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INVESTIGATION OF GENE POLYMORPHISMS ASSOCIATED WITH ATOPIC DERMATITIS IN THE KAZAKH POPULATION

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Abstract

Introduction. Atopic dermatitis belongs to a group of allergic diseases, including food allergies, allergic rhinitis, and asthma. Atopic dermatitis is a common chronic heterogeneous inflammatory skin disease characterized by relapses. The main factors contributing to its development include genetic predisposition, epidermal barrier disruption, and immune system dysfunction. The aim of this study is to investigate the polymorphisms of atopic dermatitis genes among the population of Kazakhstan.

Materials and methods. Our case-control study involved 322 people with atopic dermatitis and 328 healthy controls. 120 SNPs were selected and genotyped using a Quant Studio 12K Flex real-time PCR system.

Results. Significant associations were identified between eight single nucleotide polymorphisms (SNPs) (rs79497729, rs12144049, rs2321443, rs3091307, rs3208007, rs10995245, rs56302621, rs72823628) and atopic dermatitis.

Conclusion. Our data confirm and expand the current understanding of the influence of SNPs on atopic dermatitis. Importantly, this study is unique in focusing on the Kazakhstani population, providing valuable insights into Central Asia, where research data are scarce or absent for this region.

Keywords: Atopic dermatitis, Single nucleotide polymorphism, Genotypes, Population study

Introduction. In recent years, atopic dermatitis (AD) has become a major global health problem. The incidence of this disease is increasing, and this increase is especially remarkable in light of progress in society. AD, also known as atopic eczema, is a common and long-lasting skin disorder affecting a large proportion of the population, with an estimated lifetime incidence of 10–20% in developed countries [1, 2]. AD is a complex condition influenced by a combination of genetic, biological, and environmental factors that can lead to skin barrier dysfunction and changes in the immune response. Living with AD can have a significant impact on a person's quality of life, affecting self-esteem, and sleep, and even creating economic problems [3]. Although AD often begins in infancy (about 50% of cases appear within the first 6 months of life), many cases resolve spontaneously. However, some people continue to suffer from Alzheimer's disease into adulthood, which can have a significant impact on their well-

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being. Interestingly, there is a growing number of patients who develop AD later in life. It is worth noting that approximately 80% of patients with AD have elevated levels of total IgE (immunoglobulin E) in the bloodstream and are sensitized to various allergens, including environmental allergens and microbes found on the skin [4]. However, a study conducted by Abuabara et al. found that the incidence of atopy, or the tendency to develop allergic reactions, can vary from 47% to 75%, depending on factors such as age at diagnosis, study size and characteristics of the patients involved [5]. From a genetic point of view, AD is a complex hereditary disease. It involves many genes that are not necessarily located on the same chromosome, as well as environmental factors that can cause symptoms and play a role in its development. Recent studies indicate that there may be more than 70 genes associated with AD in different populations [6]. The filaggrin gene (FLG), located on chromosome 1q21.3, is a significant risk factor for the development of AD [7]. This gene encodes a protein that is critical for skin integrity by linking intermediate keratin filaments. It is initially synthesized as a polyprotein called profilaggrin, which undergoes proteolytic processing into functional filaggrin molecules [8]. As such, FLG plays a vital role in maintaining skin health and is associated with various skin diseases and developmental processes [9, 10]. The GLB1 gene serves a dual purpose, controlling the production of two different proteins. The primary product is beta-galactosidase, an enzyme required for various metabolic processes. In addition, this gene encodes an elastin-binding protein, which together with cathepsin A and neuraminidase 1 forms the elastin receptor complex. This complex is vital for the construction of elastic fibers that participate in the supporting framework of the body's connective tissue [11]. Th2-dominant immune responses are thought to play a role in the development of AD, especially in the early stages. Studies have shown that in acute skin lesions of AD patients, there are higher levels of cells expressing interleukin IL-4, IL-5 and IL-13 mRNA, whereas in chronic skin lesions, there is increased expression of GM-CSF subunit and IL-13 mRNA. 12p40. Further studies of skin biopsies from AD patients revealed an increased presence of Th2 cells expressing IL-4 and IL-13 mRNA [12]. IL-13 is associated with two types of receptors: a heterodimer consisting of IL-13Rα1 and IL-4Rα, responsible for IL-13 signaling, and IL-13Rα2, which acts as a non-signaling decoy receptor. The short cytoplasmic tail of IL-13Rα2 lacks any obvious signaling motif, so it does not trigger signaling pathways upon IL-13 binding [13]. This study is based on multiple GWAS of AD conducted in both East Asian and European populations. Through extensive replication and meta-analysis, these studies have identified multiple AD susceptibility loci located in different genomic regions. The main aim of this study was to get the association between specific genetic variants AD in the Kazakh population. To achieve this, we identified and selected genetic variants that demonstrated the strongest correlation with AD in previous studies. These variants were then used to genotype individuals diagnosed with AD within the Kazakh population. Our specific objectives included: assessing the frequency of these variants in AD patients compared to a control group, evaluating their potential role as genetic risk factors for AD in this population, and testing the hypothesis that certain variants contribute to an increased susceptibility to AD in Kazakh.

Materials and Methods

Participants

The study employed a case-control design with a total cohort of 650 participants. This comprised 322 individuals diagnosed with AD and a control group of 328 subjects with no indications of AD or related atopic conditions.

Participants were sourced from diverse regions across Kazakhstan. Specifically, they were enrolled in multi-disciplinary hospitals situated in 17 regions within the Republic of Kazakhstan.

Institutional Review Board Statement

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The study was approved by the Local Ethics Committee of the S.D. Asfendiyarov Kazakh National Medical University, Almaty, Republic of Kazakhstan (protocol of the Local Ethics Commission No. 12 (118) dated 28.09.2021). In addition, this investigation also was approved by the Central Bioethics Commission of the Ministry of Healthcare of the Republic of Kazakhstan (protocol No. 14 dated 24.11.2021). Moreover, the study was registered with ClinicalTrials.gov (NCT05090631). All methods were performed according to the relevant guidelines.

Informed Consent Statement

Informed consent was obtained from all subjects and/or their legal guardians. During the evaluation phase, all enrolled subjects provided their written informed consent, endorsing their voluntary participation in the study, allowance for biological material sampling (specifically blood), and authorization for potential publication of results.

Inclusion Criteria

Individuals with diverse manifestations of a medically confirmed diagnosis of AD. The participant age ranged from 18 to 45 years and above—individuals of Kazakh descent, evidenced by both paternal and maternal grandparents being ethnically Kazakh. Participants demonstrated the capacity and willingness to provide informed written consent. Participants exhibited the capability and intent to comply with the established research protocol.

Exclusion Criteria

Detailed exclusion criteria can be accessed on the clinical trial portal.

Covariates

Licensed dermatologists rigorously confirmed diagnoses of AD. All control participants underwent comprehensive clinical evaluations to validate the absence of AD and other skin or atopic disorders. These disorders included but were not limited to asthma, hay fever, allergic conjunctivitis, and sensitization to various allergens like air pollutants, food, medication, domestic animals, and indoor allergens. Furthermore, participants' family history was scrutinized for the presence of atopic diseases.

The severity of AD among patients was assessed using the SCORAD (SCORing Atopic Dermatitis) index. SCORAD = (0.1 x Erythema + 0.1 x Edema + 0.1 x Oozing/Crusting + 0.1 x Lichenification + 0.6 x Area Affected) + (0.025 x Patient's Assessment of Itchiness + 0.025 x Patient's Assessment of Sleep Quality) [14]. Based on their scores, patients were stratified into:

- Severe category (SCORAD > 50; n = 39)
- Moderate category (SCORAD 25-50; n = 112)
- Mild category (SCORAD < 25; n = 170)

Genotyping

Information pertinent to single-nucleotide polymorphisms (SNPs) was sourced from the GWAS (Genome-Wide Association Study) Catalog (https://www.ebi.ac.uk/gwas/home). For this study, 120 SNPs were identified and selected as polymorphic markers.

Genomic DNA was isolated from 200 μL of whole blood utilizing the KingFisher Flex-Ready DNA Ultra 2.0 Prefilled Plates (USA). The procedure adhered strictly to the manufacturer's guidelines.

The concentration and purity of the extracted genomic DNA were quantitatively assessed employing the NanoDrop One/OneC Microvolume UV-Vis Spectrophotometer (Thermo Scientific, USA) and the Qubit Fluorometric Quantification system (Thermo Scientific, USA). Post-quantification, DNA samples were standardized to ensure uniformity in concentration. The standardized samples were then preserved at a temperature of -20°C.

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Genotypic determination was accomplished using the QuantStudio 12K Flex Real-Time PCR System (Thermo Fisher Scientific, USA). Data extraction and subsequent analysis were facilitated through the QuantStudio Real-Time PCR Cloud Software [15].

Statistical analysis

Statistical analyses were performed using the R Studio software. For continuous variables, comprehensive descriptive statistics were derived. This encompassed the arithmetic mean (X), median (Me), standard deviation (SD), coefficient of variation (v%), as well as the minimum (min) and maximum (max) observed values. Such descriptive metrics elucidate the data's distribution characteristics and inherent variability. Odds ratios (OR) accompanied by their 95% confidence intervals (CI) were computed to assess the strength and direction of associations. $\chi 2$ tests were harnessed to determine any discernible differences in genotype and allele frequencies between the AD patient cohort and the control group, aiming to substantiate their clinical implications. Corrections for multiple comparisons were made after the FDR analysis.

The Student's t-test was invoked for contrasting biophysical measures between the AD and control groups. Throughout the analyses, a p-value threshold of $P < 0.05$ was adopted to denote statistical significance.

Results. The study FDR (False Discovery Rate) analysis was employed to account for multiple comparisons when testing a multitude of SNPs (Table 1) [16]. According to the study of this table 1, there was a low p-value in rs2259735 = 2.22e-37, indicating strong statistical significance. According to the padj-value (FDR) statistic, which adjusts the p-value for multiple comparisons, the SNP rs2259735 has an adjusted value of 1.443e-35, which still indicates a significant association. The highest significance p-value (rs10053502 = 0.758) and the corresponding padj-value (0.831) indicate no statistical significance.

Table 1. Results of FDR analysis to account for multiple comparisons when testing multiple SNPs

№	SNP	p-value	p_{adj} -value (FDR)
1	rs10053502	0.758272879	0.8313332365
2	rs10152544	0.073720161	0.218327525
3	rs10174949	0.050065499	0.16271287175
4	rs1059513	0.689644471	0.8313332365
5	rs10995245	1.48405e-06	1.205790625e-05
6	rs10995251	0.709307367	0.8313332365
7	rs11130215	0.709778045	0.8313332365
8	rs11171739	0.488525608	0.721685557272727
9	rs112111458	0.000522893	0.00308982227272727
10	rs11303055	0.767384526	0.8313332365
11	rs12144049	6.34092e-11	6.86933e-10
12	rs1214598	0.760013044	0.8313332365
13	rs12153855	0.677833593	0.8313332365
14	rs12295535	0.003504471	0.015186041
15	rs12465939	0.820322219	0.860015229596774
16	rs1295686	0.077003666	0.218327525
17	rs1409123	0.109929813	0.266981279259259
18	rs16948048	0.754525176	0.8313332365

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19	rs16960052	0.589956296	0.782595086530612
20	rs17389644	0.414101165	0.651534911547619
21	rs176095	0.110899916	0.266981279259259
22	rs17881320	0.002852108	0.01324193
23	rs1861246	0.417507656	0.651534911547619
24	rs2041733	0.259848266	0.496768743823529
25	rs20541	0.078727423	0.218327525
26	rs22124344	0.095639466	0.2486626116
27	rs2212434	0.002698335	0.01324193
28	rs2259735	2.22e-37	1.443e-35
29	rs2271404	0.475247711	0.718397702674419
30	rs2321443	4.44089e-16	5.773157e-15
31	rs2426500	0.581596274	0.782595086530612
32	rs2766664	0.007424496	0.030162015
33	rs28558565	0.888416651	0.888416651
34	rs2897442	0.206057306	0.4185539028125
35	rs3091307	2.26e-36	4.89666666666667e-35
36	rs3208007	7.82773e-05	0.00050880245
37	rs34290285	0.715971968	0.8313332365
38	rs35073649	0.08061324	0.218327525
39	rs35568883	0.395792936	0.651534911547619
40	rs35766269	0.74649525	0.8313332365
41	rs3917265	0.165485355	0.347595432096774
42	rs45605540	0.013637453	0.0521432026470588
43	rs4713555	0.375199361	0.641788380657895
44	rs479844	0.420991789	0.651534911547619
45	rs4821544	0.2309617	0.454924560606061
46	rs56101042	0.560113549	0.782595086530612
47	rs56302621	1.32028e-08	1.22597428571429e-07
48	rs593982	0.165776283	0.347595432096774
49	rs61865882	0.359463752	0.631490375135135
50	rs61878692	0.001532289	0.00829989875
51	rs61961401	0.30203198	0.545335519444444
52	rs6461503	0.855423527	0.882579829444445
53	rs6473227	0.290197483	0.538938182714286
54	rs6720763	0.63165418	0.821150434
55	rs6943506	0.037340765	0.127744722368421
56	rs72823628	1.26e-36	4.095e-35
57	rs72943976	0.143772603	0.324741936551724
58	rs7512552	0.57560686	0.782595086530612
59	rs759382	0.788462997	0.840165488606557
60	rs7717955	0.872646168	0.886281264375
61	rs79497729	3.15e-36	5.11875e-35

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62	rs8086340	0.144884864	0.324741936551724
63	rs847	2.00355e-05	0.000144700833333333
64	rs848	0.015423672	0.0556965933333333
65	rs909341	0.516747091	0.746412464777778

The study encompassed 328 (50.46%) controls and 322 (49.54%) AD patients (Table 2) with the control group predominantly living in rural areas, and the AD group split between urban and rural residents. Controls averaged 42.4±10.6 years of age, while AD patients averaged 33.8±11.9 years. AD symptom recurrence varied among patients, with triggers identified as food, household chemicals, stress, pollen, and others. Hereditary patterns were evident, with many AD patients having family members affected by atopic diseases. Comorbidities in AD patients ranged from gastrointestinal diseases to lifestyle habits like smoking and alcohol consumption. Clinical manifestations of AD varied, and while some didn't undergo hormone therapy, others opted for local, systemic, or a combination of both.

Table 2. Phenotypic and clinical characteristics of the study participants

Parameters		**Controls**	**AD patients**
N		328 (males-173, females-155)	322 (males-96, females-221)
Age, years (min-max), mean ± SD, %		42.4±10.6(77-18)	33.8±11.9(68-13)
Region of residence: urban/rural area		0/328	187/135
Number of recurrences per year:	once a year	-	118
	2 times a year	-	85
	3 times or more	-	121
Dermographism	white	-	173
	red	-	53
	mixed	-	96
The reason for this exacerbation	food	-	177
	household chemicals	-	118
	stress	-	121
	pollen	-	80
	other	-	19
Heredity	children	-	44
	one parent	-	132
	both parents	-	7
	grandma or grandpa	-	13
	siblings, sisters	-	57
Comorbidities:	diseases of the gastrointestinal tract	-	139
	hay fever	-	51
	frequent acute respiratory infection	-	31
	parasitosis	-	16
	smoking	-	49
	alcohol	-	63

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Itching degree:	mild	-	109
	moderate	-	123
	severe	-	89
Clinical form	in remission	-	2
	exudative	-	2
	erythematous-squamous	-	43
	lichenification	-	58
	lichenoid	-	123
	pruriginous	-	16
Hormone therapy	not use	-	84
	systemic	-	15
	local	-	184
	and system and local	-	38

Table 3 showcases the single nucleotide polymorphism (SNP) markers that were genotyped in the case-control samples. These markers are associated with various genes, their chromosomal positions, specific functions, and minor allele frequencies (MAF) as indicated by reference [17]. The gene GLB1 is linked to the SNP marker rs79497729 located on chromosome 3p22.3 at position 33043419. Its function is within an intron and has an MAF of 0.1771. The genes LCE5A and FLG-AS1 are related to the SNP marker rs12144049 found on chromosome 1q21.3 at position 152468434. This marker's function is intergenic with an MAF of 0.2648. IRAK1BP1 and MEI4 are connected to the SNP marker rs2321443 positioned on chromosome 6q14.1 at 78495243. Its function is also intergenic, having an MAF of 0.2306. The gene TH2LCRR correlates with the SNP marker rs3091307, which is on chromosome 5q31.1 at 132653444. This SNP functions within an intron and possesses an MAF of 0.3311. RTEL1 and RTEL1-TNFRSF6B associate with the SNP marker rs3208007 located on chromosome 20q13.33 at 63690935. This marker is synonymous in function and holds an MAF of 0.2819. The genes ALDH7A1P4 and ZNF365 link to the SNP marker rs10995245 found on chromosome 10q21.2 at 62631615. Its function is intronic with an MAF of 0.4858. CCDC80 and LINC02042 are connected to the SNP marker rs56302621 located on chromosome 3q13.2 at 112658770. The function is intergenic, having an MAF of 0.4894. Finally, the genes IL18R1 and IL1RL1 associate with the SNP marker rs72823628, which is found on chromosome 2q12.1 at 102312157. Its function is intronic with an MAF of 0.1577.

Table 3. SNP markers genotyped in the case-control samples

Gene	RS number	Chromosome	Position	Function	MAF [21]
GLB1	rs79497729	3p22.3	33043419	Intron	0.1771
LCE5A, FLG-AS1	rs12144049	1q21.3	152468434	Intergenic	0.2648
IRAK1BP1, MEI4	rs2321443	6q14.1	78495243	Intergenic	0.2306
TH2LCRR	rs3091307	5q31.1	132653444	Intron	0.3311
RTEL1, RTEL1-TNFRSF6B	rs3208007	20q13.33	63690935	Synonymous	0.2819
ALDH7A1P4, ZNF365	rs10995245	10q21.2	62631615	Intron	0.4858

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CCDC80, LINC02042	rs56302621	3q13.2	112658770	Intergenic	0.4894
IL18R1, IL1RL1	rs72823628	2q12.1	102312157	Intron	0.1577

Table 4 details the allele frequencies of eight SNPs in patients with AD and controls. For each SNP, the genotype frequencies among the cases (AD patients) and controls are compared, and the statistical significance is assessed. rs79497729 had three genotypes, A/A, A/G, and G/G, with respective frequencies in cases being 0.86, 0.12, and 0.02. The minor allele frequency (MAF) for the allele (G) in the cases was 0.15. This SNP displayed a significant association with AD, given the very low p-value of $5\times10^{(-35)}$ and an odds ratio (OR) of 12.59 with a confidence interval (CI) of 8.06 to 19.67 for the A/A genotype. rs12144049 demonstrated significant association with AD with a p-value of $6\times10^{(-10)}$. The genotypes C/C, C/T, and T/T had frequencies of 0.72, 0.26, and 0.02 in the cases, respectively. The MAF for the allele (C) was 0.39. rs2321443 showed a strong association with AD with a p-value of $5\times10^{(-15)}$. The genotypes C/C, C/T, and T/T had frequencies of 0.35, 0.27, and 0.38 in AD patients. The MAF for allele (C) was 0.39. rs3091307 presented a very strong association with AD, having a p-value of $3\times10^{(-35)}$). Genotypes A/A, A/G, and G/G had respective frequencies in cases of 0.65, 0.29, and 0.06. The MAF for allele (G) was 0.28. rs3208007 also showed an association with AD with a p-value of 0.0005088. The genotypes C/C, C/T, and T/T displayed frequencies of 0.21, 0.44, and 0.35 in the cases. The MAF for allele (T) was 0.53. rs10995245 indicated a significant association with AD with a p-value of $1\times10(^{-5})$. Genotypes A/A, A/G, and G/G had frequencies of 0.14, 0.48, and 0.38 in the cases. The MAF for allele (A) was 0.52. rs56302621 demonstrated a significant association with AD, having a p-value of $1\times10^{(-7)}$. The genotypes G/G, G/C, and C/C showed frequencies of 0.13, 0.51, and 0.36 in the cases. The MAF for allele (C) was 0.58. rs72823628 was strongly associated with AD with a p-value of $4\times10^{(-35)}$. The genotypes G/G, G/A, and A/A had respective frequencies in cases of 0.79, 0.20, and 0.01. The MAF for allele (A) was 0.19.

Table 4. Allele frequencies of eight SNPs in patients with AD

rs number	**Genotype Frequency**			X^2	**p-value**	**OR**	**CI**	
	Genotypes	Cases	Controls					
rs79497729	A/A	0,86	0,33	163,494	5×10^{-35}	12,59	8,06	19,67
	A/G	0,12	0,26			0,41	0,25	0,65
	G/G	0,02	0,42			0,03	0,01	0,07
MAF	(G)	0,15	0,85					
rs12144049	C/C	0,72	0,60	46,963	6×10^{-10}	1,73	1,17	2,56
	C/T	0,26	0,19			1,52	0,97	2,38
	T/T	0,02	0,21			0,07	0,03	0,18
MAF	(C)	0,39	0.61					
rs2321443	C/C	0,35	0,41	70,864	5×10^{-15}	0,76	0,52	1,11
	C/T	0,27	0,52			0,34	0,23	0,50
	T/T	0,38	0,06			9,03	4,99	16,32
MAF	(C)	0,39	0,61					
rs3091307	A/A	0,65	0,02	223,455	3×10^{-35}	109,93	39,50	305,98

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	A/G	0,29	0,92			0,04	0,02	0,06
	G/G	0,06	0,07			0,95	0,46	1,97
MAF	(G)	0,28	0,72					
rs3208007	C/C	0,21	0,36	18,911	0.0005088	0,49	0,34	0,72
	C/T	0,44	0,28			1,98	1,39	2,83
	T/T	0,35	0,36			0,94	0,66	1,34
MAF	(T)	0,53	0,47					
rs10995245	A/A	0,14	0,07	26,841	1×10^{-5}	2,25	1,12	4,53
	A/G	0,48	0,73			0,34	0,22	0,51
	G/G	0,38	0,20			2,45	1,56	3,84
MAF	(A)	0,52	0,48					
rs56302621	G/G	0,13	0,36	36,286	1×10^{-7}	0,26	0,17	0,42
	G/C	0,51	0,39			1,57	1,10	2,25
	C/C	0,36	0,24			1,78	1,20	2,62
MAF	(C)	0,58	0,42					
rs72823628	G/G	0,79	0,32	140,262	4×10^{-35}	8,37	5,57	12,57
	G/A	0,20	0,36			0,43	0,29	0,65
	A/A	0,01	0,32			0,02	0,00	0,07
MAF	(A)	0,19	0,8					

Discussion. AD is a complex disease caused by a combination of multiple genetic and interacting environmental factors. Therefore, identifying genetic factors contributing to the development of AD is important for the development of new strategies for the treatment and prevention of this disease [18]. Although GWAS and meta-analyses have been conducted in several studies and many AD susceptibility loci have been identified, our analysis strongly suggests that certain polymorphisms, including rs79497729, rs12144049, rs2321443, rs3091307, rs3208007, rs10995245, rs56302621 and rs72823 628 ($p \leq 0.05$) close associated with asthma. Notably, individuals carrying at least one such polymorphic allele, whether heterozygous or homozygous, show a reduced susceptibility to AD compared with their counterparts homozygous for the major alleles. This highlights potential genetic mediators of AD vulnerability and lays the foundation for detailed therapeutic strategies. Previous historical studies have shed light on the role of mutations rs79497729, rs10995245, and rs56302621 in the GLB1, ZNF365 and CCDC80, LINC02042 genes, respectively, in modulating the occurrence of dermatitis. At the same time, many recent genome-wide association studies (GWAS) have shown that SNPs nested within the GLB1 gene may increase the risk of AD [19, 20]. These previous results are consistent with the insights gained from our current efforts. The odds ratio (OR) associated with the C rs12144049 risk allele located in the FLG gene as shown in our study (OR = 1.73–1.52) reflects OR rates previously reported in European-based genome-wide association studies: OR = 1.53 and OR = 1.39 [21]. The work of Simard M et al. 2021 clarified the connection between the genetic marker rs2321443 and the incidence of AD. The implications of this genetic variant about AD require further research and accumulating supporting evidence. A 2015 study by Schaarschmidt H. et.al. (2015) presented a comprehensive GWAS covering over 1.6 million genetic markers, evaluating 924 patients diagnosed with AD versus 5506 controls in a German population [22]. Their results revealed strong associations reaching genome-wide significance ($p < 5x10^{-7}$), especially for the

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polymorphic site rs3091307, which appears to influence the etiology of AD. Our data echo and confirm these findings, further strengthening the association between the rs3091307 locus and AD susceptibility. Alsabbagh M. and Ismail A., 2022 reported that SNPs (rs3091307 located within TH2LCRR and adjacent to RAD50) on chromosome 5q31.1 are significantly associated with AD [23]. In our result, SNP rs3091307 located TH2LCRR was found to have an association signal. Earlier studies have convincingly demonstrated a strong association between the genomic region rs3208007, located in the RTEL1-TNFRSF6B gene, and the manifestation of asthma and a variety of allergic diseases. This association emerged from a rigorous meta-analysis that supported the premise of a deep genetic link between the rs3208007 locus and susceptibility to these respiratory and allergic syndromes [24].

Conclusion. This research underscores a probable link between the polymorphisms rs79497729, rs12144049, rs2321443, rs3091307, rs3208007, rs10995245, rs56302621, and rs72823628 and a reduced susceptibility to AD among the Kazakh populace. Additionally, the results proffer a theoretical framework for deciphering the roles of the GLB1, LCE5A/FLG-AS1, IRAK1BP1/MEI4, TH2LCRR, RTEL1/RTEL1-TNFRSF6B, ALDH7A1P4/ZNF365, CCDC80/LINC02042, and IL18R1/IL1RL1 genes vis-à-vis AD. Ultimately, a nuanced understanding of the ensemble of AD-related risk factors is of paramount importance in sculpting efficacious primary prevention strategies and shaping informed public health directives.

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ҚАЗАҚСТАН ПОПУЛЯЦИЯСЫНДАҒЫ АТОПИЯЛЫҚ ДЕРМАТИТТІҢ ГЕН ПОЛИМОРФИЗМДЕРІН ЗЕРТТЕУ

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Түйіндеме

Кіріспе. Атопиялық дерматит тағамдық аллергия, аллергиялық ринит және астма сияқты аллергиялық аурулар тобына жатады. Атопиялық дерматит рецидивтермен сипатталатын кең таралған созылмалы гетерогенді қабынатын тері ауруы. Оның дамуына ықпал ететін негізгі факторлар – генетикалық бейімділік, эпидермиялық барьердің бұзылуы және иммундық жүйенің дисфункциясы. Бұл зерттеудің мақсаты Қазақстан тұрғындары арасында атопиялық дерматит гендерінің полиморфизмін зерттеу.

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Материалдар мен әдістер. Біздің жағдайда, зерттеуге атопиялық дерматитпен ауыратын 322 адам және 328 сау бақылау тобы қатысты. Барлығы 120 бірнуклеотидтік полиморфизм (SNP) Quant Studio 12K Flex нақты уақыттағы ПТР жүйесі арқылы скринингтен өтті және генотиптелді.

Нәтижелер. Сегіз SNP (rs79497729, rs12144049, rs2321443, rs3091307, rs3208007, rs10995245, rs56302621, rs72823628) және атопиялық дерматит арасында маңызды байланыстар анықталды.

Қорытынды. Біздің деректеріміз атопиялық дерматитте SNP әсерінің қазіргі түсінігін растайды және кеңейтеді. Зерттеу маңызын атап өтсек, зерттеу Қазақстан популяциясының ерекшеліктеріне назар аударуымен ерекшеленеді және зерттеу мәліметтері аз немесе мүлдем жоқ Орталық Азия жөнінде құнды ақпарат береді.

Түйінді сөздер: атопиялық дерматит, бірнуклеотидтік полиморфизм, генотиптер, популяциялық зерттеу

ИЗУЧЕНИЕ ПОЛИМОРФИЗМА ГЕНОВ АТОПИЧЕСКОГО ДЕРМАТИТА В ПОПУЛЯЦИИ КАЗАХСТАНА

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Аннотация

Введение. Атопический дерматит относится к группе аллергических заболеваний, включая пищевую аллергию, аллергический ринит и астму. Атопический дерматит – распространенное хроническое гетерогенное воспалительное заболевание кожи, характеризующееся рецидивами. Основными факторами, способствующими его развитию, являются генетическая предрасположенность, нарушение эпидермального барьера и дисфункция иммунной системы. Целью данного исследования является изучение полиморфизма генов атопического дерматита среди населения Казахстана.

Материалы и методы. В нашем исследовании случай-контроль приняли участие 322 человека с атопическим дерматитом и 328 здоровых лиц. Было отобрано и генотипировано 120 однонуклеотидных полиморфизмов (SNP) с использованием системы ПЦР в реальном времени Quant Studio 12K Flex.

Результаты. Значимые ассоциации были выявлены между восемью SNP (rs79497729, rs12144049, rs2321443, rs3091307, rs3208007, rs10995245, rs56302621, rs72823628) и атопическим дерматитом.

Заключение. Наши данные подтверждают и расширяют текущее понимание влияния SNP на атопический дерматит. Важно отметить, что это исследование уникально тем, что фокусируется на популяции Казахстана, предоставляя ценную информацию о Центральной Азии, где данные исследований скудны или отсутствуют для этого региона.

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Ключевые слова: атопический дерматит, однонуклеотидный полиморфизм, генотипы, популяционное исследование