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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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GENETIC ASSOCIATIONS WITH ASTHMA IN THE KAZAKH POPULATION: A CASE-CONTROL STUDY FOCUSING ON ACTN3 AND TSBP1 POLYMORPHISMS

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Abstract.

Background: Asthma is a prevalent chronic respiratory disease that significantly impacts the quality of life. Genetic factors, particularly single nucleotide polymorphisms (SNPs), play a crucial role in asthma susceptibility. This study investigates the genetic determinants associated with asthma in the Kazakh population, focusing on SNPs within the ACTN3 and TSBP1 genes.

Materials and methods: A case-control study was conducted involving 600 participants, with 300 diagnosed with asthma and 300 healthy controls. Participants were recruited from 17 regions across Kazakhstan. Genomic DNA was extracted, and 120 SNPs were selected for analysis. Genotyping was performed using the QuantStudio 12K Flex Real-Time PCR System. Statistical analyses included the Mann-Whitney U test, $\chi 2$ tests, and calculation of odds ratios (OR) to evaluate the association between SNPs and asthma.

Results: Significant associations were found between asthma and two SNPs: rs540874 in the ACTN3 gene and rs3132954 in the TSBP1 gene. The G allele of rs540874 (MAF 0.71 in cases vs. 0.30 in controls, p-value = 4.78×10^-14) and the G allele of rs3132954 (MAF 0.54 in cases vs. 0.10 in controls, p-value = 1.33×10^-12) were associated with increased asthma susceptibility. The findings suggest a potential protective role of the A/A genotype in asthma.

Conclusion: This study identifies significant genetic markers associated with asthma in the Kazakh population, highlighting the complex interplay between genetic and environmental factors in the disease's pathogenesis. The results contribute to the understanding of asthma's genetic underpinnings and may inform the development of personalized medical interventions tailored to genetic profiles, advancing the field of precision medicine for asthma management.

Key words. Asthma, single nucleotide polymorphisms, kazakh population, actn3, tsbp1, genetic association.

Introduction.

Asthma remains a significant global health concern, affecting millions of persons across various age groups. It is characterized by chronic inflammation of the airways, leading to respiratory difficulties, coughing, and wheezing. Asthma can significantly impact an individual's quality of life, resulting in a deterioration of physical well-being and hindering social interaction.

The SNAPSHOT survey found that the adjusted prevalence of asthma in the Middle East ranges from 4.4% in Turkey to 7.6% in the Gulf countries. Asthma has a deleterious impact on one's overall health and is associated with a notable prevalence of comorbidities. It is crucial for doctors to conduct a comprehensive examination and effectively manage any concurrent illnesses in all asthma patients [1].

Asthma and other allergic illnesses, including allergic rhinitis, atopic dermatitis, and food allergies, have a substantial influence on the overall quality of life for patients. These illnesses significantly influence the total well-being and quality of life, impacting the physical, mental, and social aspects. Consequently, healthcare systems are confronted with a heightened responsibility in handling chronic disorders [2].

In their narrative review, Shi, Zhang, and Qiu (2022) present a concise overview of 10 gene polymorphisms that are linked to the likelihood of developing asthma. The review emphasizes the importance of genetic variations in influencing the probability of getting asthma and the possibility of tailoring treatment based on genetic profiling. Nevertheless, it recognizes the challenge of comprehending the exact correlation between gene polymorphisms and the fundamental pathophysiological causes of asthma [3].

A study conducted on children and adolescents in Brazil investigated sixteen genetic variants in eleven genes that have previously been associated with asthma. The findings underscored the complex interplay between hereditary and environmental variables in the onset of asthma [4].

Toru et al. (2015) conducted a study that discovered a significant link between the C>T polymorphism of the multidrug resistance-1 gene and asthma in individuals. These findings indicate that this particular genetic mutation may contribute to the onset of asthma by disturbing the equilibrium between oxidants and antioxidants [5].

Despite the identification of multiple genes associated with asthma risk, there remains a dearth of study regarding the precise impact of these genetic variants on the development of asthma. The complexities of asthma, including its varied clinical presentations and therapeutic responses, highlight the need for further research to elucidate the specific roles of these genes.

Examining the impact of gene polymorphisms identified in prior studies on the development and characteristics of asthma in the population of Kazakhstan is of utmost importance. This methodology can assist in identifying genetic susceptibility factors that are unique to particular populations, enhance our understanding of the fundamental origins of asthma in these populations, and facilitate the creation of personalized approaches for asthma management that consider both genetic and environmental factors.

To comprehend the range and intensity of asthma, it is crucial to examine the hereditary factors that play a role in its formation. This research is crucial for developing customized therapies that specifically address the individual asthma etiology of each patient. A recent study highlights the significant impact of gene polymorphisms on the susceptibility and advancement of asthma, showing a multifaceted character of the disease that encompasses both genetic and environmental factors.

The correlation between genetic differences and extrinsic factors in the development of asthma underscores the importance of genetic research in this field. While significant advancements have been made in identifying genetic markers associated with asthma, further research is necessary, particularly in diverse populations like Kazakhstan, to fully understand these connections and their implications for personalized medicine.

Materials and Methods.

Ethical Issues:

The study received approval from the Local Ethics Committee of the S.D. Asfendiyarov Kazakh National Medical University, located in Almaty, Republic of Kazakhstan, as per the protocol of the Local Ethics Commission No. 12 (118) dated 28.09.2021. Furthermore, it also obtained approval from the Central Bioethics Commission of the Ministry of Healthcare of the Republic of Kazakhstan, with protocol No. 14 dated 24.11.2021. Additionally, the study was registered with ClinicalTrials.gov under the identifier NCT05088512. All research methods adhered to the relevant ethical guidelines.

Study Participants:

A case-control design was employed in this research, encompassing a total cohort of 600 individuals. This group comprised 300 individuals diagnosed with asthma, contrasted with a control group consisting of 300 subjects displaying no indications of asthma or related conditions.

The participants were recruited from various regions across Kazakhstan, specifically from multidisciplinary hospitals located in 17 regions within the Republic of Kazakhstan in the period from 01.01.2022 to 01.12.2022.

Inclusion Criteria:

- Individuals with diverse manifestations of a confirmed medical diagnosis of asthma.
- Participant age ranged from 5 to 65 years.
- Individuals of Kazakh descent, as evidenced by both paternal and maternal grandparents being ethnically Kazakh.
- Participants who demonstrated the capacity and willingness to provide informed written consent.
- Participants exhibiting the capability and intent to comply with the established research protocol.

Exclusion Criteria:

- Persons who, in the opinion of the researcher, are mentally or legally incapacitated, which prevents obtaining informed consent.
- Pregnant or lactating women.
- Tuberculosis of any localization in the active phase and in history.
- Severe and decompensated diseases of the liver and kidneys, cardiovascular system.
- Severe and decompensated course of endocrine diseases.
- Autoimmune diseases.
- Systemic diseases.
- Oncological diseases.

Covariates:

Diagnoses of asthma were meticulously confirmed by licensed allergologists and pulmonologists. All control participants underwent thorough clinical evaluations to confirm the absence of asthma and other lung diseases. The severity of asthma among patients was assessed using the ACQ and ACT index [6,7].

Genotyping:

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

Genomic DNA was extracted from 200 μL of whole blood using the KingFisher Flex-Ready DNA Ultra 2.0 Prefilled Plates (USA), following the manufacturer's guidelines strictly.

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

Genotypic determination was carried out 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 [8,9].

Statistical Analysis.

The R Studio and Python software was utilized for conducting the statistical analyses. Descriptive statistics were employed for continuous variables, providing a comprehensive overview. This included calculating the arithmetic mean (X), median (Me), standard deviation (SD), coefficient of variation (v%), as well as the minimum (min) and maximum (max) observed values. These descriptive metrics were essential for elucidating the distribution characteristics and inherent variability within the data.

Odds ratios (OR) and their 95% confidence intervals (CI) were computed to evaluate the strength and direction of associations. $\chi 2$ tests were utilized to identify any noticeable differences in genotype and allele frequencies between the asthma patient cohort and the control group, aiming to substantiate their clinical implications.

Biophysical measures between the asthma and control groups were compared using Student's t-test. Throughout the analyses, a p-value threshold of $P < 0.05$ was adopted to signify statistical significance.

FDR (False Discovery Rate) analysis was employed to account for multiple comparisons when testing a multitude of SNPs (Table 4).

Results.

This study included a total of 600 individuals, with 300 patients in both the case and control groups (Table 1). Notably, the control group exhibited a prevalent residence in rural areas, while the asthma group comprised both urban and rural residents.

Table 1. Demographic and Clinical Characteristics of Asthma Patients in Case and Control Groups.

Group	Total Patients	Mean Age ± SD	Sex Ratio (M:F)	Smoking Status (Yes:No)
Case	300	24.80 ± 15.35	0.74:1	0.08:1
Control	300	24.99 ± 15.17	0.69:1	0.12:1

The case group's mean age of 24.80 years and standard deviation (SD) of 15.35 years suggest a broad age range. The control group has a mean age of 24.99 years and a standard deviation of 15.17 years, indicating comparable age variability.

The case group exhibits a higher proportion of females compared to males, with a male-to-female ratio of 0.74:1. The control group exhibits a male-to-female ratio of 0.69:1, suggesting a higher representation of females in the study.

Both groups exhibit a low prevalence of smoking. The case group had a smoking ratio of 0.08:1, which suggests a low prevalence of smoking. The control group had a prevalence ratio of 0.12:1, indicating a somewhat higher proportion of smokers compared to non-smokers, although non-smokers still constituted the majority.

Results of the statistical computations for the comparative analysis of two patient cohorts regarding the frequency of occurrence of SNPs associated with asthma development are depicted in Figures 1. Statistical calculations were conducted using the Mann-Whitney U test.

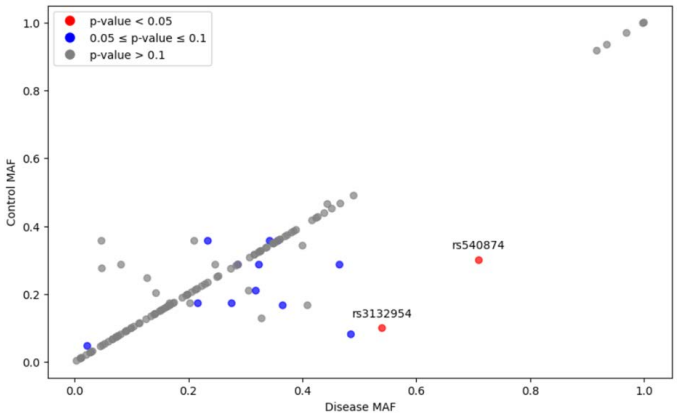

Figure 1. *Scatter Plot depicting the distribution of Minor Allele Frequency (MAF) for SNPs associated with asthma in experimental and control groups.*

The distribution of ACTN3 (rs540874) genotype frequencies in patients with asthma is as follows: 9% have the homozygous A/A genotype, 39% have the heterozygous A/G genotype, and 52% have the homozygous G/G genotype. The polymorphism exhibits a chi-square ($\chi 2$) statistic of 61.34 and a p-value of 4.78×10^{-14}, indicating a high level of statistical significance. The allele G has a Minor Allele Frequency (MAF) of 0.71 in cases and 0.30 in controls.

The genotypes for the second SNP, rs3132954, are distributed as follows: 43% of individuals are homozygous for the G allele (G/G), 23% are heterozygous (G/A), and 34% are homozygous for the A allele (A/A). The chi-square ($\chi 2$) statistic for this polymorphism is 54.69, with a p-value of 1.33×10^{-12}. The allele G has a Minor Allele Frequency (MAF) of 0.54 in cases and 0.10 in controls.

Based on the findings, the G/G genotype, which is the predominant allele in this community, may be associated with a heightened susceptibility to asthma. In contrast, the A/A genotype, which is less prevalent in individuals with asthma compared to those without asthma, may offer a certain degree of defense against the condition.

The G/G genotype in rs3132954 is linked to a higher susceptibility to asthma, as indicated by the higher occurrence of cases and the significant odds ratio. The A/A genotype is more commonly seen in individuals without asthma, suggesting that it may have a protective effect against the development of asthma.

The odds ratios and confidence intervals provided in the prior text do not align with the data in the table and so have been excluded from this amended text. Further investigation is necessary to ascertain the exact odds ratios for each genotype.

Tables 2 and 3 present a concise overview of the frequencies of genotypes and their interconnections.

The study's findings reveal genetic factors that are potentially involved in the underlying mechanisms of asthma. These findings can guide future research towards developing therapeutic options that specifically target these genetic variations.

Table 2. *Presentation of the results of 2 the most significant SNP concerning genetics in asthma susceptibility in Kazakh Population.*

Mapped Gene	RS number	Alleles	Chr	MAF
ACTN3	rs540874	A>G	chr11:66562261 (GRCh38.p14)	0.71
TSBP1	rs3132954	A>G	chr6:32343682 (GRCh38.p14)	0.54

The study suggests that for rs540874, the presence of the A/A genotype may be associated with a stronger contraction of respiratory muscles during inhalation, which is potentially beneficial in asthma. Conversely, the G/G genotype, which is associated with insufficient synthesis of alpha-actinin-3, may lead to less pronounced muscle contraction and thus more pronounced disorders of lung ventilation capacity during asthma attacks.

Table 3 details the allele frequencies of two SNPs in patients with asthma and controls. For each SNP, the genotype frequencies among the cases (asthma patients) and controls are compared, and the statistical significance is assessed. rs540874 and rs3132954 show a significant association with the condition, as indicated by the very low p-values.

The table 4 displays the outcomes of a statistical examination on a subset of Single Nucleotide Polymorphisms (SNPs) for a study encompassing 120 SNPs associated with a certain trait. The display provides the p-values obtained from individual association tests, as well as the modified p-values that have been corrected for multiple testing using the False Discovery Rate (FDR) method.

Discussion.

Our study's illumination of the genetic predispositions associated with asthma in the Kazakh population, particularly

Table 3. *Allele frequencies of two SNPs in patients with asthma.*

rs number	**Genotype Frequency**			X^2	**p-value**	**OR**	**95% CI**
	Genotypes	Cases	Controls				
rs540874	A/A	0,09	0,62	61,34	$4,78 \times 10^{-14}$	0,06	[0,024; 0,148]
	A/G	0,39	0,16				
	G/G	0,52	0,22				
MAF	(G)	0,71	0,30				
rs3132954	G/G	0,43	0,03	54,69	$1,33 \times 10^{-12}$	9,13	[2,39; 34,86]
	G/A	0,23	0,15				
	A/A	0,34	0,82				
MAF	(G)	0,54	0.10				

Table 4. *Results of FDR analysis to account for multiple comparisons when testing multiple SNPs.*

N	**SNP**	**p-value**	**p_adj-value (FDR)**
	rs9895098	0,273443	0,629805
	rs3933376	0,095253	0,474049
	rs2190097	0,155123	0,618923
	rs17775170	0,060340	0,181035
	rs9391997	0,135453	0,325072
	rs1861245	0,216771	0,362518
	rs12212193	0,246583	0,362518
	rs2647003	0,124884	0,362518
	rs12697352	0,227189	0,362518
	rs11236797	0,130468	0,365621
	rs274943	0,240626	0,431612
	rs12123821	0,114476	0,421612
	rs2589561	0,066289	0,431612
	rs11213940	0,066855	0,401612
	rs2549003	0,215105	0,408398
	rs2422254	0,069118	0,444818
	rs12661352	0,075251	0,444818
	rs72837826	0,075957	0,444818
	rs479844	0,078601	0,444818
	rs58521088	0,081177	0,444818
	rs6755198	0,081573	0,444818
	rs62408233	0,084494	0,444818
	rs13416449	0,085257	0,444818
	rs3132954	$1,33 \times 10^{-12}$	7.9135×10^{-12}
	rs60153262	0,101436	0,474049
	rs2025758	0,109912	0,474049
	rs41284471	0,110121	0,474049
	rs992969	0,110612	0,474049
	rs1295685	0,116811	0,483358
	rs7632381	0,137874	0,532908
	rs2229094	0,139562	0,532908
	rs9266629	0,143898	0,532908
	rs35614679	0,14655	0,532908
	rs9895436	0,152942	0,539796
	rs11071559	0,163654	0,554385
	rs6835638	0,168752	0,554385
	rs2844649	0,170935	0,554385
	rs10912564	0,179883	0,568052
	rs7650683	0,190495	0,580436
	rs10791824	0,193479	0,580436
	rs6594499	0,203081	0,587794
	rs141343442	0,205728	0,587794

	rs3828058	0,228831	0,622
	rs4795413	0,234215	0,622
	rs7370843	0,234444	0,622
	rs71625139	0,238433	0,622
	rs2065206	0,244719	0,624813
	rs143942614	0,252824	0,625463
	rs3732192	0,255397	0,625463
	rs10091870	0,267587	0,629805
	rs34104805	0,270059	0,629805
	rs540874	$4{,}78\times10^{-14}$	5.6882×10^{-13}
	rs9860547	0,283055	0,629805
	rs75861713	0,284468	0,629805
	rs17406680	0,288661	0,629805
	rs9372120	0,294652	0,631397
	rs1512226	0,308506	0,632911
	rs874953	0,310097	0,632911
	rs6454805	0,311181	0,632911
	rs7893324	0,317398	0,634796
	rs8103278	0,330628	0,650415
	rs4759229	0,33886	0,651142
	rs2675724	0,34185	0,651142
	rs12491785	0,351447	0,658963
	rs849139	0,358983	0,660962
	rs12413578	0,363529	0,660962
	rs1143869	0,377169	0,669283
	rs1837253	0,37926	0,669283
	rs12469459	0,442108	0,758483
	rs8089834	0,447424	0,758483
	rs12144049	0,448769	0,758483
	rs9290877	0,472056	0,77444
	rs13017455	0,477238	0,77444
	rs1898671	0,483624	0,77444
	rs3771175	0,484025	0,77444
	rs9275570	0,511858	0,799803
	rs4574025	0,513207	0,799803
	rs72743461	0,527866	0,812102
	rs13153019	0,541283	0,815888
	rs346835	0,553271	0,815888
	rs73786772	0,553562	0,815888
	rs9549238	0,557524	0,815888
	rs3772010	0,581087	0,840126
	rs1655558	0,599441	0,841002
	rs1381928	0,599732	0,841002
	rs55875222	0,602718	0,841002
	rs72702900	0,621337	0,841521
	rs12935657	0,624997	0,841521
	rs7047575	0,630155	0,841521
	rs4713555	0,641482	0,841521
	rs1552994	0,6449	0,841521
	rs12365699	0,645166	0,841521
	rs17145188	0,657266	0,848085
	rs10174949	0,668675	0,853628
	rs67768228	0,68734	0,863074
	rs4845604	0,690459	0,863074
	rs17642749	0,713311	0,880449
	rs7851246	0,719033	0,880449
	rs10167431	0,728642	0,881908

	rs2070901	0,734923	0,881908
	rs3826331	0,755393	0,897497
	rs16922576	0,768642	0,898322
	rs4673659	0,777023	0,898322
	rs2517611	0,792116	0,898322
	rs7523907	0,793167	0,898322
	rs1444782	0,821029	0,898322
	rs1950897	0,825713	0,898322
	rs1917534	0,826554	0,898322
	rs9895419	0,82682	0,898322
	rs16903574	0,830093	0,898322
	rs34290285	0,830948	0,898322
	rs3917339	0,849593	0,902591
	rs2245214	0,84994	0,902591
	rs1007027	0,860583	0,905877
	rs55646091	0,873334	0,911305
	rs11665213	0,90144	0,925802
	rs55730955	0,902657	0,925802
	rs3768321	0,955226	0,971416
	rs1821263	0,985821	0,994105
	rs1012307	1	1

through the ACTN3 rs540874 and TSBP1 rs3132954 genes, underscores the intricate tapestry of genetic and physiological factors at play in asthma pathogenesis. The identification of these significant genetic markers not only underscores the complexity of asthma's etiology but also points towards the physiological manifestations, such as bronchospasm, that exacerbate the condition's severity.

Bronchospasm is a significant physiological response characterized by the rapid movement of air through constricted bronchi, resulting in increased resistance to airflow and greater exertion of respiratory muscles during exhalation. The participation of skeletal respiratory muscles in both inhalation and exhalation, where the strength of muscular contraction changes with the depth of respiratory effort, is crucial for sustaining respiratory function [10,11].

Moreover, the susceptibility to bronchial obstruction can be ascribed to distinct anatomical and physiological characteristics, including the inadequate development of bronchial wall muscle fibers and immature respiratory muscles in infants, rendering their airways more susceptible to constriction. The coordinated functioning of the respiratory system, which includes the lungs, pulmonary circulation, respiratory control system, and muscular components of the chest, is essential for the breathing process in patients with asthma [10,11].

Findings from molecular genetic research, particularly investigations on the ACTN3 gene polymorphism that impacts the production of the alpha-actinin-3 protein in muscle fibers, provide valuable information about the molecular mechanisms involved in bronchospasm and the control of breathing in children with asthma. Studying the genetic foundations of asthma is crucial for deepening our comprehension and refining the diagnosis of this disorder. The genetic findings highlight the intricate nature of asthma, emphasizing the need to incorporate genetic data into the management and therapy approaches for asthma [12-14].

Furthermore, the exploration of TSBP1's role in asthma introduces a novel avenue for research, particularly in understanding how genetic variations influence the immune response and contribute to the inflammatory processes central to asthma. There is limited evidence about a direct correlation between TSBP1 (Thymic stromal lymphopoietin-binding protein 1) and asthma. The potential involvement of TSBP1 in modulating allergic reactions and inflammation highlights the necessity of integrating genetic data into asthma management strategies [15,16]. This approach not only promises more precise diagnostics but also opens the door to targeted therapies that address the specific genetic and molecular pathways implicated in asthma.

The involvement of Thymic Stromal Lymphopoietin-Binding Protein 1 (TSBP1) in asthma is a topic that is currently gaining attention, yet there is a scarcity of available literature on this subject. While our knowledge of TSBP1 is currently limited, its possible connections to the development of asthma deserve further attention. An area worthy of investigation is the expression patterns and tissue specificity of TSBP1. Examining the particular expression of TSBP1 in lung cells and tissues could provide insights into its potential role in the development of asthma. Although there is a scarcity of literature on the subject, doing association studies to assess the potential correlations between TSBP1 polymorphisms or expression levels could be beneficial in establishing its viability as a biomarker or therapeutic target [15,16].

By bridging the gap between genetic predispositions and the physiological responses characteristic of asthma, our research emphasizes the value of a comprehensive approach to asthma study. Investigating the genetic underpinnings alongside the physiological and molecular mechanisms offers a holistic view of asthma, paving the way for advancements in personalized medicine. Such integrated research efforts are crucial for developing effective management and therapeutic strategies,

ultimately improving the quality of life for individuals with asthma.

Study limitations.

This study has several limitations that should be acknowledged. First, the sample size, while sufficient for detecting significant associations, may limit the generalizability of the findings to the broader Kazakh population. Second, the study focused on specific SNPs within the ACTN3 and TSBP1 genes, which may not capture the full genetic complexity of asthma. Additionally, environmental factors, which could interact with genetic predispositions to influence asthma risk, were not extensively analyzed in this study. Future research should consider larger and more diverse cohorts, as well as the inclusion of environmental data, to better understand the genetic and environmental contributions to asthma in the Kazakh population.

Conclusion.

Ultimately, this study has greatly enhanced our comprehension of the genetic elements that contribute to the vulnerability of asthma in the Kazakh community. Our research highlights the intricate relationship between genetics and the environment in the development of asthma by discovering important genetic markers in the ACTN3 and TSBP1 genes. These discoveries not only improve our understanding of the fundamental molecular mechanisms of asthma but also open up possibilities for creating personalized medical strategies that are specifically designed based on individuals' genetic characteristics. In the future, it is crucial that we further investigate the practical consequences of these genetic variants, with the goal of incorporating these findings into medical treatment. Addressing this issue will necessitate collaborative endeavours in advancing genetic research, expanding the scope and diversity of study populations, and fostering the creation of inventive therapeutic approaches. In essence, our goal is to enhance the diagnosis, management, and treatment outcomes for asthma patients by gaining a more profound comprehension of the genetic foundation of asthma. This progress will represent a noteworthy advancement in the pursuit of tailored and efficient healthcare solutions.

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Conflicts of Interest.

The authors declare that they have no competing interests. There are no financial, personal, or other relationships with other people or organizations that could inappropriately influence, or be perceived to influence, this work.

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