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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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RELATIONSHIP OF ALLERGIC DISEASES, POLLEN EXPOSURE AND COVID-19 IN GEORGIA

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Abstract.

Allergic diseases have been recognized as one of the global health issues and affect about a third of the worldwide population. COVID-19 pandemic has raised concerns about the risk of infection and the severity of COVID-19 infection in patients with asthma and allergic rhinitis. The aim of our study was to define the relationships between pollen exposures and SARS-CoV-2 infection rates in Georgia, as well as to characterize the Covid-19 autoimmune and antiviral responses in Georgian allergic patients with different sensitization patterns.

Data on daily COVID-19 positivity rates, case fatality rates, and pollen concentrations from February 2020 to November 2022 were collected in Tbilisi, Kutaisi, and Batumi. Diagnostic parameters, including total IgE, specific IgE, eosinophil counts, anti-nuclear antibodies, and Covid-19 antibodies, were assessed in 181 atopic patients and 24 healthy controls with confirmed SARS-CoV-2 infection.

Laboratory findings revealed significant variations in eosinophil counts and total IgE levels among the groups. ANA positivity did not exhibit substantial differences between atopic patients and healthy controls. Individuals with indoor allergies displayed lower SARS-CoV-2-specific antibody levels, potentially explained by variations in adaptive immune responses. There was no correlation between pollen concentration and COVID-19 epidemiological characteristics, indicating that pollen had no effect on virus epidemiology.

Key words. Allergic diseases, pollen exposure, Covid-19.

Introduction.

Allergic diseases have been recognized as one of the global health issues and affect about third of the worldwide population. COVID-19 pandemic has raised concerns about the risk of infection and the severity of COVID-19 infection in patients with asthma and allergic rhinitis. A study conducted by Jackson et al. [1] found that allergic diseases and allergen exposure has an inverse relation with angiotensin-converting enzyme 2 (ACE-2) expressions, where COVID-19 requires this receptor to enter the host body [2,3]. A growing body of evidence indicates a reduced risk of both SARS-CoV-2 infection and COVID-19 severity associated with atopy. Increasing evidence suggests that atopic disease protects against severe COVID-19 illness owing to the underlying type 2 inflammatory process. COVID-19 may trigger the onset of autoimmune pathology; various autoantibodies have been described in association with COVID-19. Furthermore, histamine and immunoglobulin E (IgE) serum levels are found to be elevated in allergic rhinitis and asthmatic patients, which can down-regulate certain anti-viral responses, i.e., hyper-inflammation that mark the severity of various respiratory diseases, including COVID-19 [4]. Like various other respiratory diseases, coronavirus might worsen asthmatic symptoms in severe or uncontrolled patients but owing to Th2-skewed immunity (pertaining to the allergic and interferon-mediated response), which drives anti-immune response may protect against COVID-19 diseases [5]. These observations were quite interesting and contrasting according to the theoretical knowledge, where allergic diseases and asthma are known to increase with viral infections. This inverse correlation might support the idea that the triggering of immune responses by airborne pollen (i.e., hay fever) makes it difficult for COVID-19 to penetrate a new host. Moreover, this gives substantial sense to the idea that an activated-immune system seems to protect against COVID-19 viruses [6].

Pollens are considered as one of the primary triggers of respiratory allergies, causing 'pollinosis'. Pollens grains are known to be allergenic [7,8] and play a vital role in immune system activation [9,10]. They are considered anti-viral substances and have also shown anti-influenza effects [11,12].

Pollen is hypothesized to either increase, decrease, or has no effect on the risk of COVID-19 infection. It may reduce the risk by acting as an inhibiting factor towards viral infections, e.g., by downregulating ACE-2 in the nasal epithelium and subsequently protecting people especially those with asthma and allergic rhinitis against COVID-19. Conversely, pollen may increase the risk of COVID-19 transmission by acting as a carrier. Experimental studies have shown that viruses can exist inside pollen grains or on its outer surface, allowing it to persist in the atmosphere for up to weeks and travel over long distances [13].

Various publications have linked the SARS-CoV-2 infection rate to the pollen concentration in a specific area, the most recent being that of Damialis et al, who reported that higher airborne pollen concentrations were related to higher COVID-19 infection rates according to the data on 31 countries around the world [14]. However, how allergen exposure per se, and pollen exposure in particular, might influence SARS-CoV-2–induced inflammation and its clinical outcomes remains unknown. In vitro allergen exposure can attenuate antiviral response to some respiratory viruses. Nonetheless, with increasing pollen exposure associated with climate change, the interplay between pollen and respiratory viruses, including SARS-CoV-2, warrants consideration. It is postulated that pollen exposure, independent of allergic status, has a direct effect on antiviral defense within

the airway epithelium and therefore enhances susceptibility to SARS-CoV-2 infection [15].

Aims.

The aim of our study was to define the relationships between pollen exposures and SARS-CoV-2 infection rates in Georgia, as well as to characterize the Covid-19 autoimmune and antiviral responses in Georgian allergic patients with different sensitization patterns. The findings of the study can help to inform evidence-based public health policy aiming at lowering the impact of Covid-19, particularly in populations plagued by allergic illnesses.

Methods.

Study participants:

181 atopic patients and 24 healthy controls with confirmed SARS-COV-2 infection were recruited in the study. The inclusion criteria were positivity of skin-prick or specific IgE testing of patients attended to the allergy clinic during the 2021-2022 years period. Atopic patients were categorized in three groups: 1) sensitized to pollen allergens (any of trees, grasses and weeds) "pollen allergy group" (59 patients); 2) sensitized to pollen and indoor allergens (house dust mites, molds and epidermal allergens) together "pollen+indoor allergy" group (55 patients) and 3) sensitized to indoor allergens only – "indoor allergy group" (67 patients). According to Covid-19 symptoms, all patients were stratified into asymptomatic, mildly symptomatic (upper respiratory tract infections only), moderately symptomatic (lower respiratory tract infections, high fever, or severe gastrointestinal symptoms) and severely symptomatic (admitted into health care facility to treat disease) using the clinical questionnaires.

Ethical considerations:

This study was approved by Institutional Ethical Committee of Center of Allergy and Immunology, Tbilisi, Georgia. All procedures were performed in accordance with the ethical standards and informed consents were obtained before the enrollment procedure based on Law of Georgia "On Health Protection" (Chapter II, Article 11).

Data collection:

Daily COVID-19 cases, positivity rate and case fatality rate in 3 main cities Tbilisi, Kutaisi, and Batumi at the period from 4th February 2020 till 29th November 2022 were obtained from NCDC data base. The information regarding hospitalization and death was not included in the analysis, as it was only 2 cases of hospitalization and no death due to Covid-19 in study population.

Pollen sampling and analysis:

The pollen data was obtained at the period from 4th February 2020 till 29th November 2022. The airborne pollen monitoring for evaluation of concentration of allergic pollen was performed in Tbilisi, Kutaisi, and Batumi with a Burkard Seven Day Volumetric Spore-trap (Burkard Manufacturing Co Ltd, UK), following the recommendations and protocols of European Aerobiology Society. Pollen concentration was calculated and expressed as the number of pollen grains per cubic meter of air (p/m^3).

Blood sampling:

Blood sampling was done for measuring of diagnostic parameters (total IgE, inhalant allergen specific IgE by ImmunoCAP, differential blood count (counts of eosinophils), anti-nuclear antibodies (IFA) and antibodies against Covid-19 during the recruitment procedure. The Immunocap test for specific and total IgE measurement was performed according to the manufacturer's instructions (Thermo Fisher Scientific, Uppsala, Sweden).

Covid -19 antiviral response:

Laboratory testing was conducted using the Abbott ARCHITECT i2000 system (Abbott Diagnostics). Chemiluminescent microparticle immunoassays (CMIA) ARCHITECT SARS-COV-2 IgG II Quant and ARCHITECT SARS-COV-2 IgG were used for detection immunoglobulin class G (IgG) antibodies to SARS-CoV-2 in serum samples. The SARS-CoV-2 IgG II Quant assay is an automated, two-step immunoassay for the qualitative and quantitative determination of IgG antibodies to the receptor binding domain (RBD) of the S1 subunit of the spike protein of SARS-CoV-2, and ≥50 AU/ml threshold was used for classification as a positive result. ARCHITECT SARS-CoV-2 IgG assay is a fully automated, two-step immunoassay for the qualitative detection of IgG antibodies to the nucleocapsid (N) protein of SARS-CoV-2. Results are reported as an Index (ratio of the chemiluminescent signal between the samples and a calibrator), with values >1.4 indicating a positive result. The procedure was performed according to the manufacturer's instructions.

Covid-19 autoimmunity response:

All patients (including controls) were screened for anti-nuclear antibodies (ANAs) by IIFA (Indirect Immunofluorescence Assay) on HEp-2 cells (Bio-Rad Laboratories, Hercules, CA). Twofold serial dilution in 0.01 M phosphate buffered saline (PBS) was used for autoantibody titration. A positive and a negative reference control were tested in each slide for quality control. Pre-diluted sera were overlaid on fixed HEp-2 cells for 20 min at room temperature. Slides were washed for 10 min with PBS overlaid with fluorescein conjugated (FITC) antiserum and incubated for an additional 20 min. The slides were evaluated with a fluorescence microscope (at x 400-fold magnification). A titer of 1:80 or higher was considered to indicate ANA positivity.

Statistical evaluation:

All the statistical analyses were performed using IBM SPSS Statistics version 21 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used with mean, minimum and maximum values to describe continuous variables; absolute number and percentage were reported for categorical variables. Intergroup difference was calculated using the analysis of variances by Anova test. The degree of relationship between the quantitative variables was analyzed using Pearson Correlation test (r). The strength of a correlation was stratifying as followings: weak (/r/<0.3), moderate (0.3≤/r/<0.7), or strong (/r/≥0.7). Statistical significance was defined as $p < 0.05$.

Results.

The mean age of studied population (including controls) was 21.1 ± 15.1 years, females 42.4%, the mean recruitment

Table 1. *Comparisons of various characteristics of study groups and health control.*

Study population characteristics	**Healthy Control (N=24)**	**Pollen allergy group (N=59)**	**Pollen + indoor allergy group (N=55)**	**Indoor allergy group (N=67)**	**Anova between groups (p-value)**
Patient characteristics					
Age years old (mean ± SD)	24,3 ± 21,0	24,9 ± 14,3	24,2 ± 14,4	14,2 ± 11,4	0,000
Sex (female) (%, 95% CI)	54,2 (32,7-75,6)	49,2 (36,0-62,3)	38,2 (24,9-51,4)	35,8 (24,0-47,6)	0,259
Months after last Covid-19 positive testing (mean, 95% CI)	3,1 (1,8 -4,3)	4,5 (3,3 - 5,6)	5,3 (4,1 - 6,5)	4,2 (3,3 - 5,2)	0,158
Fully Covid-19 vaccination status (%, 95% CI)	33,3% (12,9-53,7)	27,1% (15,4-38,8)	23,6% (12,0-35,2)	29,8% (18,6-41,0)	0,806
Laboratory characteristics					
ANA postivity (%, 95% CI)	8,3% (3,5-20,2)	23,7% (12,5-34,9)	16,3% (6,3-26,5)	14,9% (6,2-23,7)	0,341
Eosinophiles (absolute# 10^9/**l**, 95% CI)	0,18 (0,12-0,25)	0,46 (0,32-0,58)	0,46 (0,26-0,65)	0,61 (0,34-0,87)	0,002
Total IgE (kU/l, geometric mean ± SE)	20,7 ±12,1	155,2±59,5	288,2±48,9	190,1±66,8	0,016
SARS-Cov-2 S1- specific antibodies (positivity %, 95% CI)	95,8% (87,2-104,4)	94,9% (89,9-100,7)	95,9% (90,1-100)	95,6% (90,5-100)	0,986
SARS-Cov-2 S1- specific antibodies (mean AU/ml, 95% CI)	10530,8 (4495,1-16566,6)	9017,7 (6062,3-13171,9)	9675,8 (6179,6-13171,9)	2725,9 (1304,8-4147,1)	0,001
Nucleocapsid protein of SARS-CoV-2 antibodies (positivity %, 95% CI)	52,2% (30,1-74,3)	68,8% (51,8-85,7)	47,6% (24,3-70,9)	64,7%(47,8-81,6)	0,361
Nucleocapsid protein of SARS-CoV-2 antibodies (mean of index, 95% CI)	2,6 (1,1-4,0)	4,8 (3,4-6,2)	2,5 (1,1-3,9)	3,1 (2,1-4,1)	0,042
Atopic diseases					
Allergic rhinitis (%, 95% CI)	N/A	96,3% (94,9-101,7)	94,5% (88,3-100,7)	83,6% (74,5-92,7)	0,007
Asthma (%, 95% CI)	N/A	8,5% (1,2-15,8)	21,8% (10,6-33,1)	16,4% (7,3-25,5)	0,140
Urticaria (%, 95% CI)	N/A	16,9% (7,1-26,8)	10,9% (2,4-19,4)	11,9% (4,0-19,9)	0,592
Atopic conjunctivitis (%, 95% CI)	N/A	42,4% (29,4-55,4)	40,0% (26,6-53,4)	4,5% (0,6 - 9,6)	0,000
Immunotherapy (%, 95% CI)	N/A	8,4% (1,2-15,8)	18,2% (7,7-28,7)	7,5% (1,0-13,9)	0,198
Family history of allergy					
Asthma (%, 95% CI)	N/A	6,0 (2,5-14,6)	6,1 (2,5 - 14,7)	16,0 (5,5 - 26,5)	0,374
Rhinitis (%, 95% CI)	N/A	39,4 (21,7-56,9)	33,3 (16,3 - 50,3)	30,0 (16,8 - 43,2)	0,738
Eczema (%, 95% CI)	N/A	0	0	4,0 (1,6 -9,6)	0,444
Allergy treatment last 12 months (%, 95% CI)	N/A	87,8 (76,1-99,6)	87,5 (75,4-99,6)	90,0 (81,4-98,6)	0,965
Steroids (%, 95% CI)	N/A	21,2 (6,5-37,0)	21,8 (6,7-37,1)	40,0 (25,9-54,1)	0,075
Anti-histamines (%, 95% CI)	N/A	78,8 (64,1-93,5)	71,8 (55,4-88,3)	78,0 (66,1-89,9)	0,843
Covid-19 symptoms					
Asymptomatic (%, 95% CI)	0,0	25 (4,2-45,8)	23,1 (5,7-40,4)	15,6 (2,3-28,9)	0,148
Mildly symptomatic (%, 95% CI)	94,4 (82,7-106,2)	60 (36,5-83,5)	61,5 (41,5-81,6)	53,1 (34,8-71,4)	0,026
Moderate symptomatic (%, 95% CI)	5,6 (0,2-17,3)	15 (0,3-32,1)	11,5 (0,1 - 24,7)	28,1 (11,7-44,6)	0,164
Severe symptomatic (%, 95% CI)	0,0	0,0	3,8 (0,4-11,8)	3,1 (0,3-9,5)	0,721

N/A - not available information for healthy control group.
P-value less than 0,05 marked by yellow color.

Table 2. *The correlation between the daily concentration of pollens and COVID-19 in three Georgian cities -Tbilisi, Kutaisi and Batumi.*

		Pearson correlation test	**Pollen grains per cubic meter**
City	%	Correlation coefficient /r/	Sig. (2-tailed)
Tbilisi	Positivity rate	-0,062	0,000
	Case fatality rate	0,002	0,952
Kutaisi	Positivity rate	0,137	0,000
	Case fatality rate	0,089	0,011
Batumi	Positivity rate	-0,028	0,390
	Case fatality rate	0,013	0,707
P-value less than 0,05 marked by yellow color			

time after COVID-19 positive test was 4.4 ± 4.1 months and vaccination rate were 27.8%. The healthy control and pollen allergy groups exhibited similar mean ages (24.3 vs. 24.9 years), while the indoor allergy group displayed a markedly lower average age (14.2 years). Sex distribution showed slight variations, but not statistically significant (Table 1).

Based on the data (Table 1) represents the percentage of individuals with positive ANA test results in different groups and the ANOVA test, there is no strong evidence to suggest significant differences in ANA positivity between the atopic patients groups. In positive cases titer was not more than 1:160 and more frequent pattern was AC-2 (according to the International Consensus on Antinuclear Antibody Patterns (ICAP)).

The analysis of laboratory results revealed that the eosinophils absolute count and total IgE levels demonstrated significant discrepancies across the groups. Particularly, the indoor allergy group exhibited the highest eosinophil count (0.61) compared to the healthy control group (0.18), while the pollen allergy and pollen + indoor allergy groups displayed intermediate values. Total IgE levels were notably elevated in the pollen + indoor allergy group (288.2 kU/1), followed by the indoor allergy group (190.1 kU/1). The healthy control group exhibited the lowest total IgE level (20.7 kU/L). Comparative analysis of immunological responses to SARS-CoV-2 revealed significant difference. Particularly, the healthy control group have the highest mean SARS-Co V-2 SI-specific antibody levels compared to the other groups, with mean value 10530.8 AU/ml (95% CI: 4495.1-16566.6 AU/ml). The lowest value (mean value 2725.9 AU/ml, 95% CI: 1304.8-4147.1) was observed among the individuals sensitized to indoor allergens only. The variance analysis by Anova test reveals significant differences in nucleocapsid protein antibody levels ($p = 0.042$) across the groups. The pollen allergy group displays the highest mean index value (4.8), followed by the indoor allergy group (3.1), pollen + indoor allergy group (2.5), and healthy control group (2.6).

Figure 1 express the difference between groups for both investigated antiviral responses; the results suggest that individuals with indoor allergies tend to have lower levels of SARS-CoV-2 SI-specific antibodies compared to individuals without allergies (healthy control group), with pollen allergies or a combination of pollen and indoor allergies. The differences between the allergy groups and the healthy control group for nucleocapsid antibodies may not be as substantial and the confidence intervals overlap, indicating some degree of uncertainty in the estimates.

Allergic rhinitis and atopic conjunctivitis were the major diagnoses for both groups sensitized to pollen allergens. Asthma was more prevalent in the pollen + indoor allergy group (21.8%), followed by the indoor allergy group (16.4%). Immunotherapy was administered in varying proportions across the allergic groups, with the highest prevalence seen in the pollen+ indoor allergy group (18.2%). Despite the observed most prevalent family history of asthma among indoor allergy group and slight difference of family history of rhinitis between groups, this is not significant and could not influence on any important characteristics. No special differences between allergy treatment strategy for atopic patients was revealed, more that 75% of them used the anti-histamine medication during the last 12 months and 40.0% of patients sensitized only to indoor allergens required steroids for management of their allergic symptoms.

As it was defined in the methodology Covid-19 symptoms were stratified in 4 groups. Healthy controls exhibited the highest proportion of mildly symptomatic cases (94.4%), while the indoor allergy group had the highest proportion of moderately symptomatic cases (28.1%). The prevalence of severe symptomatic cases was minimal in all groups, as among recruited patients it was only 2 cases of hospitalization due to Covid-19.

In Figure 2 we can see the graph corresponding to the three investigated cities of Georgia in which a correlation between

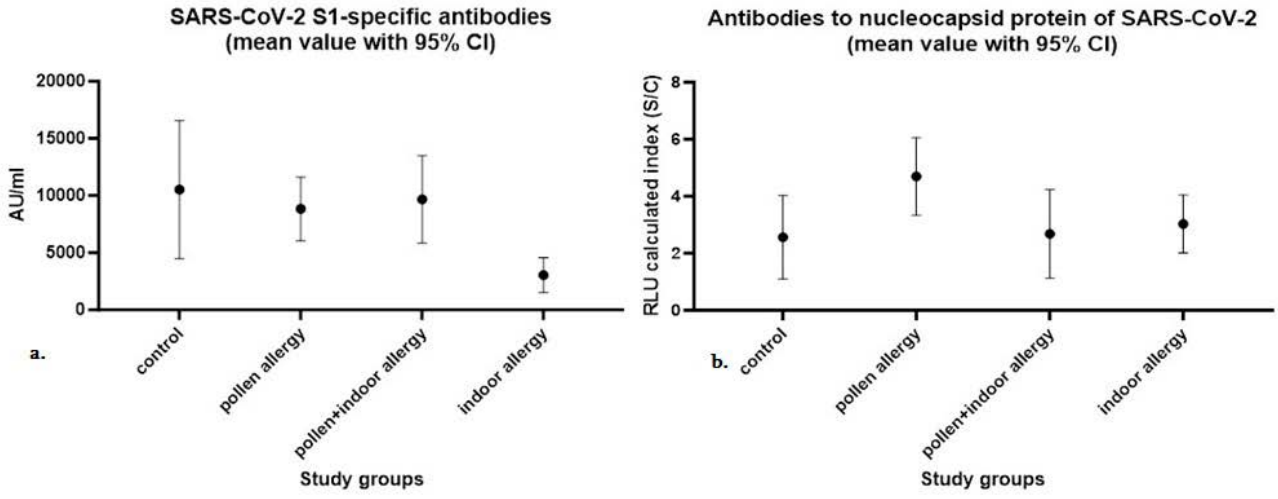

Figure 1. *Comparison SARS-CoV-2 IgG antibodies responses in study groups and health control.*

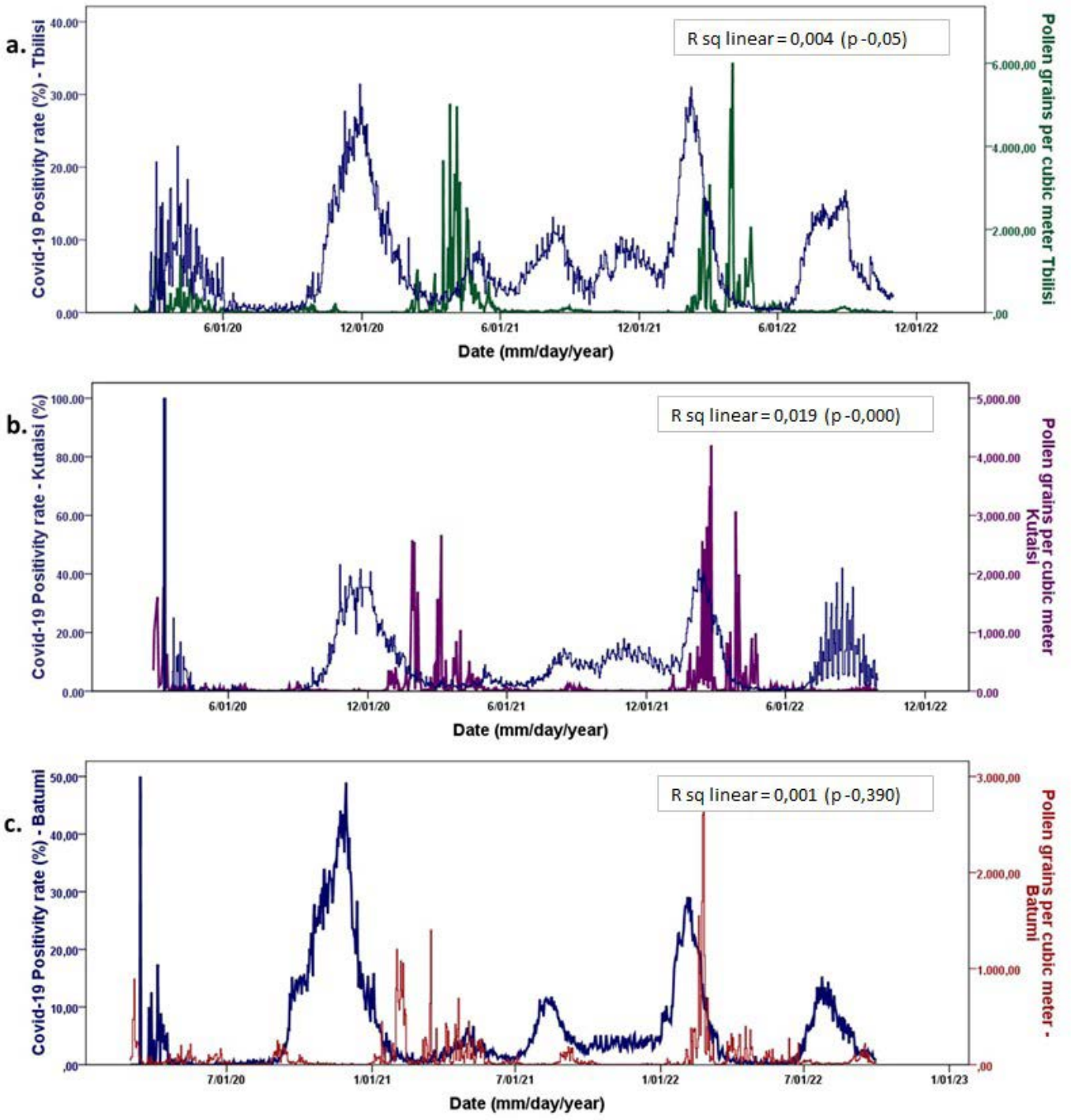

Figure 2. *The correlation between the daily concentration of pollens and Covid-19 positivity rate in three Georgian cities at the period of February 2020 - November 2022 (a. - Tbilisi, b. - Kutaisi and c.- Batumi). "R sq linear" represents the coefficient of determination for a linear regression model, but observed low R-squared value in all three cities may not well explaining the variability in the data.*

total daily pollen concentrations and daily cases of COVID-19 between 4th of February 2020 and 29th of November 2022 is carried out.

By statistical analysis of the data, we found that there slightly different relationship between the daily cases of COVID-19 and the total daily concentration of pollen between investigated cities - Tbilisi, Kutaisi, and Batumi. Once these data were available, a Pearson correlation was performed to determine whether there was a significant relationship between total pollen concentrations and Covid-19 positivity and case fatality rates (Table 2).

In Kutaisi weak positive correlation of daily pollen concentration and Covid-19 both rates (for positivity r =0.137, p 0.000 and case fatality r =0.089, p – 0.011) was obtained. In Tbilisi positivity rate and pollen concentration correlation was weakly negative (r=-0.062, p – 0.000).

Discussion.

The impact of allergic disorders on the progression of Covid-19 is controversial. Recent studies have revealed fascinating findings that allergic diseases may provide some sort of protection against Covid-19 [16,17]. However, there is contradictory information, as another study suggests that Covid-19 can be more severe in patients with allergic rhinitis and asthma, particularly non-allergic asthma [18].

In our research, we focused on individuals sensitized to both pollen and indoor allergens. The examinations occurred several months after Covid-19 testing, with an average duration of 4.4 months, aiming to uncover distinctive features in the laboratory characteristics of these patients. It is widely recognized that persistent exposure to allergens in individuals with inhalational allergies can result in chronic inflammation of the airways and skin, consequently heightening susceptibility to infections [19,20]. In our cohort, inhalational allergies (allergic rhinitis up to 96.3% and atopic conjunctivitis up to 42.4%) were prevalent and accompanied by increased values for some laboratory characteristics (total IgE and absolute eosinophil count), especially observed in patient groups sensitized to indoor allergens. Our results align with previous researches indicating a strong connection between elevated total IgE levels (> 100 kU/l) and a history of wheezing, asthma, and allergic manifestations, as well as atopy. Additionally, there is an association between increased absolute eosinophil count and the presence of allergic diseases, along with specific IgE antibodies to grass pollen and mites, consistent with findings in other studies [21-23]. The elevated absolute eosinophil count observed in patients after Covid-19 may be linked to the activation of mast cells and eosinophils by SARS-CoV-2 [24]. In a study by Licari et al. (2020), it was demonstrated that allergic children exhibit higher eosinophil counts without experiencing dyspnea symptoms compared to COVID-19 patients. Eosinophils are immune cells known to aid in the recovery from specific viral infections, including COVID-19 [25,26].

Antibodies directed against nuclear, cytoplasmic, and soluble autoantigens have been thoroughly documented following viral infections [27,28]. However, their precise significance has remained unclear. In this investigation, we employed highly sensitive assays to identify ANA (anti-nuclear antibodies) in individuals following SARS-CoV-2 infection. Our findings revealed a slightly higher ANA positivity in atopic patients compared to healthy controls. Nevertheless, as the difference did not reach statistical significance, interpreting the diagnostic value of autoantibody positivity several months after recovering from acute viral infections proves challenging.

Serological tests are a powerful tool in the monitoring of infectious diseases and the detection of host immunity, thus the testing for SARS-CoV-2-specific antibodies is most important for assessment of the degree of protection. In keeping with previous literature, we observed that SARS-Cov-2 S1 and nucleocapsid protein antibodies still have detectable levels up to 4.4 months after natural infection, ranging from 95.6% to 95.9% and 47.5% to 68.8% respectively (across all groups and healthy controls) and nucleocapsid protein antibodies tend to disappear more quickly than SARS-Cov-2 S1 antibodies [29]. A noteworthy discovery in this study was the variation in antibody levels among the groups, with individuals sensitized to indoor allergens exhibiting the lowest SARS-Cov-2 S1 value at 2725.9 AU/ml. This finding could theoretically be attributed to differences in adaptive immune responses among atopic patients sensitized to various aeroallergens. This is supported by previous knowledge [30] indicating that in hosts sensitized to specific predicted aeroallergens, such as Dermatophagoides species and Aspergillus fumigatus, identified similarities with the SARS-CoV-2 proteome might confer protection by preventing an overwhelming Th1 response and the associated cytokine storm. Additionally, allergen-specific T cells may develop a memory response against heterologous SARS-CoV-2 epitopes, offering a faster and more efficient immune reaction. Conversely, such heterologous immune responses could have an adverse outcome by attenuating the antiviral response.

COVID-19 presents a range of clinical manifestations, spanning from asymptomatic cases to mild and severe forms. Interestingly, individuals with allergic diseases do not appear to exhibit distinct symptoms or an elevated risk of severe disease, which contradicts the typical pattern seen in viral infections that tend to exacerbate asthma and other allergic conditions. This raises the question of what specific features in allergic diseases or asthmatic patients might be associated with a reduced potential for COVID-19 severity. Through a comparison of COVID-19 symptoms across groups, we discovered that the indoor allergy group had a lower percentage of individuals with mild symptoms (53.1% compared to 94.4% in healthy controls or 60% in the pollen allergy group) and a higher proportion with moderate symptoms compared to other groups. Notably, there was no observed association between the use of oral corticosteroids in the year before COVID-19 infection and an increased risk of more severe symptoms. Further studies are needed to explore the involved pathogenetic mechanisms and potential clinical implications of underlying aeroallergen sensitization on the immune response to SARS-CoV-2.

Co-exposure to airborne pollen enhances susceptibility to respiratory viral infections, regardless of the allergy status [31]. Pollen exposure weakens the body's innate defense against respiratory viruses. According to a recent report of 31 countries [15], higher airborne pollen concentrations correlate with increased SARS coronavirus-2 infection rates. To explore this association, we examined the relationship between SARS-CoV-2 infection rates and pollen concentrations in three major cities in Georgia – Tbilisi, Kutaisi, and Batumi.

According to the document published on 4 August regarding the epidemiological situation in Georgia on the basis of data from January 2020 to June 2022, the first case of COVID-19 was detected in Georgia on February 26, 2020. In the period from 2020 to 2022, the positivity rate for testing was 9.4%. The maximum positivity rates for each year were recorded in November 2020 – 25.2%, August 2021 – 10.3% and February 2022 – 29.9% [source in Georgian language only].

Upon analyzing the datasets pertaining to pollen counts and Covid-19 in three Georgian cities, it becomes evident that the correlation between daily pollen concentration and two key epidemiological indicators of COVID-19 (positivity rate

and case fatality rate) varies among cities. Specifically, there is a weak negative correlation for Tbilisi and a weak positive correlation for Kutaisi. These observed differences may be attributed to various environmental factors, as the cities are situated in different regions (the West and East parts of the country) with distinct climate zones. Notably, the most significant outcome from this segment of our investigation is the very weak correlation between COVID-19 positivity rate and daily pollen concentration for Tbilisi (/r/ 0.062) and Kutaisi (/r/ 0.137), with the association not being statistically significant for Batumi. Consequently, we can assert that, at present, there is no discernible association between pollen exposure and COVID-19 in Georgia. However, a definitive conclusion cannot be drawn due to limited evidence, underscoring the need for further research to elucidate how pollen bio-aerosols might influence virus survival.

This study has several limitations. Firstly, the study cohort was randomly selected from the outpatient allergy clinic database based on sensitization to aeroallergens (pollen and indoor) and a positive COVID-19 test conducted a few months prior. As a result, the study cohort was relatively young, with a mean age of 21 years, impacting both vaccination status and certain laboratory outcomes. Secondly, only two patients among the atopic individuals under study were hospitalized due to COVID-19. Consequently, we lacked the opportunity to assess and compare atopic patients experiencing severe Covid-19 symptoms. Thirdly, the data for present study are collected on average 4.4 months after COVID-19 positivity and not include the acute phase of the virus, which still requires future research. Fourthly, our analysis focused on the daily concentrations of pollen and specific epidemiological rates of Covid-19, excluding other environmental variables (such as temperature, humidity, etc.) from the analysis.

Conclusion.

In conclusion, we can state that, in Georgia, there is no association between pollen concentration and COVID-19 epidemiological parameters, thus we didn't find an influence of pollen on virus epidemiology. The investigation Covid-19 autoimmune and antiviral responses in Georgian allergic patients with different sensitization patterns revealed that the individuals with indoor allergies exhibited the lowest levels of SARS-CoV-2-specific antibodies, potentially explained by differences in adaptive immune responses.

Conflict of interest.

The authors declare that they have no conflict of interest.

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