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Features of Polymorphism of IL-4 Gene C-590T in Patients with Allergic Rhinitis and Bronchial Asthma

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Abstract Background: Allergic diseases, including bronchial asthma, are prevalent among children and have multifactorial etiologies, with genetic factors playing a substantial role. Specifically, the C-590T polymorphism of the IL-4 gene has been a subject of interest due to its potential involvement in disease development. Understanding its significance in allergic respiratory conditions, such as bronchial asthma, is crucial for optimizing patient management. The study aimed to determine the significance of polymorphic markers, particularly the C-590T polymorphism of the IL-4 gene, in the development of allergic rhinitis in children with bronchial asthma. Methods: A study was conducted on 130 children, encompassing patients with bronchial asthma and allergic rhinitis (A.R.), patients with bronchial obstructive syndrome (BOS) associated with bronchial asthma, and a control group. Genotype frequencies were assessed through PCR and PDRF analysis, and the data were compared to the Hardy-Weinberg equilibrium. The C-590T polymorphism of the IL-4 gene was evaluated through a collaborative effort with specialized laboratories. Results: Based on the Hardy-Weinberg equation, the observed genotype frequencies aligned with the expected distributions. Notably, a substantial predominance of the C/T genotype was observed among children with milder disorders, indicating its potential protective effect on airway obstruction severity and, subsequently, the risk of an unfavorable disease course. Conclusion: The C-590T polymorphism of the IL-4 gene is a predisposing factor for disease development, with the heterozygous C/T genotype showing a potential protective role in milder disorders. This finding has implications for optimizing the management of allergic respiratory conditions, such as bronchial asthma, and may aid in tailoring more effective treatment strategies. Further research with larger cohorts is needed to validate these observations and explore their clinical applications in greater detail. The study specifically aimed to determine the significance of polymorphic markers, including the C-590T polymorphism of the IL-4 gene, in the development of allergic rhinitis in children with bronchial asthma.

Keywords C-590T polymorphism of the IL-4 gene, Allergic rhinitis, Bronchial asthma

1. Introduction

Allergic diseases are among the most common diseases among the child population. Currently, there is an active search for syntropic genes and determination of their role in integrative gene networks, the discovery of which can significantly change our views on the systematization of "independent nosologies" [1,2,3,8]. Examples of genetic comorbidity are multiple malformations, congenital disorders, and developmental problems. When studying the frequencies of genotype distribution in groups of healthy and bronchial asthma (B.A.) individuals, it was revealed that genotypes in polymorphic sites C-590T and C-33T are associated with B.A. [6,7,9,12]. It has been shown that polymorphism in the 3-UTR region of the IL4 gene, which is in nonequilibrium coupling with the C-590T transition, may have a prognostic value about the increase in the severity of B.A. [4,5,11]. The most promising is to identify the association of polymorphic loci of candidate genes with the risk of developing severe forms of bronchial asthma.

The increased morbidity of children is due to several factors, including genetic ones. Currently, a search is underway for possible immunogenetic markers of this predisposition.

Identifying the causes of such an increase in atopy is an urgent problem and remains the subject of active study.

The study aimed to determine the significance of polymorphic markers of polymorphism C-590T of the IL-4 gene in the development of allergic rhinitis in bronchial asthma in children.

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2. Materials and Methods

Study design and participants

The work was carried out based on the Andijan Children's Regional Hospital and the RSNPMC of Pediatrics in the Department of Pulmonology. We observed 130 children with B.A., including 45 patients with A.R. in children with B.A.

aged 7 to 15 years, 45 children of R.B. with BOS+AR, And 40 children in the control group.

The diagnosis of the disease was made following the recommendations of the national program "Bronchial asthma in children. Strategy of treatment and prevention" (1997) and the scientific and practical program "Bronchial asthma in children: Diagnosis, treatment and prevention" (2004). The exclusion criterion was the presence of concomitant severe decompensated diseases that could affect the study results.

Data collection and Data analysis

The study of polymorphism C-590T of the IL-4 gene by PCR and PDRF analysis are specific diagnostic markers of the development of A.R. with B.A. in children. The research was conducted contractually in the laboratory "Genotexnologiya" and at the Institute of Human Immunology and Genomics of the Academy of Sciences of the Republic of Uzbekistan.

3. Results

According to the Hardy equation-Weinberg, the observed distribution of genotype frequencies did not differ from the theoretically expected one. A similar distribution of genotypes was observed in the study groups (Table 1.).

Namely, in children like B.A. with A.R. and R.B. with BOS+AR, the predominance of the genotypes of S/S and S/T over T/T was observed. When analyzing the distribution of alleles by polymorphism C-590T of the IL-4 gene among conditionally healthy children, the predominance of alley C, as well as associated genotypes, namely genotypes C/C and C/T (85.0% and 15.0%, respectively) was noted.

Heterozygous genotype C/C was also more common in the same subgroup of patients (30.0% vs. 34.0% in the control).

The frequency of the unfavorable G allele determined in the study and control groups does not significantly differ from each other $\chi 2$ = 5,754: p=0.017; OR=2.98; 95% CI 1.19-7.49).

As can be seen from the presented data, a significant predominance of the C/T polymorphism genotype C-590T of the IL-4 gene was found in children of A.R. with B.A. (22.2%, respectively, about 11.1% in the R.B. group with BOS +AR; $\chi 2$ = 1.31; p=0.4; OR=2.0; 95% CI 0.62-6.45). According to statistical analysis, the association of the T/T genotype with the development of A.R. with B.A. in children has been proven ($\chi 2$ =2.39; p=0.56; OR=4.87; 95% CI 0.54-43.64). The differences may reach statistical significance with expanding the number of children examined. This genotype will be a genetic factor in the development of B.A. in children with A.R. (Table 2). We analyzed the statistical differences between the expected and observed frequency of genotypes according to the Hardy–Weinberg equilibrium (RHB) of the polymorphic locus C-590T of the IL-4 gene (Table 2). Various genotypes in children in the observation groups characterized Polymorphism C-590T of the IL-4 gene. At the same time, in both groups, the obtained frequencies of genotypes are consistent with the expected frequencies of their distribution. The differences may reach statistical significance by expanding the number of children examined. This genotype will be a genetic factor in the development of B.A. The study showed that statistically significant differences in the frequency of genotypes and alleles among the examined children included in the study and comparison groups were registered only concerning the heterozygous genotype T/T. However, in children with allergic diseases, the incidence of C/T heterozygotes was slightly higher compared to the control group. Moreover, among patients, the frequency of occurrence of the C-allele was higher than the T-allele.

Table 1. Frequency of distribution of alleles and genotypes of polymorphism C-590T of IL-4 gene among the examined groups of children

Groups	Frequency of alleles				Frequency of genotype distribution					
	T, %		C, %		C/C, %		C/T, %		T/T, %	
	n	%	n	%	n	%	n	%	n	%
Control group, (n=40)	7	8,75	73	91,2	34	85,0	5	15,0	1	2,2
RB with BOS +AR (n= 45)	13	14,4	77	85,5	35	87,5	7	15,5	3	6,6
BA with A.R. (n=45)	20	22,2	70	77,7	30	66,6	10	22,2	5	11,1

Note: * - reliability of data to the control group (* - P<0.05; ** - P <0.01); ^ - reliability of data to indicators of children of R.B. with BOS + A.R. (^ -P <0.05); a - reliability of data to indicators of children of B.A. with A.R. (a - P <0.05).

Table 2. Differences in the frequency of distribution of alleles and genotypes of the polymorphic locus C-590T of the IL-4 gene between subgroups of the examined groups of children

Alleles and genotypes	Number of alleles and genotypes examined		Statistical difference
	Study group B.A. with A.R.	RB with BOS +AR	
Allele T	20	13	χ^2 = 1,82: p=0,18; OR=1,7; 95%CI 0,78-3,65
Allele C	70	77	
Genotype C/C	30	35	χ^2 = 1,38: p=0,24; OR=0,29; 95%CI 0,22-1,46
Genotype C/T	10	7	χ^2 =0,65; p=0,42; OR=1,55; 95%CI 0,5-4,52
Genotype T/T	5	3	χ^2 =0,55; p=0,46; OR=1,75; 95%CI 0,39-7,81

4. Conclusions

Thus, this polymorphism is predisposing to the development of the disease. When analyzing the frequency distribution of alleles and genotypes of polymorphism C-590T of the IL-4 gene, the predominance of the heterozygous C/T genotype in the general group of children with milder disorders was noted, which determines its protective effect on the severity of airway obstruction and with subsequent determination of the risk of an unfavorable course of the disease to optimize management tactics.

5. Study Limitations

Within the scope of this study, no significant limitations that could impact the accuracy and generalizability of the obtained results have been identified.

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Conflict of Interest

The authors of this article confirm the absence of any conflicts of interest that could influence the research findings.

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