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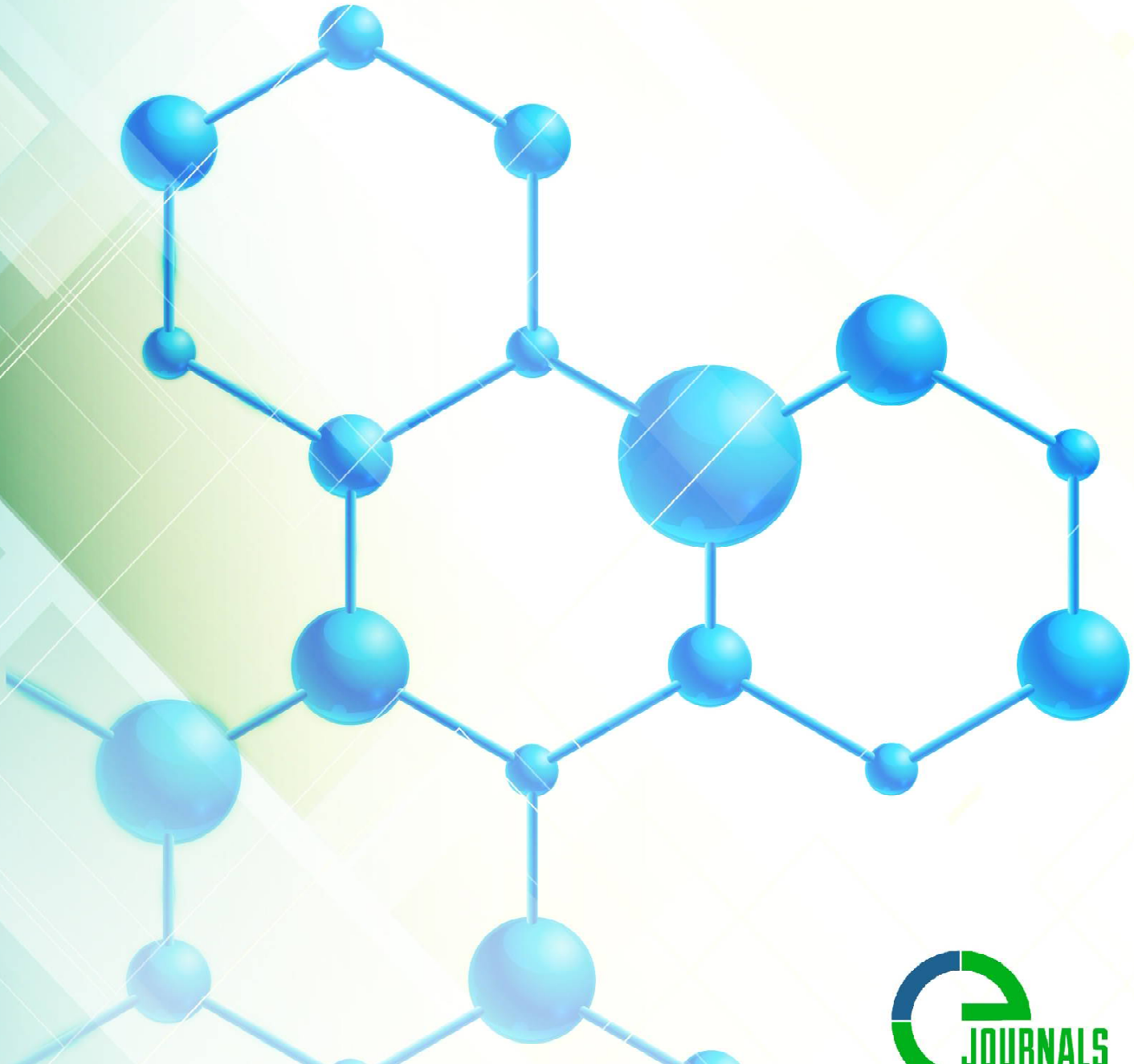

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Features of the distribution of allelic polymorphisms of inflammatory (TNF (G308A), IL2 (T330G), IL6 (C174G), IL10 (C592A)) cytokine genes in pyoinflammatory diseases of the middle ear

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Abstract: We have studied the results of the distribution of single nucleotide polymorphisms of the inflammatory cytokine genes TNF (G308A), IL2 (T330G), IL6 (C174G) and IL10 (C592A), which are currently common among the population of the Republic of Uzbekistan, involved in the processes of inflammation initiation in individuals with inflammatory diseases. diseases (n=87) and in healthy people without inflammatory diseases (n=71), we conducted a study aimed at studying the characteristics of the distribution. In the studied groups, all genotypic variants of the studied genetic polymorphisms (TNF (G308A), IL2 (T330G), IL6 (C174G), IL10 (C592A)) were analyzed for compliance with the Hardy-Weinberg equilibrium (RHB, p>0.05).

Keywords: chronic suppurative otitis media, allelic polymorphisms of inflammatory cytokine genes, genetic polymorphism

Relevance: Chronic inflammation of the middle ear, despite significant progress in prevention, diagnosis and treatment, remains one of the most common and dangerous childhood diseases. This is due to many medical and social reasons, as well as such adverse effects as hearing loss and the risk of intracranial complications caused by exacerbations of a chronic process in the middle ear. The modern definition of chronic purulent otitis media (CHSO), summarizing the main features of this disease, was given by V.T. Palchun et al . [one]. CHSO is a chronic purulent inflammation of the middle ear that occurs with persistent perforation of the tympanic membrane, persistent or recurrent suppuration from the ear, and hearing loss of varying degrees, gradually progressing with a long course of the disease [1, 2]. In addition, to date, CHSO is also dangerous as a source of formidable intracranial complications (mastoiditis, meningitis, brain abscess, sinus thrombosis).

Objectives: to study the distribution of single nucleotide polymorphisms of the inflammatory cytokine genes TNF (G308A), IL2 (T330G), IL6 (C174G) and IL10 (C592A),

Materials and methods: We examined persons with inflammatory diseases of the middle ear (n=87) and persons without inflammatory diseases (n=71), we conducted a study aimed at studying the distribution of polymorphic genes.

In the studied groups, all genotypic variants of the studied genetic polymorphisms (TNF (G308A), IL2 (T330G), IL6 (C174G), IL10 (C592A)) were analyzed for compliance with the Hardy-Weinberg equilibrium (RHB, p>0.05).

Results: With regard to the distribution of the proportions of the genotypes of the single nucleotide polymorphic gene TNF-? (G308A) in the general group of patients (group I), it was found that H o - observed frequencies of G / G and G / A genotype variants were 0.87 and 0.13, while their values H e - expected frequencies corresponded to 0.88 and 0.12, respectively. Along with this, o and H e frequencies of the mutant A/ A genotype were equal to zero. A similar statistical analysis carried out among patients with mild purulent-inflammatory diseases of the middle ear (group II) made it possible to determine the frequency distribution of the genotypes of the single-nucleotide polymorphic gene TNF-? (G308A) without deviations from RCM (p>0.05).

An analysis conducted among patients with moderate purulent-inflammatory diseases of the middle ear (group III) also showed that the frequency distribution of the genotypes of the single-nucleotide polymorphic gene TNF-? (G308A) corresponded to RCM (p>0.05).

Namely, for G / G and G / A genotypes H o amounted to 0.84 and 0.85 with their values of H e equal to 0.16 and 0.14, respectively (? 2 =0.37; P=0.52; df =1) . In this case, the heterozygosity index (D) between the expected and observed heterozygosity in group III patients (H o =0.16 and H e =0.14 at D = 0.09) and healthy (H o = 0.13 and H e = 0.12 at D = 0.07) also had insignificant differences, which may be due to a smaller sample of patients compared to the control.

In the IV group of healthy individuals studied, the differences between the H o and H e frequencies of the genotypic variants T/T (H o =0.73 and H e =0.73), T/ G (H o =0.24 and H e = 0.25) and G / G (H o =0.03 and H e =0.02) for the single nucleotide polymorphic gene IL2 (T330G) also corresponded to RHV (? 2 =0.18; P=0.643; df =1). (see Table 4.2).

In this regard, the study of the features of the distribution of the single nucleotide polymorphic gene TNF-? (G308A) and its contribution to the development of pyoinflammatory diseases of the middle ear in Uzbekistan seemed interesting and necessary. The given values in the general group of patients (group I) and the control group (group IV) show the correspondence of the frequencies of occurrence in them of alleles (G and A) and genotypes (G / G and G / A) for the TNF polymorphic gene (G308A), which indicates about the absence of the contribution of the studied gene in the mechanisms of formation of purulent-inflammatory diseases of the middle ear in general . Further, it seemed interesting to study the distribution of alleles and genotypes for the TNF-? (G308A) polymorphic gene among patients depending on the severity of the disease. So, in group II (n = 36) patients with a mild course of the disease, compared with groups I and IV , the proportion of the main allele G increased to 95.8% (n =69), while the minor allele A, on the contrary, decreased to 4.2% (n =3). With these characteristics, there is an increase in the proportion of the main G/G genotype by 91.7% (n=33), and the proportion of the heterozygous G/A genotype decreased by 8.3% (n=3). Thus, according to the results of the analysis, the genotypic variants of the polymorphism and the allele of the TNF-A gene (G308A) have the same frequency in the general group of patients and in the group of healthy people, and a low frequency is also known. Thus, analyzing the results of studying the distribution features in the frequencies of occurrence of alleles and genotypes according to the polymorphism of the TNF-? (G308A) gene among the studied groups of patients with purulent-inflammatory diseases of the middle ear and healthy ones, their identical carriage was found in the general group of patients (I group) and healthy (group IV), which was naturally characterized by the absence of statistically significant differences in their proportions (for allele A and for genotype G / A - ? 2 <3.84; P=0.99).

When analyzing the results of the carriage of alleles and genotypes for the polymorphic IL2 gene (T330G) between the general group (group I) and healthy (group IV), revealed a clear tendency to increase the frequency of the minor allele G among patients by 1.6 times (21.8% vs. 14.8%; ? 2 =2.6; P=0.2; O R =1.6; 95% CI: 0.9-2.89) compared with healthy ones, which indicates an increased risk of pyoinflammatory diseases of the middle ear among carriers of the minor allele G for the polymorphic gene IL2 (T330G) by 1.6 times Thus, analyzing the results of a comparative assessment of differences in the frequency distribution of alleles and genotypes of the single-nucleotide polymorphic IL2 gene (T330G) in groups of patients with pyoinflammatory diseases of the middle ear and healthy people, it was found that the carriers of the G

allele of the minor gene of the IL2 polymorph (T330G) had 1 .6 times (?2=2.6? R=0.2), and the heterozygous T/G genotype increases the risk of the disease by 1.5 times (?2=1.3? R=0.3).).

Characterization of single nucleotide polymorphism IL6 (C174G) in patients with purulent inflammation of the middle ear and its role in the mechanisms of the disease formation. When comparing the results, the minor allele G was 1.2 times (25.4% vs. 28.2%; ?2=0.3? R=0.6; OR=1.2; 95% CI: 0.7-1 ,91) more often among patients than among healthy people, but statistical analysis revealed this difference in its indicators, which does not differ from a reliable amount. Thus, analyzing the results of studying the distribution of the frequencies of occurrence of alleles and genotypes for the polymorphic gene IL6 (C174G) among the studied groups of patients with purulent-inflammatory diseases of the middle ear and healthy people among carriers of the heterozygous C/ G genotype , a tendency to an increase in the risk of purulent- inflammatory diseases was found. diseases of the middle ear of the lung course 1.5 times (? 2 =1.1; P=0.3) compared with the control and 2.4 times (? 2 =3.8; P=0.1) compared with the moderate and severe course of the disease, as well as among carriers of the mutant genotype G / G revealed a tendency to increase the probable risk of pyoinflammatory diseases of the middle ear with moderate and severe course compared with the control 2.2 times (? 2 =1.5; P=0.3). These differences are likely to be statistically significant. In this regard, the S/G and G/G genotypes of the polymorphic IL6 gene (C174G) can be considered as genetic predictors of a high risk of pyoinflammatory diseases of the middle ear in Uzbekistan.

Characterization of single nucleotide polymorphism IL10 (C592A) in patients with purulent inflammatory disease of the middle ear and its role in the mechanisms of the formation of the disease showed that single nucleotide polymorphism IL10 (C592A) was observed in patients of group I with purulent inflammatory disease. of the middle ear and healthy people in the control group A molecular genetic study of the gene made it possible to establish the presence of differences in the distribution of its allelic and genotypic variants. If the relative frequency of major alleles C and minor alleles A was determined in 83.1% (n=118) and 16.9% (n=24) of cases in the control group of healthy people, then the percentage of carriage of the major allele S decreased to 75.9% (n = 132) in patients of group I, while the percentage of the minor allele A increased by 24.1% (n = 24). Thus, analyzing the results of studying the distribution features in the frequency of occurrence of alleles and genotypes of the IL10 gene polymorphism (C592A) among the studied groups of patients with purulent-inflammatory diseases of the middle ear and healthy people, it was found that the minor allele A may contribute to the initiation of inflammatory processes that implement the onset of purulent-inflammatory diseases of the middle ear, increasing the risk of their development in general by 1.6 times (? 2 =2.5; P=0.2).

Conclusions : It was found that the A minor allele (?2=4.3? R=0.05) is associated with an increased risk of mild purulent-inflammatory diseases of the middle ear. In addition, three genotypes (S/S - ?2=3.2, R=0.1; A/G - ?2=1.3, R=0.3; OR=1.7; A/ A - ?2= 1.9, R=0.2) IL10 (C592A) It has been established that the risk of developing a mild course of the disease increases the polymorphic gene.

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