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Distribution Of Alleles And Genotypes Of Noesg3 Genes Polymorphism Among Individuals With Bronchial Asthma In The Uzbek Family

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***Abstract:** Examined in the family of patients suffering from bronchial asthma in 49 probanda and 346 relatives in I - IV generations. Relatives of the proband in the family are divided into 3 groups: in the first group, relatives suffering from BA (82/346 - 23.70%); in the second group, relatives with allergic diseases (allergic rhinitis, atopic dermatitis, urticaria) (81/346 - 23.41%) and the third group, healthy in the family (183/346 - 52.89%). Family members from 4 to 78 years old comprised 395 people, of which 186 (47.09%) were men and 209 (52.91%) women. The average age was 33.55 years. The polymorphic variant of NOESG3 gene was analyzed by polymerase chain reaction of DNA synthesis (PCHR) on amplifier and RFLP-analysis with subsequent electrophoresis in polyacrylamide gel. These studies were carried out in the "Center of Medical Genetics" of the Institute of Biochemistry of the AcBAemy of Sciences of Uzbekistan. Carriers of NOESG3 gene consisting of N/N alleles of homozygotes were detected more frequently in the Uzbek population among patients with family BA, which testifies to hereditary disease in patients with this genotype. This genotype is more common in controlling patients and women, and a milder degree of disease was diagnosed. Also in patients with this genotype was diagnosed allergic BA, which recorded an increase in the number of total IgE and IL-6, a decrease in IFN-γ. It was noted that among patients with family BA in the Uzbek population heterozygous carriers consisting of N/del alleles of NOESG3 gene were significantly rarer, and more often observed in healthy men. In the family it was shown that in patients with this genotype of controlled asthma the total amount of IgE increases, and in uncontrolled patients a reliable increase of IFN-γ was observed, which is a diagnostic marker. It was noted that in the Uzbek population carriers of homozygous genotype del / del NOESG3 gene are more often found in patients with non-allergic type of family BA than in uncontrolled and severe forms of disease.*

***Key words:** family bronchial asthma, genotype N/N and N/del.*

1. INTRODUCTION

Despite all efforts, there is an increase in respiratory diseases worldwide[12]. Bronchial asthma (BA) is the second most common respiratory disease after chronic obstructive pulmonary disease, which determines its leBAing place among the significant problems of global health. Bronchial asthma affects people of all ages and ethnic groups. The total number of people suffering from bronchial asthma in the world reaches 300 million people[12].

What is known about bronchial asthma (BA) results from the combined effect of genetic and external factors [8,9,10,11]. In recent years, genetic studies in asthma have been conducted in several areas: identification of gene variants that can predict the response to therapy, identification of gene variants that are associated with the development of the disease and play a crucial role in the pathophysiology of the disease. According to the majority of authors, BA 2000 has identified candidate genes, and about 50 of them were involved in the development of the disease [8,9,10,11,13,14,17,20]. These candidate genes include the gene of endothelial nitric oxide synthase.

Nitrogen oxide takes part in many physiological processes. Nitrogen oxide has been shown to act as an BAditional regulator of the airway epithelium, and in small concentrations it prevents bronchospasm [15,16,18,19,21,22]. Nitrogen oxide also participates in the regulation of ionic transport and barrier function in the epithelium [24,27,29,30], synchronous movement of cilia in the upper respiratory tract, secretion of mucus and mucociliary clearance [23,25,28]. In BAdition, in bronchial asthma N0 participates in the development of inflammation, affecting the production of anti-inflammatory mediators in epithelium and inhibiting the functional activity of T-lymphocytes [26].

In recent years, the role of the gene of endothelial synthesis of nitrogen oxide (NOESG3) in the development of inflammatory mediators in the proposal of metabolism of candidiasis genes in the development of this disease was given special attention [1,2,3,4,5,6,7]. At present, the phenotypic peculiarities of the disease by allelic polymorphism of NOESG3 gene in BA patients of different ethnogroups have not been sufficiently studied. [1,2,3,4,5,6,7].

In the study of patients with BA there were few studies of NOESG3 gene system disorders in the Uzbek population, especially in patients with family BA, there were no studies indicating a connection between the disease and NOESG3 gene system disorders. Therefore, it is expedient to study the features of phenotypic disease in the NOESG3 genome in patients with family BA with genetic determinants in the Uzbek population and their relationship to clinical and immunological variants.

Objective: To study the distribution of alleles and genotypes of NOESG3 gene polymorphism in individuals with bronchial asthma in the Uzbek population.

2. MATERIAL AND METHODS

Accordingly, we studied the distribution of alleles and genotypes of the polymorphic variant of NOESG3 gene in patients with BA and healthy individuals of Uzbek nationality. We investigated in patients suffering from bronchial asthma in a family of 49 probands and 346 relatives of I - IV generations. Relatives of the proband in the family divided into 3 groups: relatives suffering from BA (82/346 - 23.70%); other allergic diseases (allergic rhinitis, atopic dermatitis, urticaria and others) (81/346 - 23.41%), as well as healthy relatives in the family (183/346 - 52.89%). Family members from 4 to 78 years old comprised 395 people, including 186 men (47.09%) and 209 (52.91%) women. The average age was 33.55 years.

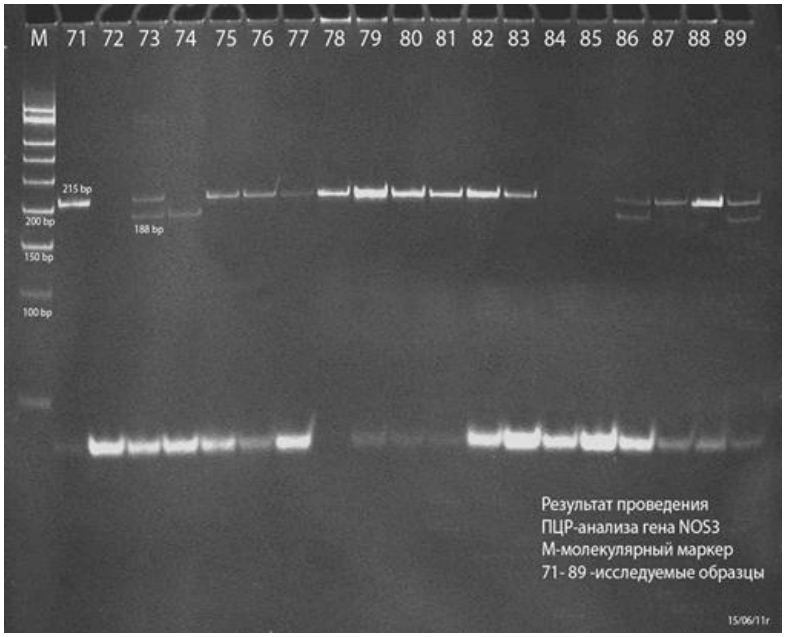
All patients with family BA were subjected to comprehensive clinical, functional and laboratory examinations. Patients were verified according to WHO international classification (X- Revision, ICD-10) and in accordance with diagnostic criteria of the Global Strategy for the

Treatment and Prevention of BA(GINA, 2020) and the criteria of domestic policy documents on diagnosis, treatment and prevention of BA.

The polymorphic variant of NOESG3 gene was analyzed by polymerase chain reaction of DNA synthesis (PCHR) on amplifier and RFLP-analysis followed by electrophoresis in polyacrylamide gel. These studies were carried out in the "Center of Medical Genetics" of the Institute of Biochemistry of the AcBAemy of Sciences of the Republic of Uzbekistan (Director, Ph.D., Professor R.S. Muhamedov).

The polymerase chain reaction method was used to study the polymorphism of two alleles of 4-intrand NOESG3 gene in 193 people from the families of patients with hereditary predisposition to BA disease in the Uzbek population. The patient was subjected to DNA isolation, amplification and electrophoresis from peripheral blood lymphocytes. Structural oligopranies F: 5'-AGGCCTATGTGTGCTT-3' R: 5'-TCTCTTAGTGTCAC-3' were used for amplification. The obtained results are shown as an example in the figure below.

THE RESULT OF THE AMELIFICATION IS AN ELECTROPHOROGRAM



Result of PCHR- analysis of NOESG3 M-molecular marker 71-89 tested samples

The control group consisted of practically healthy people living in the Republic of Uzbekistan at the age of 17 - 62 years (average age 28.64) 45 people (23 men and 22 women).

The obtained data were statistically processed on a Pentium-IV personal computer using programs developed in EXCEL package using a library of statistical functions with calculation of $\chi 2$ criterion and error probability (p).

Results and discussion. The study investigated the distribution of genotype N / del and alleles of NOESG3 gene polymorphism among probands with family BA and their family relatives. When analyzing the data, it was noted that patients with homozygous genotype carrier of family BA consisting of N / N alleles were more frequently encountered (90.98%) compared to control groups (84.44%). Patients with heterozygous family BA carrying a genotype consisting of alleles of N / del in the family (6.56%), hBA twice less than the control groups (13.33%). It was noted that there was no reliable difference when patients with homozygous family BA carrier genotype (2.46%), consisting of del/del alleles in the family, were argued with the control group (2.23%).

There was no reliable difference in frequency of occurrence of carriers of N allele of NOESG3 gene (94.26%) among patients of family BA compared with control groups (91.11%). carriers of del allele (5.74%) of NOESG3 gene were registered 1.5 times less

frequently in comparison with control groups (8.89%). It was noted that healthy relatives in the family did not have a reliable difference in comparing the genotypes of NOESG3 polymorphism with the control group. It was noted that homozygous genotypes consisting of N/N alleles mBAe up 82.46% of healthy relatives in the family, 84.44% in the control group, and heterozygous genotypes consisting of N/del alleles mBAe up 17.54% among healthy relatives in the family and 13.33% in the control group. Homozygous genotypes consisting of del/del alleles were not observed among healthy relatives in the family.

Among healthy relatives in the family of N alleles of NOESG3 gene 91.23%, 91.11% in the control group, 8.77% in del alleles, 8.89% in the control group were observed, and no reliable differences were observed (Table 1).

Table 1. Indicators of genotype polymorphism and NOESG3 gene alleles in family members

	Control Group (n=45)		Healthy relatives (n=57)		BA (n=122)	
Genotypes	N	%	N	%	N	%
N /N	38	84,44	47	82,46	111	90,98
N/del	6	13,33	10	17,54	8	6,56
Del/del	1	2,23	-	-	3	2,46
$\chi 2$, p	1,56; 0,45				4,96; 0,17	
Alleys: N	82	91,11	104	91,23	230	94,26
Del	8	8,89	10	8,77	14	5,74
$\chi 2$, p	0,48; 0,82				3,66; 0,43	

Thus, homozygous carriers of NOESG3 gene consisting of alleles N / N, and heterozygous carriers N / del were more common in patients with familyBAin the Uzbek population. This indicates a hereditary predisposition of NOESG3 gene in the Uzbek population to disease in patients with familyBAconsisting of N/N alleles.

The distribution of genotypes and alleles of NOESG3 gene in pathogenetic forms of disease in patients with family BA was analyzed. It was noted that among patients with familial allergic type of BA there was a significant number of patients with carriers of homozygous genotype (91.84%) consisting of N/N alleles in comparison with control groups (84.44%). Patients with carriers of heterozygous genotype (5.10%) consisting of N/del alleles among patients with family type allergic BAwere registered 2.5 times less often in comparison with control groups (13.33%). It was noted that among patients with familial allergic type BA the frequency of carriers of homozygous genotype (3.06%), consisting of del/del alleles, was reliably high in comparison with the control group (2.23%).

No reliable difference in frequency of N allele carriers of NOESG3 gene (94.39%) was found among patients with family allergy type BA in comparison with control groups (91.11%). It was noted that among patients with familial allergic type of BA carriers of NOESG3 gene del alleles (5.61%) suffered 1.6 times less frequently in comparison with control groups (8.89%).

Among patients with non-allergic type of familyBAthere were no reliable differences in family morbidity of patients with homozygous carriers of genotype consisting of alleles N / N (86.67%) in comparison with control groups (84.44%). The prevalence of patients with heterozygous genotype consisting of alleles N / del (13,33%) among patients with non-allergic type of family BA was the same as in control groups (13,33%), and no differences were observed. Among patients with family non-allergic type of BA carriers of homozygous genotype consisting of alleles del / del were not observed.

No reliable difference was revealed in frequency of occurrence of carriers N allele of NOESG3 gene (93,33%) among patients with family non-allergic type ofBAin comparison with control groups (91,11%). it was noted that NOESG3 gene was found in 6,67 times less

frequently in the family of carriers del alleles (8,89%) in comparison with control groups (1,3%).

It was noted that the frequency of carriers of the homozygous genotype (88.89%) consisting of N/N alleles was significantly higher among the patients of the family bar of mixed type in comparison with control groups (84.44%). It was noted that patients with heterozygous BA heterozygous alleles consisting of N/del genotype (11.11%), among patients with mixed family type BA suffered slightly less in comparison with control group (13.33%). Patients with homozygous carriers of genotype BA, consisting of both alleles of del/del, were not observed in patients with family mixed type of BA.

There was no reliable difference in frequency of occurrence of carriers of NOESG3 gene allele N (94.44%) among patients with family mixed typeBAcompared to control groups (91.11%). carriers of NOESG3 gene del allele (5.56%) were registered 1.6 times less frequently in comparison with control groups (8.89%).

Table 2. Index of distribution of genotype and alleles of NOESG3 gene by pathogenetic forms of the disease

	Control Group (n= 45)		Allergic BA (n=93)		Non-allergic BA (n=15)		Mixed BA (n=9)	
Genotypes	N	%	N	%	N	%	N	%
N /N	38	84,44	89	95,70	11	73,33	8	88,89
N/del	6	13,33	3	3,22	2	13,33	1	11,11
del/del	1	2,23	1	1,08	2	13,33	-	-
$\chi 2$, p	1,56; 0,45		4,98;0,02		0,34; 0,84		0,24; 0,88	
Alleys: N	82	91,11	181	97,31	24	80,00	17	94,44
Del	8	8,89	5	2,69	6	20,00	1	5,56
$\chi 2$, p	0,48; 0,82		4,65; 0,03		0,08; 1,0		4,98; 1,0	

Thus, in Uzbek population it was found that carriers of homozygous genotype NOESG3 of del/del gene were diagnosed more with family BA of non-allergic type. It was noted that carriers of heterozygous genotype N / del less often suffered from familyBAallergic and mixed type.

The distribution of occurrence of the genotype and alleles of NOESG3 gene by the severity of the disease in patients with familial BA was analyzed. It was noted that the frequency of patients with homozygous carriers of the genotype consisting of N/N alleles (96.42%) among patients with mild familyBAwas significantly higher in comparison with control groups (84.44%). Among patients with light familyBAthe probability in patients with heterozygous carriers of genotype consisting of alleles N / del (3.58%) was 3.7 times less in comparison with control groups (13.33%). Among patients with light familyBAthere were no homozygous carriers of genotype consisting of alleles del / del.

No reliable difference in frequency of occurrence of carriers of NOESG3 gene allele N (98.21%) among patients with light familyBAcompared to control groups was revealed (91.11%). Among patients with light familyBAcarriers of del-allele of NOESG3 gene (1.79%) hBA 5 times lower frequency of occurrence in comparison with control groups (8.89%). It was noted that the frequency of carriers of homozygous genotype (84.44%), consisting of N/N alleles, among patients with familyBAof medium severity was the same in comparison with control groups (84.44%). It was noted that patients with carriers of heterozygous genotype consisting of N/del alleles (8.89%) were 1.5 times less likely to experience tachycardia than the control groups (13.33%) among patients with medium severe family BA. Among patients

with family BA of medium severity in patients with homozygous genotype of carriers of del/del alleles (6.67%) a 3-fold increase was registered in comparison with the control group (2.23%).

No reliable difference in frequency of occurrence of carriers of NOESG3 del allele gene N (88.89%) was revealed among patients with family BA of medium severity in comparison with control groups (91.11%). It was noted that carriers of NOESG3 del allele gene (11.11%) experienced reliably high frequency of occurrence in comparison with control groups (8.89%).

Among patients with severe family BA there was a reliable burden in comparison with control groups (9%) of patients with carriers of homozygous genotype (84.44%) consisting of N/N alleles. It was noted that among patients with severe familyBAcarriers of heterozygous genotype consisting of N/del alleles (9.53%) suffered 1.4 times less in comparison with control groups (13.33%). Among patients with severe family BA, homozygous carriers of the genotype consisting of del/del alleles were not registered.

No reliable difference in frequency of occurrence of carriers of NOESG3 gene N allele (95.24%) among patients with severe familyBAwas revealed in comparison with control groups (91.11%). 1.9 times less than in control groups (8.89%) were recorded in patients carrying NOESG3 gene del allele (4.76%). (table-3)

Table 3 Comparative indices of bronchial asthma severity at the level of genotype and alleles of eNOS gene

Genotypes	Control Group (n= 45)		Lightweight BA (n=56)		Medium Heavy BA (n=45)		Heavy BA (n=21)	
	N	%	N	%	N	%	N	%
N /N	38	84,44	54	96,42	38	84,44	16	76,19
N/del	6	13,33	2	3,58	7	15,55	2	9,52
del/del	1	2,23	-	-	-	-	3	14,28
X^2,p	1,56; 0,45		4,64; 0,09		1,4; 0,48		0,68; 0,70	
Alleys:								
N	82	91,11	110	98,21	82	91,11	36	85,71
Del	8	8,89	2	1,79	8	8,8	6	14,28
X^2,p	0,48; 0,82		3,94; 0,04		0,62; 0,8		0,23; 0,63	

Thus, in the Uzbek population of carriers of homozygous genotype N / N NOESG3 gene more often BA a mild degree of family BA. Carriers of heterozygous N / del genotype were less likely to have a mild degree of familial BA. Carriers of homozygous genotype del / del were found to be more likely to suffer from a severe degree of familial BA. It was found that the allele del carriers have a milder degree of familial BA.

The distribution of genotype and alleles of NOESG3 gene by the degree of disease control in patients with familyBAwas analyzed. It was noted that the incidence of patients with carriers of homozygous genotype, consisting of alleles N / N (96.05%), among controlled patients with family BA increased significantly compared with control groups (84.44%). Among controlled patients with familyBAin patients with heterozygous genotype, carriers of N / del alleles (3.95%), the probability of disease is 3.4 times lower than in patients of control groups (13.33%). Among controlled patients with familyBAthere were no homozygous carriers of genotype consisting of N / del alleles.

The frequency of allele N carriers of NOESG3 gene (98.03%) among controlled familyBApatients did not significantly differ in comparison with control groups (91.11%).

Patients carrying the NOESG3 del allele (1.97%) were 4.5 times less likely than patients in control groups (8.89%).

Frequency of occurrence of patients with homozygous carriers of genotype consisting of N/N alleles (82.61%) among uncontrolled familyBApatients practically did not differ in comparison with control groups (84.44%). Among carriers of heterozygous genotype consisting of alleles N / del (10.87%) among uncontrolled familyBApatients, it was significantly lower compared with the control groups (13.33%). Among uncontrolled patients with family BA, patients with homozygous genotype consisting of N / del alleles (6.52%) were 2.9 times more likely than patients in the control group (2.23%).

It was noted that family BA among uncontrolled patients was much less common than the control groups (91.11%) of carriers of NOESG3 gene allele N (88.04%). Patients with NOESG3 gene allele del (11.96%) were found to be slightly more common in comparison with control groups (8.89%) [Table 4].

Table 4 Distribution of genotype and alleles of NOESG3 gene by the degree of control of bronchial asthma in the family

Genotypes	Control Group (n=45)		Controlled by BA groups (n=76)		Uncontrolled BA group (n=46)	
	N	%	N	%	N	%
N /N	38	84,44	73	96,05	38	82,61
N/del	6	13,33	3	3,95	5	10,87
del/del	1	2,23	-	-	3	6,52
X2, p	1,56; 0,45		5,45; 0,06		1,08; 0,5	
Alleys:						
N	82	91,11	149	98,03	81	88,04
del	8	8,89	3	1,97	11	11,96
X2, p	0,48; 0,82		4,7; 0,02		0,18; 0,66	

Thus, in the Uzbek population it was noted that the NOESG3 gene is more commonly found in controlled patients with family BA, which carries a homozygous genotype consisting of alleles N / N, and less often among patients with heterozygous genotype consisting of alleles N / del. It was noted that patients with homozygous genotype consisting of alleles del / del NOESG3 gene, are more common among patients with uncontrolled family BA.

The distribution of occurrence of genotype and allele of NOESG3 gene by sex in patients with familyBAwas analyzed. It was noted that NOESG3 gene in a family is somewhat less common in patients (37.70%) with homozygous genotype carrying familyBAconsisting of N / N alleles, compared with control groups (44.44%). Patients with heterozygous carriers of the genotype consisting of alleles N / del (4.10%) were significantly less frequently compared with control groups (6.67%) in men with family BA. Among men with family BA(0.82%) of patients homozygous genotype consisting of the alleles of del / del, in men of the control group this genotype was not registered.

The frequency of allele N carriers of NOESG3 gene (93.27%) among men with familyBBAid not differ significantly from the control group (90.83%). Patients with NOESG3 gene allele del (6.73%) were less likely to be reliable compared to the control groups (9.17%).

It was noted that the NOESG3 gene in the family was more reliable than the control groups (40.0%) of women (53.28%) with homozygous carriers of the genotype alleles N / N in the control group (40.0%).

Among women with familyBAthe probability of patients with heterozygous carriers of the genotype consisting of N / del alleles (2.46%) was 2.7 times less compared to the control groups (6.67%). Among women with familyBApatients with homozygous carriers of the

genotype consisting of N / del alleles (1.64%) were 1.4 times less likely than women in the control group (2.22%).

It was noted that allele N carriers of NOESG3 gene (95.0%) were significantly more likely to be found among women with family BA compared to the control groups (88.64%). Patients with NOESG3 gene allele del (5.0%) were 2.3 times less likely than those in the control group (11.36%).

When analyzing the sex distribution of the genotype and alleles of the NOESG3 gene in healthy relatives in the family, it was noted that the NOESG3 gene in the family was less reliable than in the control group (44.44%) of men with homozygous genotype consisting of N/N alleles (31.48%). It was noted that healthy relatives in the family were 1.6 times more likely to be men (10.53%) with heterozygous genotypes consisting of alleles N / del, compared with the control groups (6.67%). Among healthy relatives, no homozygous genotype consisting of N/ del alleles was observed in the family.

The occurrence of NOESG3 alleles N (87.5%) in men of healthy relatives in the family was significantly lower compared to the control groups (90.83%). The NOESG3 alleles del gene (12.5%) was 1.4 times more common than in the control groups (9.17%).

The homozygous genotype of NOESG3 gene consisting of N/N alleles (50.88%) was found to be more common in women with healthy relatives than in the control groups (40.0%). Among women of healthy relatives in the family, the heterozygous genotype of NOESG3 gene consisting of N/ del alleles (7.01%) showed no significant difference compared to the control groups (6.67%). No cases of homozygous allele genotypes del / del among women of healthy relatives have been registered in the family.

The frequency of alleles N of NOESG3 gene (93.94%) among women of healthy relatives in the family did not significantly differ in comparison with the control groups (88.64%). In healthy women alleles del of NOESG3 gene (6.06%) were 1.9 times less common than in control groups (11.36%) [Table 5].

Table 5 Sex distribution of genotype and alleles of NOESG3 gene in patients with bronchial asthma in the family

Genotypes	Control Group (n=45)				BA (n=122)				Healthy relatives (n=57)			
	Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	N	%	N	%
N /N	21	46,6	17	37,8	46	37,7	65	53,2	18	31,5	29	50,8
N/del	3	6,7	3	6,7	5	4,10	3	2,4	6	10,5	4	7,0
del/del	-	-	1	2,2	1	0,82	2	1,6	-	-	-	-
χ^2, p					18,6;0,20		7,63;0,02		3,79; ,06		4,1; 0,12	
Alleys:												
N	45	93,8	37	88,1	97	93,2	133	95,0	42	87,5	62	93,9
Del	3	6,2	5	11,9	7	6,73	7	5,0	6	12,5	4	6,0
χ^2, p					2,5; 0,10		12,7; 00		1,06;0,30		7,4; 0,06	

Thus, homozygous carriers of NOESG3 gene genotype consisting of N / N alleles were found in Uzbek population of female patients with family BA. It was noted that in healthy men heterozygous carriers of genotype consisting of alleles of N / del of NOESG3 gene were observed.

The correlation of genotype and alleles of NOESG3 gene polymorphism with immunological parameters in patients with bronchial asthma in the family has also been studied. It is important to study the specific association of immunoregulatory cytokines and

total IgE with genotypes of N/ del polymorphism of NOESG3 gene in patients with family BA. The study showed that the average level of total IgE in the total group of patients with genotype N /N BA in the family was 346.Z pg/ml, which was significantly higher than the average (196.3 pg/ml) in patients with genotype N / del in this group. The average value of total IgE (517.3 p g/ml) in patients with genotype N /N allergic BA in the family was almost 3 times higher than the average (178.4 p g/ml) in patients with genotype N/del in this group. No reliable correlation of N / del polymorphism genotypes of NOESG3 gene was found inBApatients in a family with inductive cytokines activity. The immune status indicators related to the genotypes of NOESG3 gene polymorphism of pathogenetic groups of bronchial asthma in the family are presented in Table 6.

Table 6. Indicators of immune status associated with genotypes of NOESG3 gene polymorphism of pathogenetic groups of bronchial asthma in the family

Patient group surveyed	Immunological indicators (pg/ml)	Genotypes		P
		N /N	N/del	
General group	IgE	196,3±23,6	346,3±33,4	0,01
	IL-6	13,5±2,9	13,2±2,9	Incorrect
	IFN-γ	7,8±1,2	7,6±1,2	Incorrect
Allergic BA	IgE	178,4±22,7	517,3±36,3	Incorrect
	IL-6	15,6±3,2	14,2±3,1	Incorrect
	IFN-γ	5,1±0,9	5,6±0,9	Incorrect
Non-allergic BA	IgE	162,8±22,3	213,7±23,8	Incorrect
	IL-6	10,9±2,6	12,6±2,9	Incorrect
	IFN-γ	13,1±1,3	11,2±1,4	Incorrect
Mixed BA	IgE	368,1±33,5	417,4±36,6	Incorrect
	IL-6	14,3±3,1	15,3±3,4	Incorrect
	IFN-γ	8,2±1,1	8,3±1,1	Incorrect

When studying the correlation between the polymorphism genotypes of N / del NOESG3 gene and immunological parameters revealed in patients with family BA, the mean total IgE in patients with family N / N genotype was 189.5 ± 26.5 pg / ml. It was noted that there was a significant decrease by 243.4 ± 28.9 pg/ml from the mean value for patients with genotype N / del in this group.

The average value of IL-6 in patients with genotype N / N in the family was 10.6 ± 2.9 pg / ml, which is significantly higher than the average value of 8.7 ± 2.6 pg / ml in patients with genotype N / del in this group. The increase was observed.

The average IFN-γ value of patients without genotype N / del control in the family was 5.6 ± 0.8 pg / ml, which is 3.5 ± 0.6 pg / ml higher than the average value of patients with genotype N / N in this group ($r < 0.05$).

Table 7 shows immune status indicators related to the genotypes of NOESG3 gene polymorphism for controlling bronchial asthma in the family.

Table 7. Indicators of immune status associated with genotypes of NOESG3 gene polymorphism in control of bronchial asthma

Group of patients surveyed	Immunological indicators (pg/ml)	Genotypes		P
		N /N	N/del	

Controlled by BA	IgE	189,5±26,5	243,4±28,9	Incorrect
	IL-6	10,6±2,9	8,7±2,6	Incorrect
	IFN-γ	4,8±0,7	4,2±0,7	Incorrect
Uncontrolled BA	IgE	456,7±36,6	505,7±38,3	Incorrect
	IL-6	15,7±3,1	16,6±3,4	Incorrect
	IFN-γ	3,5±0,6	5,6±0,8	0,05

Thus, the increase of general IgE level in patients with controlled genotype N / del with BA and reliable increase of IFN-γ level in uncontrolled patients was a diagnostic marker.

Among family members average values of IgE, IL-6, IFN-γ in patients with NOESG3 N / N genotype of BA (497,9; 14,0; 7,1) were higher than average values of patients with N / del genotype of BA (285,6; 12,4; 5,1) significantly increased.

Among family members NOESG3 gene averaged IgE, IL-6 and IFN-γ in healthy people with N / N genotype (274,9; 9,3; 4,8) to average value in healthy people with N / del genotype (234,5; 8,8; 5,2) relatively no significant differences were observed. Indicators of immune status related to the genotypes of NOESG3 gene polymorphism in individuals in the family are shown in Table 8.

Table 8 . Indicators of immune status associated with NOESG3 gene polymorphism genotypes in individuals in the family

Family members	Immunological indicators (pg/ml)	Genotypes		P
		N /N	N/del	
BA	IgE	285,6±29,6	497,9±38,9	0,01
	IL-6	14,0±2,6	12,4±2,3	Incorrect
	IFN-γ	7,1±1,1	5,1±0,8	Incorrect
Healthy relatives	IgE	234,5±26,8	274,9±29,4	Incorrect
	IL-6	9,3±2,9	8,8±2,4	Incorrect
	IFN-γ	4,8±0,8	5,2±0,9	Incorrect

Thus, there is an increase in total IgE and IL-6 in patients with allergic BA N / N genotype, reduction of IFN-γ, increase in total IgE in patients with N / del genotype and increase in IFN-γ in uncontrolled patients among family members. A reliable increase in IFN-γ indicates that these parameters are inherited in patients with the appropriate genotype.

3. CONCLUSION

Homozygous carriers of NOESG3 gene, consisting of alleles N / N, are common in the Uzbek population among patients with family BA, indicating that the disease is inherited from patients with this genotype. It was found that this genotype is more common in patients suffering from this disease, and more often in women with higher morbidity. Patients of this genotype also BA allergic BA, which showed an increase in total IgE and IL-6, a decrease in IFN-g.

In the Uzbek population, heterozygous carriers of NOESG3 gene, consisting of N / del, were less often found in patients with family BA and more often in healthy men. In the family, an increase in total IgE in controlled patients with this genotype and a reliable increase in IFN-g in uncontrolled patients indicated a diagnostic marker.

In the Uzbek population, carriers of del / del homozygous genotype eNOS gene were more susceptible to family non-allergic type of BA, and the disease was more common in uncontrolled and severe patients.

Thus, identification of allelic variants of NOESG3 gene of family BA in Uzbek population has diagnostic and prognostic importance and plays an important role in prevention of primary groups and risk groups.

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