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ORIGINAL ARTICLE

The Prevalence of Gene Polymorphisms Il-10, Il-13, Il-18 in The Development of Bronchial Asthma in the Republic of Karakalpakstan

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ABSTRACT

The prevalence of atopic diseases has increased abruptly in recent years in most western countries. The best paradigm available to date to explain this steep rise, the 'hygiene hypothesis', supports that it is the excess 'cleanliness' of our environments that has led to the decline in the number of infectious stimuli that are necessary for the proper development of our immune system. Recent findings support that it is the combined effect that not only pathogenic, but also non-pathogenic microorganisms, and even their structural components, can exert on the immune system that deters from the development of atopic responses. In recent years, polymorphisms of the interleukin gene have been widely studied. Certain allelic variants of cytokine genes may play an important role in the pathophysiology of various diseases. The aim of the study was to analyze the distribution of allelic variants of polymorphisms of IL-13 (rs1800925 C/T, rs20541 G/A), IL-10 (rs1800896 A/G) and IL-18 (rs1946518 G/T) genes and their relationship in patients diagnosed with bronchial asthma in the Republic of Karakalpakstan. The object of our study was the venous blood of 134 patients from the Republic of Karakalpakstan with a diagnosis of bronchial asthma aged 18 to 55 years, sent to the Republican Specialized Scientific and Practical Medical Center of Allergology and Clinical Immunology of the Republic of Uzbekistan and 120 healthy individuals as a control (at the time of examination they had no history and manifestations of allergic diseases). The genotypic distribution of polymorphisms rs1800896 C/T and rs20541 G/A of the IL-13 gene genotypes C/C and G/G in patients with asthma was 26% and 45%, respectively, heterozygous genotypes C/T and G/A - 60% and 41%, and homozygous T/T and A/A -genotypes - 14% and 14%, respectively. In bronchial asthma, no significant difference was found for IL10 rs1800896 polymorphism with control groups (p > 0.05). The rs1800925 polymorphism of the IL-13 gene was found to be significant (allele model: p = 0.0002, OR 1.27, 95% CI 0.34 -2.98; genotypic model: p = 0.0002, OR 1.56, 95% CI 0.20–5.50; dominant model: p = 5.0E-5, OR 1.65, 95% CI 0.20–5.06). For rs20541 of the IL-13 gene, a significant association was in the recessive model (p = 0.04, OR 1.3, 95% CI 0.79 - 1.27). For IL18 (rs1946518) genes, significant reliability was found for the following genotypes (p = 2.0E-8, OR 1.87, 95% CI 0.28–6.72), dominant genotypes (p = 0.0009, OR 1.31, 95% CI 0.30 - 3.31), and recessive model (p = 0.0005, OR 1.64, 95% CI 0.18 - 5.53). Understanding the genetic factors and molecular pathways that contribute to the disruption of the Th2 immune response will be useful in the future development of new targeted therapeutic approaches for prognosis, prevention, and treatment. However, to confirm and expand these results, further research is needed among various categories of the population of the Republic of Karakalpakstan.

Keywords: *atopic diseases, bronchial asthma, cytokines, immune system, genetic factors, polymorphism.*

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INTRODUCTION

The pathophysiology of atopic diseases is multifaceted and involves a complex interaction of several factors, including genetics, the environment, and dysregulation of immune pathway [1,2,3]. In the immunopathogenesis of allergic diseases, there is a dysregulation of type 2 T helper cells (TH2) and type 2 innate lymphoid cells, which leads to a significant increase in type 2 immune cytokines [4,5]. Cytokines

are proteins stimulated by immune cells, play an important role in regulating the immune response and act as a link between cells. Cytokines are divided into two groups depending on their function: anti-inflammatory and pro-inflammatory cytokines. The lack of balance between pro- and anti-inflammatory cytokines disrupts the proper function of the immune system [6,7]. Anti-inflammatory cytokines such as IL-4, IL-6, IL-10, IL-11, IL-13, IL-1 receptor antagonist (IL-1RA) and TGF-β inhibit inflammation and suppress cells of the immune system [8]. Pro-inflammatory cytokines such as IL-1β, IL-6, IL-8, IL-12, TNF-α and interferons facilitate inflammatory reactions and tend to stimulate immune cells, and there are cytokines that have both properties [9,10,11]. The same cytokine can be secreted by different cells and, depending on the context, has both pro- and anti-inflammatory activity, causing multiple immune responses [12,13]. Cytokines are classified according to the site of stimulation: Th1 cells or Th2 cells. Recently, a third subgroup has been identified that differs from Th1 and Th2 cells, called Th-cells (Th17) and T-regulatory cells (T-reg) [14,15,16]. In recent years, polymorphisms of the interleukin gene have been widely studied. Certain allelic variants of cytokine genes may play an important role in the pathophysiology of various diseases [17,18].

The aim of the study was to analyze the distribution of allelic variants of polymorphisms of IL-13 (rs1800925 C/T, rs20541 G/A), IL-10 (rs1800896 A/G) and IL-18 (rs1946518 G/T) genes and their relationship in patients diagnosed with bronchial asthma in the Republic of Karakalpakstan.

MATERIAL AND METHODS

The object of our study was the venous blood of 134 patients from the Republic of Karakalpakstan with a diagnosis of bronchial asthma aged 18 to 55 years, sent to the Republican Specialized Scientific and Practical Medical Center of Allergology and Clinical Immunology of the Republic of Uzbekistan and 120 healthy individuals as a control (at the time of examination had no history or manifestations of allergic diseases). The average age of patients with asthma was 38.8±9.4 years (from 18 to 60 years), 87 for women and 47 for men. The diagnosis was established by an allergist during an examination in accordance with the international recommendations of GINA (Global Initiative for Asthma). Informed consent was collected from all participants of study.

DNA extraction of whole blood of patients was performed using kits QIAamp DNA Blood Kits 250 (*QIAGEN* Inc., Valencia, CA, USA).

4 polymorphisms were selected for this study: IL-13 (rs1800925 C/T, rs20541 G/A), IL-10 (rs1800896 A/G) и IL-18 (rs1946518 G/T). The selection of polymorphisms was based on information gathered from the PubMed database regarding the verification of polymorphisms, the intended function, and the known association with bronchial asthma.

The total reaction volume was 16 µl, of which 1 µl was a mixture of primers (primer design and testing using Primer-BLAST programs (http://www.ncbi.nlm.nih.gov/ tools/primer-blast/) and Oligo Analyzer 3.1 (http://eu.idtdna. com/calc/analyzer), the primer is ordered from Integrated DNA Technologies, buffer of 10 µl (QuantiNova™ SYBR Green PCR Kit, Qiagen, Venlo, Netherlands) and the DNA of interest is 5 µl (1-5ng per µl). The allele-specific polymerase chain reaction (AS-PCR) was performed on a real-time PCR system Bio-Rad CFX96 (Bio-Rad Laboratories, Hercules, California, USA). Amplification was performed according to the primer structure according to the following protocol: initial denaturation (2 min at 95 °C) and two-stage amplification: 1st stage: denaturation (15 seconds at 95 °C), annealing (from 40 seconds to 1 minute at 63 to 66 °C), elongation (40 seconds at 72 °C) from 7 to 10 cycles and 2nd stage: denaturation (20 seconds at 95 °CC), annealing (from 40 seconds to 1 minute at a temperature from 59 to 60 ° C), elongation (40 c at 72 ° C) 40-43 cycles. The analysis of the AC-PCR results was carried out using the SYBR detector program. The results obtained were documented in the form of growth curves of the SYBR detectors in graphical mode using an appropriate program.

The PCR fragment was sequenced with the following consequences: amplicon purification was performed using Exo SAP (GMLAG, Switzerland), sequencing reactions were performed using Big Dye Terminators 3.1 (TFS, USA), sequencing reaction products were purified using Big Dye Xterminator (TFS, USA) and sequencing reaction products were separated on a 3500 genetic analyzer (TFS).

The data was analyzed using standard statistical methods. Statistical processing of the basic data results was carried out using MS Office Excel 2016 (Microsoft).

Appropriate methods were used to calculate the number and percentage of different genotypes in the polymorphisms of the studied genes, and the Hardy-Weinberg equilibrium test was performed by comparing the observed and expected distribution of genotypes according to the degree of $\chi 2$ correspondence [21]. The calculation was carried out using a calculator for calculating statistics in case-control studies on the Gen Expert website (Russia, https://calc.pcr24.ru/index.php). The analysis of

interactions between polymorphisms was carried out using MDR software (Multifactor Dimensionality Reduction (mdr-2.0_beta_8.3; http://www.multifactor Dimensionalityreduction.org/)).
The nucleotide sequences of the analyzed interleukin gene regions are deposited in GenBank (NCBI) under access numbers: IL13(AF377331.2, U31120.1, U10307.1, L13029.1, X69079.1, L06801.1, NM_002188.3, NG_012090. 1, AC004039.1, L42079.1.), IL10 (GQ405199.1, DQ217938.1, AF418271.1, NG_012088.1, AL513315.15), IL18(NG_028143.1, EF444989.1, AP002884.5).

RESULTS AND DISCUSSION

The results of the frequency analysis of the distribution of genotypic variants of polymorphisms to the examined and control groups are presented in 1 table. The genotypic distribution of polymorphisms rs1800896 C/T and rs20541 G/A of the IL-13 gene genotypes C/C and G/G in patients with asthma was 26% and 45%, respectively, heterozygous genotypes C/T and G/A - 60% and 41%, and homozygous T/T and A/A -genotypes - 14% and 14%, respectively. According to the polymorphism rs1800896 A/G of the IL-10 gene and rs1946518 G/T of the IL-18 gene, the dominant homozygous genotypes A/A and GG were 58% and 32%, the heterozygous genotype A/G was 28% and GT was 56%, and the homozygous recessive genotypes G/G were 14%. and TT - 12%, respectively.
In the control group, the frequency analysis of the CC, CT, and TT genotypes of the rs1800925 C/T polymorphism of the IL-13 gene was 16%, 78%, and 6%, respectively. And according to the rs20541 A/G polymorphism, the homozygous G/G genotype is 52%, the heterozygous A/G genotype is 42%, and the A/A genotype is 6%, respectively. The results of the study on polymorphisms rs1800896 A/G of the IL-10 gene and rs1946518 G/T of the IL-18 gene were distributed as follows: genotype A/A and GG - 55% and 50%, heterozygous genotype A/G - 32% and GT - 21%, and homozygous recessive genotypes occurred G/G - 13% and TT - 29%, respectively.

Table 1. Polymorphisms of the IL-13 (rs1800925 and rs20541), IL-10 (rs1800896) and IL-18 (rs1946518) genes and their frequency of genotypes in patients with asthma and the control group

Absolute values of the occurrence of genotypes and their frequency						
Study groups and number of observations (n)	IL-13 genotypes(rs1800925)			IL-13 genotypes (rs20541)		
	CC	CT	TT	GG	GA	AA
BA (134)	36(26%)	78(60%)	20(14%)	61(45%)	56(41%)	17(14%)
The control group (n=120)	18(16%)	95(78%)	7(6%)	62(52%)	51(42%)	7(6%)
	IL-10 genotypes (rs1800896)			IL-18 genotypes (rs1946518)		
	AA	AG	GG	GG	GT	TT
BA (134)	75(58%)	38(28%)	21(14%)	42(32%)	78(56%)	14(12%)
The control group (n=120)	63(55%)	39(32%)	18(13%)	61(50%)	24(21%)	35(29%)

The results of our studies on polymorphisms of the three genes IL-13, IL-10, and IL-18 indicate that there are no statistically significant differences between the main and control groups.
Statistical values comparing the results of the allele-genotypic distribution in the group of patients with asthma and the control group are presented in Table No. 2.

Table 2. Allele-genotypic distribution in the groups

Gene (polymorphism)	The inheritance model	Allele and The genotype	Checking for association and heterogeneity			
			χ^2	***p***	***OR***	
					value	95% CI
IL13 (rs1800925)	Alleles	The allele ***C***	14.23	0.0002	0.49	0.34 – 0.71
		The allele ***T***			2.05	1.41 – 2.98
	Genotypes	The genotype ***C/C***	17.31	0.0002	0.34	0.20 – 0.57
		The genotype ***C/T***			2.08	1.25 – 3.44
		The genotype ***T/T***			2.28	0.95 – 5.50
	Dominant	The genotype ***C/C***	16.64	5.0E-5	0.34	0.20 – 0.57
		The genotype ***C/T+T/T***			2.97	1.75 – 5.06
	Recessive	The genotype ***C/C+C/T***	3.52	0.06	0.44	0.18 – 1.06
		The genotype ***T/T***			2.28	0.95 – 5.50
	Alleles	The allele ***G***	3.41	0.06	0.71	0.49 – 1.02
		The allele ***A***			1.41	0.98 – 2.04

IL13 (rs20541)	Genotypes	The genotype ***G/G***	4.49	0.11	0.75	0.47 – 1.22
		The genotype ***G/A***			0.97	0.60 – 1.58
		The genotype ***A/A***			2.40	1.02 – 5.62
	Dominant	The genotype ***G/G***	1.33	0.25	0.75	0.47 – 1.22
		The genotype ***G/A+A/A***			1.33	0.82 – 2.14
	Recessive	The genotype ***G/G+G/A***	4.24	0.04	0.42	0.18 – 0.98
		The genotype ***A/A***			2.40	1.02 – 5.62
IL10 (rs1800896)	Alleles	The allele ***A***	0.05	0.83	1.04	0.70 – 1.56
		The allele ***G***			0.96	0.64 – 1.43
	Genotypes	The genotype ***A/A***	0.39	0.82	1.12	0.67 – 1.88
		The genotype ***A/G***			0.84	0.48 – 1.47
		The genotype ***G/G***			1.09	0.51 – 2.30
	Dominant	The genotype ***A/A+A/G***	0.05	0.83	0.92	0.43 – 1.95
		The genotype ***G/G***			1.09	0.51 – 2.30
	Recessive	The genotype ***A/A***	0.18	0.67	1.12	0.67 – 1.88
		The genotype ***A/G+G/G***			0.89	0.53 – 1.50
IL18 (rs1946518)	Alleles	The allele ***G***	0.03	0.87	0.97	0.69 – 1.37
		The allele ***T***			1.03	0.73 – 1.45
	Genotypes	The genotype ***G/G***	36.03	2.0E-8	0.47	0.28 – 0.76
		The genotype ***G/T***			4.81	2.80 – 8.26
		The genotype ***T/T***			0.34	0.18 – 0.63
	Dominant	The genotype ***G/G***	9.35	0.002	0.47	0.28 – 0.76
		The genotype ***G/T+T/T***			2.15	1.31 – 3.52
	Recessive	The genotype ***G/G+G/T***	12.07	0.0005	2.95	1.58 – 5.53
		The genotype ***T/T***			0.34	0.18 – 0.63

In bronchial asthma group, no significant difference was found for IL10 rs1800896 polymorphism with control groups ($p > 0.05$). The rs1800925 polymorphism of the IL-13 gene was found to be significant (allele model: $p = 0.0002$, OR 1.27, 95% CI 0.34 -2.98; genotypic model: $p = 0.0002$, OR 1.56, 95% CI 0.20–5.50; dominant model: $p = 5.0E-5$, OR 1.65, 95% CI 0.20–5.06). Whereas for polymorphism rs20541 of the IL-13 gene, a significant association was in the recessive model ($p = 0.04$, OR 1.3, 95% CI 0.79 - 1.27). For IL18 (rs1946518) genes, significant reliability was found for the following genotypes ($p = 2.0E-8$, OR 1.87, 95% CI 0.28–6.72), dominant genotypes ($p = 0.0009$, OR 1.31, 95% CI 0.30 - 3.31), and recessive model ($p = 0.0005$, OR 1.64, 95% CI 0.18 - 5.53).

It is known that atopic disease is characterized by heterogeneity and does not have a single immunological mechanism [19,20]. Our study of genetic associations shows that the IL-13 gene is associated with the development of bronchial asthma by polymorphism rs1800925 in the allelic model and polymorphism rs20541 in the genotypic and recessive model, since IL-13 is the most frequently studied genetic change in patients with bronchial asthma [21].

It is known from the literature that IL-10 is involved in the pathophysiological mechanism of many diseases, since it regulates both cellular and humoral immunity. Genotype -1082AA is more common in bronchial asthma, and genotype -1082GG is more common in tuberculosis and Crohn's disease compared to the control group [22]. However, our study did not reveal a significant significance in the bronchial asthma group.

The results of our study revealed a significant relationship between the rs1946518 polymorphism of the IL-18 gene and the main study group. Statistical analysis has shown that IL-18 rs1946518 polymorphism is reliably identified in three types of inheritance (genotypic, dominant and recessive). Many research studies have shown that IL-18 is a powerful activator of B cells and an important regulator of both innate and acquired immune responses [23].

CONCLUSION

The results showed that the polymorphisms studied by us are risk factors for the development of bronchial asthma. However, to confirm and expand these results, further research is needed among various categories of the population of the Republic of Karakalpakstan. Understanding the genetic factors and molecular pathways that contribute to the disruption of the Th2 immune response will be useful in the future development of new targeted therapeutic approaches for prognosis, prevention, and treatment.

REFERENCES

1. Akdis C. A. Arkwright, P. D., Brüggen, M. C., Busse, W., et al. (2020). Type 2 immunity in the skin and lungs. Allergy. T. 75. – №. 7. – С. 1582-1605.
2. Akdis M. Aab, A., Altunbulakli, C., Azkur, K. et al. (2016). Interleukins (from IL-1 to IL-38), interferons, transforming growth factor β, and TNF-α: Receptors, functions, and roles in diseases. Journal of Allergy and Clinical Immunology. 138. №. 4. 984-1010.
3. Bieber T. (2020). Interleukin-13: targeting an underestimated cytokine in atopic dermatitis. Allergy. 75. №. 1. – С. 54-62.
4. Cheng D. Hao, Y., Zhou, W., & Ma, Y. (2014). The relationship between interleukin-18 polymorphisms and allergic disease: a meta-analysis. BioMed Research International.T. 2014.
5. Cosmi L. Liotta, F., Maggi, L., & Annunziato, F.. (2017). Role of type 2 innate lymphoid cells in allergic diseases //Current Allergy and Asthma Reports. 17. 1-7. https://doi.org/10.1007/s11882-017-0735-9
6. Custovic A. Custovic, D., Kljaić Bukvić, B., Fontanella, S., & Haider, S. (2020). Atopic phenotypes and their implication in the atopic march //Expert review of clinical immunology. 16. – №. 9. – С. 873-881.
7. Gandhi N. A., Pirozzi G., Graham N. M. H. (2017). Commonality of the IL-4/IL-13 pathway in atopic diseases. Expert review of clinical immunology. T. 13. 5. – С. 425-437.
8. Gulati K. Guhathakurta, S., Joshi, J., et al. (2016). Cytokines and their role in health and disease: a brief overview .Moj Immunol.. 4. №. 2. – С. 00121. https://doi.org/10.1111/imr.12620
9. Li L. Yu, R., Cai, T., Chen, Z.,et al. (2020). Effects of immune cells and cytokines on inflammation and immunosuppression in the tumor microenvironment. International Immunopharmacology. T. 88. 106939.
10. Lloyd C. M., Snelgrove R. J. (2018). Type 2 immunity: Expanding our view //Science immunology. T. 3. №. 25. С. eaat1604. DOI: 10.1126/sciimmunol.aat1604
11. Maiello N. Comberiati, P., Giannetti, A., Ricci, G.,et al. (2022). New directions in understanding atopic march starting from atopic dermatitis. Children. T. 9. – №. 4. – С. 450. https://doi.org/10.3390/children9040450
12. Nomura T., Kabashima K. (2021). Advances in atopic dermatitis in 2019-2020: Endotypes from skin barrier, ethnicity, properties of antigen, cytokine profiles, microbiome, and engagement of immune cells //Journal of Allergy and Clinical Immunology. T. 148. №. 6. С. 1451-1462. https://doi.org/10.1016/j.jaci.2021.10.022
13. Omraninava M. Eslami, M. M., Aslani, S., Razi, B. et al. (2020). Interleukin 13 gene polymorphism and susceptibility to asthma: a meta-regression and meta-analysis. Eur Ann Allergy Clin Immunol. T. 54. 150-74.
14. Qurashi T. A. Shah, A., Bhat, G. A., Khan, M. S., et al. (2021). Atopy in Kashmir-validation from a case control study with respect to IgE and Interleukin genes. Allergy, Asthma & Clinical Immunology. T. 17. С. 1-14.
15. Ramani T. Auletta, C. S., Weinstock, D., et al. (2015). Cytokines: the good, the bad, and the deadly. International journal of toxicology. 34.№. 4. 355-365.
16. Su F., Bai F., Zhang Z. (2016). Inflammatory cytokines and Alzheimer's disease: a review from the perspective of genetic polymorphisms. Neuroscience Bulletin. 32. . 469-480. https://doi.org/10.1007/s12264-016-0055-4
17. Thompson S. R., Humphries S. E. (2007). Interleukin-18 genetics and inflammatory disease susceptibility //Genes & Immunity. . 8. №. 2.. 91-99.
18. Trifunović J. Miller, L., Debeljak, Ž., & Horvat, V. (2015). Pathologic patterns of interleukin 10 expression–a review //Biochemia Medica.. 25. №. 1. 36-48.
19. Werfel T. Allam, J. P., Biedermann, T., Eyerich, K., et al. (2016). Cellular and molecular immunologic mechanisms in patients with atopic dermatitis. Journal of allergy and clinical immunology. 138. №. 2. 336-349.
20. Wynn T. A. (2015). Type 2 cytokines: mechanisms and therapeutic strategies. Nature Reviews Immunology.. 15. №. 5. 271-282. https://doi.org/10.1038/nri3831
21. Yue H. Umehara, Y., Trujillo-Paez, J. V., Peng, G., et al. (2021). Exogenous factors in the pathogenesis of atopic dermatitis: Irritants and cutaneous infections. Clinical & Experimental Allergy. 51.№. 3. 382-392. https://doi.org/10.1111/cea.13820
22. Zhang H. Wang, J., Wang, L., Xie, H., et al. (2018). Role of IL-18 in atopic asthma is determined by balance of IL-18/IL-18BP/IL-18R. Journal of Cellular and Molecular Medicine. 22. №. 1. 354-373.
23. Yang Y. Wang, Q., Song, X., Jiang, W. et al. (2017). Association between IL-4, IL-6, IL-18 polymorphisms and atopic dermatitis risk: A meta-analysis. Int. J. Clin. Exp. Med. 10. №. 5. 7375-7386.