AEP319 - ANGIOTENSIN-CONVERTING ENZYME GENE (I/D) POLYMORPHISM IN ASSOCIATION WITH THE DIABETIC NEPHROPATHY

Taner Hasan[1]*, Slavica Josifovska[2], Cvetanka Volkanovska Ilievska[3], Ivana Trajkovska[1], Natasha N. Minova[1]

[1] Department of Endocrinology, Diabetes and Metabolism, 8th September City General Hospital, Skopje, Macedonia, [2] Laboratory for Molecular Biology, Institute of Biology, Faculty of Natural Sciences, Ss. Cyril and Methodius University, Skopje, Macedonia, [3] PHI University Clinic for Endocrinology, Diabetes and Metabolic disorders, Medical Faculty, Ss. Cyril and Methodius University, Skopje, Macedonia

Introduction: Polymorphisms in the Angiotensin-converting enzyme (ACE) gene have been associated with development of Diabetic nephropathy (DN), a major microvascular complication of the Type 2 Diabetes mellitus (T2DM). Since the genetic predisposition plays an important role in development of DN in patients with T2DM, genetic testing might largely contribute to better assessment of the risk of DN in such patients. The aim of this study is to investigate the association of the ACE gene's I/D polymorphism with DN in T2DM patients.

Materials and methods: The study is designed as a case-control, prospective, observational, genetic association study. The samples from 88 patients with T2DM were analyzed, including 57 patients with DN and 31 without DN. The duration of T2DM was similar in both subgroups. The study includes also 26 healthy controls. The demographic, clinical and laboratory data are analyzed in addition to the genetic profiling of the patients for the ACE gene. The determination of polymorphisms in the ACE gene was with the TaqMan probes containing a nucleotide sequence specific to the amplified region of the gene. The resulted curves were analyzed with an integral software of the system, the StepOne (Applied Biosystems) by the method of allelic discrimination leading to determination of the genotype of each patient: DD (homozygous for deletion), ID (heterozygous carrying both alleles) or II (homozygous for insertion).

Results: The results of the analyzes of the frequencies of the genotypes and the I/D alleles of the ACE gene compared to the occurrence of nephropathy are presented in Chart 1. A statistically significant association of genotypes D/D and I/D with the occurrence of nephropathy compared to the homozygous I/I genotype was revealed. In the group of patients with T2DM, the carriers of the D/D or I/D genotypes have 7.687 folds higher odds and 1.857 folds higher relative risk for developing nephropathy than the carriers of I/I genotype (Table 1). The results confirmed the correlation of the genetic polymorphism and the development of the DN in patients with T2DM.

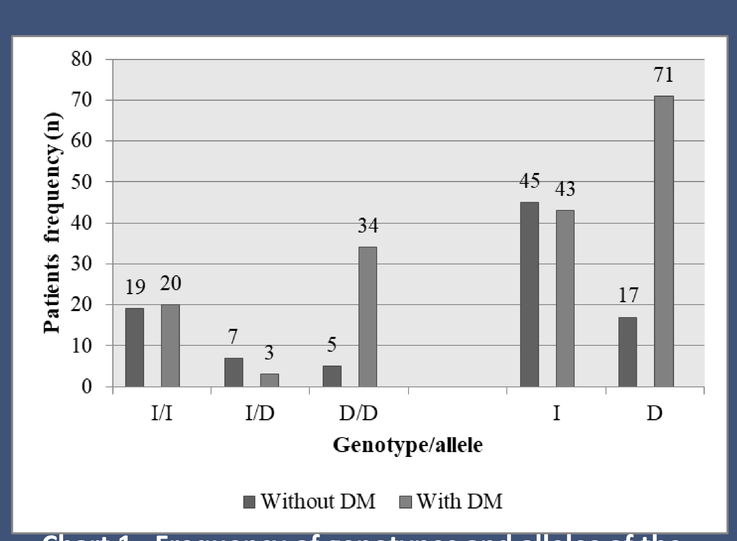

Chart 1. Frequency of genotypes and alleles of the *ACE* gene in the non-DN and DN patients with T2DM

Table 1. Applicability of the polymorphism ACE I/D as a potential predictive biomarker for development of DN in patients with T2DM

Statistic parameter	Value	Lower bound (95%)	Upper bound (95%)
Sensitivity, %	59.65	46.67	71.36
Specificity, %	83.87	66.75	93.25
False positive rate (%)	16,13	3,94	28,31
False negative rate (%)	40,35	28,04	52,66
Prevalence (%)	64,77	54,79	74,75
Positive Predictive Value (PPV)	0.872	0.767	0.977
Negative Predictive Value (NPV)	0.531	0.391	0.670
LR+ (Positive likelihood ratio)	3,698	1,612	8,487
LR- (Negative likelihood ratio)	0,481	0,339	0,684
Relative risk, folds	1.857	1.354	2.548
Odds ratio, folds	7.687	2.670	22.131

Corresponding author: MD, PhD Taner Hasan
taner_hasan@yahoo.com

Conclusion: The results of our study indicate that the ACE I / D polymorphism is associated with the onset of nephropathy in patients with T2DM emphasizing the potential predictive value of the determination of this polymorphism. Therefore, the determination of the I / D polymorphism in the ACE gene in patients with T2DM can help differentiate patients with a higher risk of developing DN and even predict the therapeutic response in such, thus subjecting them to a certain hygiene-dietary regime, frequent controls, and modification of therapy and/or administration of appropriate kidney-protective drugs.

Conflict of Interest: The authors declare that they have no conflict of interest regarding presentation of this poster.