ORIGINAL ARTICLE

Association of Polymorphic Markers Aluins/Del-DAce T-786C Gene Enos3 in Diabetic Nephropate Progressing for Type 2 Diabetes Mellitus

Ozimboy O Jabbarov1, Botir T Daminov2, Kodirjon T Boboev3, Laylo D Tursunova1, Maxsuma X Tashpulatova1, Lola I Maksudova4

1 Department of faculty and hospital therapy No.2, Farabi 2, Tashkent - 100109, Uzbekistan
2 Department of Propaedeutics of Internal Diseases, Hospital and Faculty Therapy, Doctor of medicine, Bagishamal str., 223. Yunusabad region, Tashkent city - 100140, Uzbekistan
3 Head of the Laboratory of Medical Genetics, Doctor of Medicine, Medical Care Department 138 Usman Nasyr street, Tashkent city - 100059, Uzbekistan
4 Department of children’s infections, Bagishamal str., 223. Yunusabad region, Tashkent city - 100140, Uzbekistan

Article History:
Received on: 10 Jul 2020
Revised on: 11 Aug 2020
Accepted on: 19 Aug 2020

Keywords:
diabetic nephropathy, Type 2 diabetes, ENOS3, Chronic kidney disease

ABSTRACT

In the current study, the development of diabetic nephropathy identified the relationship between the polymeric marker of AC genes and the NS3 gene. One hundred twenty-nine patients with type 2 diabetes were tried. Patients in the principle gathering: 65 people with diabetes nephropathy preserved kidney function (33 patients), and kidney function weakness (32 patients), 64 patients with Diabetes were enduring more than 10-20 years, diabetic nephropathy preserved the chain of genotyping polymers carry out kidney function (31 patients). The study showed a link between eNOS3 genes in the development of diabetic nephropathy in Type 2 diabetes patients, supported by the ACE gene.

INTRODUCTION

Diabetic nephropathy (DN) is a microvascular complex of Diabetes, which develops under the control of a completely combined effect of work and hemodynamic substances (Colombo et al., 2003). In addition to the above elements, there are also genetic trends that interact with the clinical manifestation of this pathology. (Ezzidi et al., 2008) Despite the similar incidence of type 1 and type 2 diabetes, patients with type 2 diabetes are more likely to die from terminal kidney failure - 45% compared to 5–10% of type 1 diabetes (Dellamea et al., 2014).

Convenient recognition of this difficulty legitimately influences the adequacy of treatment, exhibits the significance and significance of the issue of reading hazard factors for DNA and shows the need to create enlightening techniques for its determination. (Dellamea et al., 2014)

To be able to diagnose and prevent DN early, it is necessary to identify markers associated with DN, which in turn will help to form danger groups for DN growth even in the preclinical step. (Ezzidi et al., 2009)

Also, it is of practical interest to study the progress of NAM for actual preventive procedures and reduction of chronic kidney failure (CRI). The cost of exceptional treatment at the terminal level of naturopathy is high. (Maslova et al., 2005; Villeneuve et al., 2014) In this way, the issue of kidney entanglements of Diabetes mellitus, notwithstanding clinical, has
obtained significant financial significance. (Hana, 2011)

Hereditary components dictate the danger of rising nephropathy before clinical preliminaries. Around 40–half of the patients by type 1 and type 2 diabetes later create DNA. Genetic plants can distress the growth of DM and 100 or work together with genes that cause heart disease. In contrast to possible genetic markers, this preventative pathology drug acts as one of the essential functions of the Medicines. (Koopal et al., 2015).

By creating such markers, physicians create risk groups for diseases. (Macisaac et al., 2014) They include an individual prognosis or diagnosis (including the earlier clinical release of the disease) in some pathologies. (Maslova et al., 2005)

The occupation of genetic signs in Diabetes relies upon the racial recurrence and racial and ethnic contrasts between the genotypes of the individuals considered. (Morshed et al., 2002). In recent years, the genetic risk of Diabetes and its complications has been widely discussed in insulin resistance genes, insulin-based genes, lipid metabolism-affected genes, angiotensin I-conversion enzyme (AC) polymorphism, and endothelial no-synthesis (NOS) (Ezzidi et al., 2009; Hana, 2011).

As indicated by the present-day hypothesis, DNA creates under the total complex impact of reciprocal, hemodynamic and hereditary parts, the activity of which prompts the clinical appearances of pathology. In the pathogenesis of DN, the activation of the local renal renin-angiotensin system (RAS) is of great importance, which leads to the development of systemic and intracellular hypertension. (Ezzidi et al., 2008) The mechanism of pathogenic effect of angiotensin II (AT-II) at DM is determined not only by vasoconstrictor action but also by proliferative, prooxidant and prothrombogenic activity, stimulation of cytokine synthesis, growth factors. Therefore, the genes encoding the components of the RAC gene of the angiotensin-converting enzyme (ACE) are of interest as candidates of diabetic nephropathy in patients with type 2 DM (Mustafina et al., 2001).

At present the pathogenesis of micro- and macrovascular complications of DM is dominated by endothelial dysfunction, accompanied by a deficit of vasodilators - nitrogen oxide (NO), and activation of local secretion of vasoconstrictors such as endothelin-1 (E-1). (Macisaac et al., 2014) In its turn, the gene of nitrogen oxide endothelial synthase (eNOS3) participates in the production of the latter as candidate genes for diabetic nephropathy and CKD (Chronic kidney disease) of type 2 SD (Ng et al., 2005).

Nevertheless, the single density and properties of AC and eNOS3 genes, which cause activation of RAAS (renin-angiotensin-aldosterone system) and endothelial dysfunction, are of interest to the study as a candidate gene that controls the trend of vascular complications in type 2 diabetes. (Rizvi et al., 2014)

Explore and distinguish the connection between the AC quality and the INS3 quality as indicators of the turn of events and movement of patients with type 2 diabetes mellitus and decide the hereditary diagnostics of the Uzbek national hazard industrial facility. (Uryasiev and Shakhanov, 2017)

There are multiple variants of the AC, and Inose3 genes for type 2 diabetes and its macrobiotic and microvascular complications have not been previously studied in Uzbek nationalities. (Villeneuve et al., 2014)

The research objective is to evaluate the contribution of polymorphic markers AluIns/Del>L of the ACE gene and T-786C of the eNOS3 gene to the danger of diabetic nephropathy.

MATERIALS AND METHODS

One hundred twenty-nine patients at The Republican Scientific and Practical Center Nephrology, based at the TMA Multidisciplinary Clinic, was tested for the diagnosis of type 2D clinical lysis; The control group included 110 healthy Uzbeks in the “case-control” policy. Patients of the key group are spread as trails: disease duration ten years, diabetic nephropathy retains renal function (33 patients) and renal impairment (32 patients), permanent normal blood and urine tests over 10-20 years 64 patients, lipid Spectrum, glycemic outline, glycosylated haemoglobin, microlamination, strawberry filtration rate (CCD-EPI), endothelin-1 level plasma, resonance, SAMD and Doppler renal vessels were studied. The eNOS3 quality was completed by Applied Biosystems 2720 (USA) utilizing test frameworks from Lightech (Russia) as indicated by the maker’s directions. STATISTICA 6 was utilized for measurable handling of materials. Information is introduced as mean qualities with standard deviations (m. SD). The Kolmogorov - Smirnov rules tried the typical dissemination. The general danger of infection in transporters of specific alleles and genotypes was determined as a marker of the extent of positivity. The OR esteem was determined to utilize online clinical insights adding machine (http://med statistic.ru/calculators.html).

Genotype share was verified for anomaly from hard balance Weinberg. The correlation coefficient was
measured utilizing the Spearman method. Differences between $P<0.05$ considered statistically significant.

RESULTS AND DISCUSSION

The frequency of alleles and genotypes of AluIns/DelI>D ACE gene polymorphism in entire analyze patients in the principal, and manageable groups are shown in Figure 1

![Figure 1: Frequency of AluIns/DelI>D polymorphism alleles and genotypes in the main and control groups of the ACE gene](image1)

According to the results obtained, the prevalence of genotypes I/I, I/D, D/D was 42.6%, 39.5%, 17.8%, and 34.5%, 46.4%, and 19.1% respectively. According to statistical calculations, there is no probability of disease development in D/D genotype carriers compared to I/I genotype carriers ($\chi^2=0.1; P=0.8; \text{OR}=0.9; 95\% \text{ CI} 0.478-1.771$). Genotype I/I was significantly higher in the control group than in the main group, at 42.6% and 34.5% respectively, and showed a protective function against disease progression by 1.4 times, but no positive difference was found ($\chi^2=1.6; P=0.2; \text{OR}=1.4; 95\% \text{ CI} 0.833-2.382$). Genotype I/D was significantly lower in the major group than in the control group by 39.5% and 46.4% respectively, and the probability of disease development was not observed ($\chi^2=1.1; P=0.3; \text{OR}=0.7; 95\% \text{ CI} 0.452-1.266$).

Genetic testing of alleles and genotypes of polymorphic marker AluIns/DelI>D on the ACE gene was compared with the main and control groups, and the probability of functional unpleasant allele D in the main group was not reliable $\text{OR}=0.8$ ($95\% \text{ CI} 0.57-1.18$), ($P>0.2$). The probability of participation of mutational homozygous DD-genotype, also causing the disease, was not found $\text{OR}=0.9$ ($95\% \text{ CI} 0.47-1.77$), ($P>0.8$). In addition, the heterozygous I/D genotype has no probability of $\text{OR}=0.8$ ($95\% \text{ CI} 0.45-1.26$), ($P>0.3$).

Similarly, the eNOS3 gene is shown in the eNOS3 gene and the frequency of the genotype and the genotype Figure 2 in all patients and control group

![Figure 2: Frequency of alleles and genotypes of eNOS3 gene polymorphism T-786S in all patients and control group](image2)

In the research, we studied the distribution of genotypes and alleles of the AluIns/DelI>D polymorphic marker of the ACE gene in primary and control patients. The prevalence of the allele of I Polymorphism AluIns/DelI>D of ACE gene in the central and control groups studied was 62.4% and 57.7% respectively. The prevalence of the adverse allele D was 37.5% and 42.3%, respectively. (Villeneuve et al., 2014)

According to statistical calculations, allele D carriers compared to allele I carriers have no probability of disease development ($\chi^2=1.1; P=0.3; \text{OR}=0.8; 95\% \text{ CI} 0.57-1.188$). Allelic I ($\chi^2=1.1; P=0.3; \text{OR}=1.2; 95\% \text{ CI} 0.842-1.755$) indicates that it has a protective effect on the disease, but no reliable difference has been found ($\chi^2=1.1; P=0.3; \text{OR}=1.2; 95\% \text{ CI} 0.842-1.755$).
These data and the consequences of our study lead us to the conclusion that the ENOS3 gene plays an important role in the DNA development of patients with type 2 diabetes in Uzbekistan (Uryasiev and Shakhanov, 2017). Consequent from the main and control rally showed that the distribution rates of the TT, TC, and CC genotypes were 50.3%, 39.5%, 10%, and 62.7%, 33.6%, and 3.6%, respectively. According to statistical calculations, this disease of CC genotype carriers is 2.9 times more common than that of TT genotype carriers, and the difference between them has real statistical significance ($\pi^2 = 3.7; \ p = 0.05; \ or = 2.9; \ 95\% \ 0.9392\text{-}9.3906$). The TT genotype was significantly lower in the main team than in the control team, was 50.3%, 62.7%, and showed a function protector against disease advancement ($\pi^2 = 3.7; \ p = 0.05; \ or = 0.6; \ 95\% \ CI \ 0.3594\text{-}13232$), was significantly lower in the dominant team than in the genotype TT control team. Genotype was less influential group than TC control group, 39.5% and 33.6%, and did not play a significant role in the development of pathology ($\pi^2 = 0.9; \ p = 0.3; \ or = 1.29); \ 95\% \ CI \ 0.7592\text{-}1919)$.

In our knowledge, we have shown a link between Inos3 gene C-light (CC genotype) infection among type 2 diabetes mellitus and diabetic nephropathy patients. The results are consistent with the information of local and foreign authors. Analysis of 32 research results published before 2016 according to a meta-analysis, three NOS3 polymorphisms link to DNA development were establish: /B/A, T-CC6C and G97T. Polymorphism 4B/A and T-786666C6666C showed a reliable correlation with all genetic models ($= 12.177$ and $11.1-11.50$). The data and the consequences of our study lead us to the conclusion that the ENOS3 gene plays an important role in the DNA development of patients with type 2 diabetes in the Uzbek country. (Villeneuve et al., 2014)

CONCLUSIONS

The research has shown that the functionally unfavourable polymorphic marker T-786S of the Inos3 gene and the alleles of mutant homozygous CC genotypes tend to develop DNA, as well as the protective nature of T-allele and TT genotypes. Consequently, the alleles and genotypes of the polymorphic marker AluIns / Dell>D of the ACE gene did not show any predisposition to the disease in the primary and control groups. However, the genotypes of polymorphic marker AluIns / Dell>D of the ACE gene showed a shielding effect in the unfavourable manifestation of eNOS3 gene in the progression of DN in patients with diabetes mellitus type 2 of the Uzbek population.

ACKNOWLEDGEMENT

The author would like to thank the Dean of the medical research paper, medical department of Russia

Funding support

The authors declare that they have no funding support for this study

Conflict of interest

The authors declare that they have no conflict of interest for this study.

REFERENCES


Hana, T. 2011. Association between Apolipoprotein E-polymorphism and Ischemic Heart Disease Patients With or Without Type 2 Diabetes Mellitus: A Preliminary Study in Kuwait- Al-M. T. Hana. Archives of Iranian Medicine, 14:385–388.


