

STUDY OF THE SPREAD OF G-308A POLYMORPHISM OF THE TNF- α GENE IN THE DEVELOPMENT OF CHRONIC GLOMERULONEPHRITIS IN THE UZBEK POPULATION

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Abstract

Chronic glomerulonephritis (CGN) is a complex immunoinflammatory disease of the renal glomeruli, which develops in the body with prolonged inflammation, autoimmune reactions, and the participation of a number of genetic factors. Since CGN does not show clinical signs for a long time and can only be detected through laboratory tests, it belongs to the category of "silent" diseases. However, over time, it leads to a progressive decrease in kidney function, and as a result, to chronic renal failure. Currently, CGN is in the center of special attention as the main cause of renal failure. Thanks to research in the field of molecular genetics in recent years, it has been established that genetic factors, in particular, the polymorphism of some genes, play an important role in the pathogenesis of CGN. In particular, the TNF- α gene (tumor necrosis factor alpha) plays an important role in the inflammatory and immune response.

Keywords: Chronic glomerulonephritis, chronic kidney disease, TNF- α (tumor necrosis factor alpha).

Introduction

The role of the gene TNF- α in the development of chronic glomerulonephritis

The TNF gene encodes the production of Tumor Necrosis Factor- α (TNF- α), one of the main cytokines. TNF- α is a strong inflammatory agent and participates in the early stages of the immune response. It affects the following processes in the body:

Stimulation of inflammation: TNF- α causes an exacerbation of inflammation by involving inflammatory cells in the walls of blood vessels or tissues.

Glomerular damage: Damage to the tissues of glomeruli in the kidney, disrupting their filtration function.

Intensification of fibrous processes: Decreases kidney function by accelerating fibrous processes in kidney tissues.





TNF- α gene polymorphism and development of CGN

Polymorphisms in the G/A TNF- α gene, especially the -308 G/A polymorphism, can contribute to the acceleration of chronic inflammatory processes. This polymorphism causes increased production of the cytokine TNF- α , which exacerbates inflammation and leads to damage to the glomerular tissue.

Also, high TNF- α production leads to faster impairment of renal function and an increased risk of renal failure associated with CGN. Certain variants of the TNF- α gene polymorphism, including the G allele, are considered as a factor accelerating the progression of kidney disease.

Prognostic significance of the TNF- α gene

In chronic glomerulonephritis, the polymorphism of the TNF- α gene can accelerate inflammatory processes and lead to a more severe course of the disease. A high level of TNF- α may be associated with a faster progression of the disease, a poor prognosis, and decreased renal function. Thus, the TNF- α gene can be used as a genetic marker to improve the prognosis of CGN and develop personalized therapy methods [10, 11].

Purpose of the study

The main objective of the study was to study the genotypes of the TNF- α (G-308A) gene in mixed and nephrotic forms of chronic glomerulonephritis and to analyze their distribution.

Materials and methods

The study was conducted in the Department of Nephrology of the Multidisciplinary Clinic of the Tashkent Medical Academy. A total of 80 patients diagnosed with CGN participated. Patients were divided into two groups as follows:

1st group - patients with CGN (n=80);

2nd group - Control group (n=125).

The age of the participants was in the range of 18-60 years, the average age in group 1 was 40.6 ± 12.35 years, and in group 2 39.7 ± 6.52 years. All participants were born in Uzbekistan and do not have any family ties.

Patients underwent the following examinations: SMAD, general urine analysis, biochemical blood tests (creatinine, total protein, albumin, cholesterol), 24-hour proteinuria, microscopic hematuria, molecular genetic studies.

DNA was isolated from the venous blood of patients using the standard phenol-chloroform method. Genotyping was performed for the following gene: TNF- α (G-308A). Genotyping was performed using the polymerase chain reaction (PCR). PCR products were visualized by agarose gel electrophoresis.

The obtained results were analyzed using Microsoft Excel and SPSS 23.0. The frequency of genotypes was expressed as a percentage. For quantitative indicators, the median (Me), the interval of quartiles (Q25-Q75) were calculated. The difference between the groups was assessed using the Mann-Whitney test, the value of $p < 0.05$ was considered statistically significant.



Results Analysis

In this study, the distribution of alleles and genotypes of the G-308A gene in the TNF- α gene in patients with chronic glomerulonephritis was analyzed. The control group consisted of individuals without chronic glomerulonephritis. Below are the results obtained for the gene.

The role of the G-308A polymorphism of the TNF- α gene in the development of chronic glomerulonephritis was studied. The prevalence of the original G allele in the studied main and control groups was 81.3% and 89.3%, respectively. The frequency of the functionally unfavorable A allele was 18.8% and 13.1%, respectively. According to the statistical report, carriers of the A allele were 1.57 times more likely to develop the disease than carriers of the G allele, but did not have a reliable significance ($\chi^2=2.25$; $p=0.134$; OR=1.57; 95%CI 0.91-2.71). The original G allele ($\chi^2=2.25$; $p=0.134$; OR=0.64; 95%CI 0.37-1.10) showed protective effectiveness in relation to the development of the disease, but this also did not have reliable significance ($p=0.134$).

According to the results obtained from the main and control groups, the prevalence of the GG, GA, and AA genotypes was 66.3%, 30.0%, 3.7%, and 78.7%, 21.3%, and 2.46% respectively. According to statistical analysis, carriers of the AA genotype had a 1.58 times higher predisposition to the development of the disease compared to carriers of the GG genotype, and the difference between them was not statistically significant ($\chi^2=0.018$; $p=0.893$; OR=1.58; 95%CI 0.31-8.05). The original GG genotype was less common in the main group than in the control group, amounting to 66.3% and 78.7%, respectively, and did not indicate a predisposition to the development of the disease, but the difference between them was not significant ($\chi^2=2.23$; $p=0.135$; OR=0.59; 95%CI 0.32-1.0). The GA genotype was more common in the main group than in the control group and amounted to 30% and 21.3%, respectively, and the probability of disease progression was 1.63, but the difference between them was not significant ($\chi^2=1.77$; $p=0.184$; OR=1.63; 95%CI 0.86-3.11) (Table 1).

Table 1 The frequency of the G-308A marker genotype of the TNF- α gene in the main and control groups.

Alleles and genotypes	Number of tested alleles and genotypes				χ^2	p	RR	OR	95%CI
	Main group		Control group						
	n=80	%	n=125	%					
G	130	81,3	218	89,3	2.25	0.134	0.93	0.64	0.37-1.10
A	30	18,8	32	13,1	2.25	0.134	1.46	1.57	0.91-2.71
G/G	53	66,3	96	78,7	2.23	0.135	0.86	0.59	0.32–1.10
G/A	24	30	26	21,3	1.77	0.184	1.44	1.63	0.86–3.11
A/A	3	3,75	3	2,46	0.018	0.893	1.56	1.58	0.31–8.05

Conclusions:

It was established that the G allele and the GG, GA genotype in the G-308A polymorphism of the TNF- α gene are significantly associated with the development of the disease, but did not have reliable significance. Therefore, the work that still needs to be done in this direction is one of the important tasks facing medical workers. In the future, it is proposed to use biomarkers that determine





individual therapy and disease prognosis based on these genetic markers. In addition, the study of polymorphisms of other inflammatory and immune genes allows for a deeper understanding of the pathogenesis of CGN.

REFERENCES

1. Исломов М. и др. Сурункали буйрак касалликларини даволашда антиоксидант препаратлардан фойдаланиш //СТУДЕНЧЕСКИЙ ВЕСТНИК Учредители: Общество с ограниченной ответственностью" Интернаука". – 2022. – С. 57-61.
2. Мирзаева, Ш. Х., Жаббаров, О. О., Максудова, М. Х., Турсунова, Л. Д., & Жуманазаров, С. Б. (2022). Сурункали буйрак касаллиги бўлган беморларда кардиоренал синдромни даволаш.
3. Турсунова Л. Д. и др. Кардиоренал синдромда ангиотензин-неприлизин рецепторлари ингибиторларининг буйрак функционал ҳолатига таъсири. – 2022.
4. Umarova Z. F. et al. Quality of life in patients with chronic kidney disease in the V stage receiving program hemodialysis and possible ways of its correction //Journal of Medicine and Innovations. – 2024.
5. Sultonov P. I. et al. EFFECT OF ARTIAGREGANT THERAPY ON KIDNEY FUNCTIONAL RESOURCES IN CHRONIC DISEASE //Theoretical aspects in the formation of pedagogical sciences. – 2023. – Т. 2. – №. 5. – С. 137-138.
6. Рахматов, А., Жаббаров, О., Қодирова, Ш., Жуманазаров, С., Мирзаева, Г., & Тожибоев, М. С. (2022). Подаграда буйраклар зарарланишининг клиник ва генетик хусусиятлари.
7. Qizi, N. N. O., Atakhanovich, J. A., Fahriddinovna, A. N., & Xayotjonovna, M. D. (2020). Lupus Nephritis In Systemic Lupus Erythematosus. The American Journal of Medical Sciences and Pharmaceutical Research, 2(10), 145-150.
8. Nazarova, N., & Jabbarov, A. (2020). STUDY OF KIDNEY DAMAGE SIGNIFICANCE OF APOL1 G1/G2 and HAS2 GENE POLYMORPHISM IN SYSTEMIC LUPUS ERYTHEMATOSUS IN THE UZBEK NATION. Материали конференцій МЦНД, 54-55.
9. Сапарбаева, Н. М., Жаббаров, О. О., & Собиров, М. О. (2017). Состояние биоценоза кишечника у больных с хронической болезнью почек II-III стадии. Биология и интегративная медицина, (2), 18-33.
10. Jabbarov, O. O., Maksudova, M. H., Mirzayeva, G. P., & Rakhmatov, A. M. (2023). The Relationship of Blood Group with Human Diseases. Web of Semantic: Universal Journal on Innovative Education, 2(3), 331-334.
11. Zhumanazarov, S. B., Jabbarov, A. A., Mirzoeva, G. P., & Eshonov ShN, B. M. (2021). Prognostic significance of clinical and pathogenetic features of the development of chronic kidney disease due to glomerular diseases. Central Asian Journal of Medical and Natural Sciences, 2(2), 175-184.

