the material, the STATISTICA 6 program was used. Data are presented as mean values with standard deviation (M ± SD). The normality of the distribution was checked by the Kolmogorov-Smirnov criterion. The relative risk of disease in carriers of a certain allele and genotype was calculated as an indicator of the odds ratio (OR - odds ratio).

**Results and its discussion:** The frequency of alleles and genotypes of the Leu28Pro polymorphism of the APOE gene in all patients (main group) and the control sample is shown in Figure 1.

In our study, we investigated the distribution of genotypes and alleles of the Leu28Pro polymorphic marker of the APOE gene in the main and control patients.

The prevalence of the Leu allele in the study and control groups was 89.5% and 95.95%, respectively. The incidence of the functional unfavourable Pro allele was 10.4% and 4.1%, respectively. The statistical report shows that carriers of the Pro allele are 2.7 times more likely to develop the disease than carriers of the Leuallele, and the difference between them is a significant statistical value ($\chi 2$ = 6.9; P = 0.008; OR = 2.7; 95% CI 1.2597-5.9608)). The Leu allele indicates that it has a protective effect against disease progression. ($\chi 2$ = 6.9; P = 0.008; OR = 0.4; 95% CI 0.1678-0.7938)

**Fig.1:Frequency of distribution of alleles and genotypes of the Leu28Pro polymorphism of the APOE gene in the study and control groups of patients with type 2 diabetes.**




In our study, we investigated the distribution of genotypes and alleles of the Leu28Pro polymorphic marker of the APOE gene in the main and control patients.

The prevalence of the Leu allele in the study and control groups was 89.5% and 95.95%, respectively. The incidence of the functional unfavourable Pro allele was 10.4% and 4.1%, respectively. The statistical report shows that carriers of the Pro allele are 2.7 times more likely to develop the disease than carriers of the Leu allele, and the difference between them is a significant statistical value ($\chi 2$ = 6.9; P = 0.008; OR = 2.7; 95% CI 1.2597-5.9608)). The Leu allele indicates that it has a protective effect against disease progression. ($\chi 2$ = 6.9; P = 0.008; OR = 0.4; 95% CI 0.1678-0.7938)

According to the results of the main and control groups, the distribution of the Leu/Leu, Leu/Pro genotypes was 79.0%, 20.9% and 91.8%, 8.2%, but the Pro/Pro genotype in our analysis of the mutational genotype. According to statistical calculations, the probability of disease in carriers of the Leu/Pro genotype is 2.9 times higher than in carriers of the Leu/Leu genotype, and the difference between them is statistically significant. ($\chi$ 2 = 7.5; P = 0.006; OR = 2.9; 95% CI 1.3308-6.6311).

The Leu/Leu genotype was significantly lower in the main group than in the control group, by 79.0%, 91.8% and showed a protective function against disease progression ($\chi 2 = 7.5$; P = 0.006; OR = 0.3; 95% CI 0.1508-0.7515).

In our study, we demonstrated an association between the carriage of the Pro allele (Leu/Pro genotype) of the APOE gene and diabetic nephropathy in patients with type 2 diabetes. The results obtained are consistent with the data of domestic and foreign authors who showed that the carriage of the Pro-allele is an independent risk factor for DN in patients with type 2 diabetes in various ethnic groups. Analysis of data from foreign studies also indicates a relationship between the polymorphic marker e2/e3/e4 of the APOE gene with the development of DN in both DM 2 and DM 1, which may indicate that disorders of lipid metabolism can play a significant role in the pathogenesis of DN. An earlier study revealed an association of the e2/e3/e4 polymorphic marker of the APOE gene with the development of DN in type 2 diabetes, that the carriage of the e3 allele and the e3 / e3 genotype of the e2/e3/e4 marker of the apolipoprotein E gene (APOE) is a factor of increased risk of DN in SD 1. Japanese authors described the association of this marker with the progression of kidney damage in type 2 diabetes from MAU to proteinuria, where the e2 allele is considered an independent risk factor for DN progression. **[9]**

These data and the results of our study allow us to conclude that the APOE gene plays an important role in the development of DN in patients with type 2 diabetes mellitus in the studied Uzbek nation. However, it should be noted that genes whose products are associated with the regulation of vascular tone in the microvasculature, such as ACE and ENOS3, also play an important role in the pathogenesis of early stages of DN. **[10]**

**CONCLUSION:** Thus, summarizing the data obtained, we can conclude that a number of lipid metabolism genes are undoubtedly involved in the development of DN in type 2 diabetes in persons of Uzbek nationality. The results of this study indicate the importance of further study of the molecular basis of the development and progression of DN, which will lead to the development of new promising directions in the prevention of this pathology.

**REFERENCES**

**1.** Jabborov OO. Features of Genetic polymorphism in population with diabetic nephropathia: Literature review. Journal of advances in medicine and medical research 2019;29(9):1-7.

**2.** Alberti G, Zimmet P, Shaw J. IDF. Epidemiology Task fores consensus group. The metabolic syndrome - a new worldwide definition. Lancet. 2005;366:1059-1062.

**3.** Jeleznyakova AV, Lebedeva NO, Vikulova OK, et al. The risk of developing chronic kidney disease in patients with type 2 diabetes mellitus is determined by polymorphism of the NOS3, APOB, KCNJ11, TCF7L2 genes. Diabetes mellitus. 2014;(3):23-30.

**4.** Jabbarov OO. Significance of the RAAS coding component of the ACE gene in the development of diabetic nephropathy in type 2 diabetes. Infection, immunity and pharmacology. 2019;(6): 47-55.

**5.** Vikulova OK. Clinical, laboratory and genetic factors for the development and progression of diabetic nephropathy in patients with type 1 diabetes mellitus: Diss. ...Cand. honey. Sciences: Vikulova Olga Konstantinovna, Mascow; 2003. 123 p.

**6.** Kuchkarova DT. Analysis of energy-saving modes of pumping machines and units at industrial enterprises. Problems of modern science and education. 2020;(1):146.

**7.** Kuchkarova DT. Energy-Saving Control Systems of Machines and Silk-Winding Units. 2021. p. 92.

**8.** Shestakova MV, Shakhmalova MSh. Diabetic nephropathy: clinical picture, diagnosis, treatment. Moscow; 2009.

**9.** Villeneuve S, Brisson D, Marchant N, Gaudet D. The potential applications of Apolipoprotein E in personalized medicine. Frontiers in Aging Neuroscience. 2014;6:154.

**10.** Koopal C, van der Graaf Y, Asselbergs F, Westerink J, Visseren F. Influence of APOE-2 genotype on the relation between adiposity and plasma lipid levels in patients with vascular disease. Int J Obes Relat Metab Disord. 2015;39(2):265–269