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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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# EPIDEMIOLOGICAL AND CLINICAL FACTORS ASSOCIATED WITH COVID-19 REINFECTION IN PATIENTS TREATED IN A HIGH-ALTITUDE REGION

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## Abstract.

**Background:** The COVID-19 pandemic has underscored the challenge of SARS-CoV-2 reinfection, particularly with the emergence of new variants. This study aimed to identify epidemiological and clinical factors associated with COVID-19 reinfection in patients treated in the Cusco Region of Peru during 2022, a high-altitude area with unique demographic and geographic characteristics.

**Methods:** A retrospective, observational, case-control study was conducted, analyzing 216 patients (108 reinfection cases and 108 primary infection controls). Data were collected from clinical records and analyzed using statistical methods, including chi-square tests and multivariate regression. The study focused on demographic, epidemiological, and clinical factors, with statistical significance set at $p < 0.05$.

**Results:** Males had a 1.51 times higher risk of reinfection compared to females ($p < 0.05$). Patients from regions outside Cusco had a 16.03 times higher risk of reinfection than local residents ($p < 0.05$). No significant associations were found between reinfection and clinical factors such as symptoms or comorbidities. The overall reinfection rate was 0.97%, consistent with global trends.

**Conclusion:** The findings suggest that high altitude may confer protective effects against reinfection, potentially due to physiological adaptations to hypoxia. Males and individuals with interregional mobility were identified as high-risk groups. These results highlight the need for tailored public health strategies in high-altitude regions, focusing on surveillance and prevention for vulnerable populations. Further research is recommended to explore the biological mechanisms underlying these findings and to assess the impact of emerging viral variants on reinfection dynamics.

**Key words.** COVID-19, reinfection, altitude, risk factors, public health.

## Introduction.

Coronaviruses (CoV) encompass a large family of viruses that cause diseases ranging from the common cold to more severe and complex illnesses. The Coronavirus Disease (COVID-19) pandemic has had a profound impact on public health, economies, and societies worldwide since its emergence in December 2019 [1,2]. While initial efforts focused on mitigating the spread of the virus and reducing the morbidity and mortality associated with primary infections, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) reinfection has emerged as a significant challenge [3]. Reinfection is defined as the confirmed detection of the virus in a previously infected individual after a period during which PCR tests were negative, suggesting a new exposure to the pathogen rather than prolonged viral persistence [4].

As SARS-CoV-2 has evolved, multiple variants with varying degrees of transmissibility and immune evasion have emerged. Variants such as Delta, Omicron, and their subvariants have demonstrated an increased ability to evade immunity generated by prior infections or vaccination, leading to a rise in reinfection cases [5]. Several studies have reported that reinfections can occur between one and three months after the initial infection, with some documented cases occurring even beyond 90 days. The clinical severity of these reinfections varies, ranging from asymptomatic cases to severe illness requiring hospitalization, highlighting the importance of understanding the factors predisposing individuals to reinfection [4].

Epidemiological and clinical factors such as age, the presence of comorbidities, individual immune responses, exposure to new variants, and vaccination coverage have been identified as determinants of susceptibility to reinfection. Additionally, recent studies have suggested that reinfection may be associated with an increased risk of long-term complications, including post-COVID-19 syndrome and higher mortality rates [6-8]. However, there are gaps in the scientific literature regarding how these factors interact in specific populations and in geographic regions with unique characteristics.

The Cusco region in Peru has particular geographic and sociodemographic conditions that could influence the dynamics of SARS-CoV-2 transmission and reinfection. Located at over 3,500 meters above sea level, it has been hypothesized that the relative hypoxia at high altitude may alter the immune response of the resident population, affecting susceptibility and the clinical course of the disease [9]. Additionally, Cusco is an international tourist destination, which implies a constant flow of visitors and the potential introduction of new viral variants. These characteristics make it imperative to conduct a detailed analysis of the factors associated with reinfection in this population.

In this context, the present study aims to determine the epidemiological and clinical factors associated with COVID-19 reinfection in patients treated in the Cusco Region. Identifying these factors will generate relevant scientific evidence for designing disease prevention and control strategies in regions with similar conditions, thereby optimizing public health policies and the healthcare response to future waves of infection.

## Methods.

### Study design:

This is an observational, retrospective, cross-sectional, case-control epidemiological study. The study design was based on a

comparison of two groups: patients with COVID-19 reinfection and patients with primary COVID-19 infection. Epidemiological and clinical factors associated with reinfection were analyzed using statistical tests to determine potential associations.

**Population and Sample:**

The study population consisted of all cases of COVID-19 reinfection treated and recorded by the Cusco Regional Health Directorate during 2022. The sample size was calculated using the EPIDAT 4.2 software from the Pan American Health Organization (PAHO). Parameters included an exposed case proportion of 50%, an exposed control proportion of 33.3%, an expected odds ratio of 2.0, a confidence level of 95%, and a power of 80%. This yielded a sample size of 108 reinfection cases and 108 primary infection controls, maintaining a 1:1 ratio.

**Inclusion and exclusion criteria:**

Cases included patients over 18 years of age with a confirmed diagnosis of COVID-19 reinfection (according to MINSA/ WHO criteria), recorded by the Regional Health Directorate of Cusco in 2022. Eligibility required complete clinical records and a minimum interval of 90 days between infections. Controls were patients with a confirmed primary COVID-19 infection, with no prior history of the disease, matched by age (±5 years), sex, and comorbidities. Exclusion criteria included incomplete records, diagnoses not confirmed by PCR or antigen testing, acute respiratory co-infections, severe immunosuppression (e.g., uncontrolled HIV, chemotherapy), and duplicate data.

**Sampling:**

Non-probabilistic sampling was used, with participants selected based on predefined inclusion and exclusion criteria. Case and control assignments were made using clinical records available at the Cusco Regional Health Directorate.

**Data Collection:**

Data were collected using a document analysis technique. The instrument used was a registration form designed to extract relevant information from the electronic medical records of patients treated in 2022.

**Statistical Analysis:**

Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) version 25. The chi-square test was applied to evaluate associations between variables, and multivariate regression analysis was conducted to determine risk factors, with a statistical significance level of $p < 0.05$.

**Ethical Considerations:**

The study was approved by the Ethics Committee of the Universidad Andina del Cusco, through report N°004-2023-CIEI-UAC, signed on December 1, 2023. The study was conducted in accordance with the ethical principles of health research. Approval was obtained from an institutional ethics committee, and the confidentiality of personal data was ensured through anonymization. Since anonymized secondary data—previously collected with signed informed consent during patient care—were used, no additional participant consent was required.

## Results.

The reinfection rate was calculated by dividing confirmed reinfection cases (n=108) by the total number of COVID-19 patients registered in DIRESA Cusco-2022 (n=11,134), following MINSA guidelines (new episode ≥90 days after the first, with positive test and symptoms) resulting 0.97. Cases without intermediate confirmation or incomplete records were excluded to ensure accuracy.

A total of 216 patients were included in the study, evenly distributed into two groups: 108 primary infection cases and 108 COVID-19 reinfection cases. Regarding demographic characteristics, the majority of primary infection cases occurred in the 27-59 age group, representing 68.5% (n = 74/108). Similarly, in the reinfection group, 76.9% (n = 83/108) belonged to the same age group. In terms of sex, primary infection cases were predominantly female (64.8%, n = 70/108), while reinfection cases were more frequent in males (54.6%, n = 59/108) (Table 1).

***Table 1.*** *Distribution of non-reinfection and COVID-19 reinfection cases according to age, sex and origin; Cusco-Peru Region.*

| | | Non-reinfection | | Reinfection | |
|---|---|---|---|---|---|
| | | N° | % | N° | % |
| Age | 0 to 5 years old | 0 | 0.0% | 0 | 0.0% |
| | 6 to 11 years old | 2 | 1.9% | 0 | 0.0% |
| | 12 to 18 years old | 2 | 1.9% | 2 | 1.9% |
| | 19 to 26 years old | 11 | 10.2% | 18 | 16.7% |
| | 27 to 59 years old | 74 | 68.5% | 83 | 76.9% |
| | Over 60 years old | 19 | 17.6% | 5 | 4.6% |
| Gender | Female | 70 | 64.8% | 49 | 45.4% |
| | Male | 38 | 35.2% | 59 | 54.6% |
| Department | Cusco | 103 | 95.4% | 104 | 96.3% |
| | Other Department | 5 | 4.6% | 4 | 3.7% |
| Total | | 108 | 100.0% | 108 | 100.0% |

In the analysis of epidemiological factors associated with COVID-19 reinfection in patients treated in the Cusco Region, two factors showed statistically significant associations ($p < 0.05$): patient sex and geographic origin. The results indicate that males have a 1.51 times higher risk of COVID-19 reinfection compared to females. Additionally, patient origin was a determining factor, as those from other regions had a 16.03 times higher risk of reinfection compared to residents of the Cusco Region (Table 2).

On the other hand, other factors analyzed, such as occupation, age over 65 years, vaccination status, number of doses received, and type of vaccine administered, did not show a statistically significant association with COVID-19 reinfection.

Regarding clinical factors, various symptoms and pre-existing conditions were evaluated, including cough, sore throat, nasal congestion, difficulty breathing, fever, chills, malaise, diarrhea, nausea, headache, anosmia, ear pain, irritability, muscle pain, abdominal pain, chest pain, joint pain, pharyngeal exudate, conjunctival injection, dyspnea, cardiovascular diseases, obesity, and pregnancy. However, none of these factors showed a statistically significant association with COVID-19 reinfection ($p > 0.05$). Although these symptoms are often related to primary

***Table 2.*** *Epidemiological risk factors associated with COVID-19 reinfection in patients treated in the Cusco-Peru Region.*

| **Reference** | | **B** | **Standard error** | **Wald** | **p** | **OR** | **95% C.I.** | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | **Inferior** | **Superior** |
| Over 60 years old | Age | | | 1.502 | 0.826 | | | |
| | 6 to 11 years old | -21.925 | 26022.411 | 0.000 | 0.999 | 0.000 | 0.000 | |
| | 12 to 18 years old | -0.107 | 1.595 | 0.005 | 0.946 | 0.898 | 0.039 | 20.462 |
| | 19 to 26 years old | 1.045 | 1.194 | 0.767 | 0.381 | 2.845 | 0.274 | 29.531 |
| | 27 to 59 years old | 0.849 | 1.033 | 0.677 | 0.411 | 2.338 | 0.309 | 17.689 |
| Male | Gender | | | | | | | |
| | Male<br>Female | -1.893 | 0.583 | 10.538 | 0.001 | **0.151** | 0.048 | 0.472 |
| Other department | **Origin** | | | | | | | |
| | Another region | 2.775 | 1.107 | 6.287 | 0.012 | **16.033** | 1.833 | 140.266 |
| | Occupation | | | 4.265 | 0.641 | | | |
| | Student | 1.427 | 1.700 | 0.705 | 0.401 | 4.167 | 0.149 | 116.601 |
| | Housewife | 0.159 | 0.836 | 0.036 | 0.849 | 1.172 | 0.228 | 6.041 |
| | Health worker | -0.557 | 0.783 | 0.507 | 0.477 | 0.573 | 0.123 | 2.657 |
| | Self-employed worker | -0.598 | 0.704 | 0.721 | 0.396 | 0.550 | 0.138 | 2.187 |
| | Dependent worker | 0.643 | 0.770 | 0.698 | 0.404 | 1.902 | 0.421 | 8.595 |
| Over 65 years old | Over 65 years old | | | | | | | |
| | No | 2.035 | 1.563 | 1.696 | 0.193 | 7.654 | 0.358 | 163.759 |
| Vaccinated | Vaccine | | | | | | | |
| | No | -0.279 | 1.535 | 0.033 | 0.856 | 0.756 | 0.037 | 15.319 |
| Sinopharm | Type of vaccine | | | 3.018 | 0.389 | | | |
| | Not received or not recorded | -1.275 | 0.742 | 2.950 | 0.086 | 0.279 | 0.065 | 1.197 |
| | AstraZeneca | -0.239 | 1.044 | 0.053 | 0.819 | 0.787 | 0.102 | 6.091 |
| | Pfizer/BioNTech | -0.306 | 0.850 | 0.129 | 0.719 | 0.737 | 0.139 | 3.897 |

***Table 3.*** *Clinical factors associated with COVID-19 reinfection in patients treated in the Cusco-Peru Region.*

| **Reference = Yes** | **B** | **Standard error** | **Wald** | **P.** | **OR** | **95% C.I.** | |
|---|---|---|---|---|---|---|---|
| | | | | | | **Inferior** | **Superior** |
| Cough | 0.416 | 0.416 | 0.998 | 0.318 | 1.516 | 0.670 | 3.429 |
| Sore throat | -0.459 | 0.410 | 1.256 | 0.263 | 0.632 | 0.283 | 1.411 |
| Nasal congestion | 0.300 | 0.341 | 0.774 | 0.379 | 1.350 | 0.692 | 2.636 |
| Difficulty breathing | 1.091 | 0.677 | 2.594 | 0.107 | 2.976 | 0.789 | 11.221 |
| Fever | 0.474 | 0.367 | 1.668 | 0.196 | 1.607 | 0.782 | 3.300 |
| Chills | -0.123 | 0.440 | 0.079 | 0.779 | 0.884 | 0.373 | 2.095 |
| General malaise | -0.419 | 0.353 | 1.405 | 0.236 | 0.658 | 0.329 | 1.315 |
| Diarrhea | 0.156 | 0.682 | 0.052 | 0.819 | 1.169 | 0.307 | 4.454 |
| Nausea | -0.628 | 0.853 | 0.541 | 0.462 | 0.534 | 0.100 | 2.843 |
| Headache | -0.244 | 0.343 | 0.507 | 0.477 | 0.783 | 0.400 | 1.535 |
| Anosmia | -0.842 | 1.556 | 0.293 | 0.588 | 0.431 | 0.020 | 9.100 |
| Ear pain | 0.784 | 0.950 | 0.680 | 0.410 | 2.190 | 0.340 | 14.108 |
| Muscle pain | 0.570 | 0.529 | 1.160 | 0.281 | 1.768 | 0.627 | 4.989 |
| Chest pain | 0.535 | 0.897 | 0.356 | 0.551 | 1.708 | 0.294 | 9.911 |
| Joint pain | 0.412 | 0.782 | 0.278 | 0.598 | 1.510 | 0.326 | 6.986 |
| Other symptoms | -1.118 | 0.927 | 1.456 | 0.228 | 0.327 | 0.053 | 2.010 |
| Cardiovascular disease | 1.963 | 1.146 | 2.934 | 0.087 | 7.122 | 0.753 | 67.322 |
| Obesity | 1.013 | 1.617 | 0.392 | 0.531 | 2.753 | 0.116 | 65.493 |

infection, their presence does not appear to influence the risk of reinfection (Table 3).

## Discussion.

The findings of this study provide evidence that certain epidemiological factors are significantly associated with COVID-19 reinfection among patients treated in the Cusco region during 2022. Notably, male sex was identified as a significant risk factor for reinfection compared to female sex, a result consistent with previous studies suggesting biological and immunological differences between sexes [10]. Men tend to exhibit a less efficient immune response to SARS-CoV-2, possibly due to higher expression of the ACE2 receptor and differential regulation of the inflammatory response [11]. Additionally, behavioral and occupational patterns, such as increased occupational and social exposure, may contribute to the higher reinfection risk observed in men [12].

Furthermore, individuals from regions outside Cusco, a city situated over 3,000 meters above sea level, were found to have a significantly higher risk of reinfection. This finding suggests that high-altitude environments may play a protective role against viral infections, aligning with previous studies conducted in high-altitude populations [13,14]. These studies have proposed that moderate chronic hypoxia induced by altitude could modulate the immune response and reduce viral replication [15,16]. Chronic exposure to hypobaric hypoxia appears to downregulate angiotensin-converting enzyme 2 (ACE2) receptor expression in respiratory tissues, potentially limiting SARS-CoV-2 viral entry points [17]. High-altitude populations demonstrate beneficial hematological adaptations, including elevated hemoglobin levels and enhanced antioxidant capacity, which may mitigate COVID-19-associated hypoxemia and oxidative stress [18]. Hypoxia-inducible factors may additionally modulate inflammatory responses, potentially preventing the cytokine storms associated with severe COVID-19.

Furthermore, the characteristic low population density and increased natural ventilation of mountainous regions likely reduce person-to-person transmission rates [19]. A recent meta-analysis confirmed that high-altitude regions exhibit lower COVID-19 incidence, supporting the hypothesis that environmental and physiological factors associated with altitude may confer protection against viral infections [20].

Regarding clinical factors such as respiratory symptoms and preexisting health conditions, none showed a statistically significant association with COVID-19 reinfection in this cohort. This result contrasts with previous studies that have identified specific symptoms or comorbidities as predisposing factors for reinfection [3,4]. However, the lack of association in our study may be attributed to individual immune response variability, differences in the severity of prior illness, or potential underestimation of exposure to new viral variants [7].

With respect to interregional mobility, patients from other departments exhibited a 16.03-fold higher risk of reinfection compared to Cusco residents. This finding is consistent with studies demonstrating that migration and travel increase the likelihood of repeated exposure to the virus, particularly in contexts where prevention strategies may vary across regions [21]. Additionally, recent research has highlighted that individuals experiencing high mobility, such as those facing homelessness, have significantly higher reinfection rates due to exposure in congregate settings and limited access to preventive measures [22].

Regarding reinfection rates, our study found a reinfection rate of 0.97%, which aligns with previous reports indicating rates ranging from 0.2% to 2.5% across different populations [5,10,23,24]. These variations may be attributed to differences in reinfection definitions, diagnostic test sensitivity, and local epidemiological contexts. For instance, a study in Iran reported a reinfection rate of 2.5 cases per 1,000 patients, suggesting that regions with higher mobility and healthcare accessibility may exhibit higher reinfection rates [25].

Finally, it is crucial to tailor public health interventions to the geographical and demographic characteristics of each region. In high-altitude areas such as Cusco, factors such as altitude and interregional mobility should be considered when designing prevention strategies [9]. Moreover, the persistence of symptoms in some recovered patients and the possibility of reinfection underscore the need for comprehensive rehabilitation programs, including clinical monitoring and psychological support [7]. Such programs would not only improve patients' quality of life but also alleviate the burden on healthcare systems, mitigating the long-term impact of the pandemic.

This study has some limitations that should be acknowledged. The retrospective and observational nature of the design may introduce selection and information biases. Additionally, reliance on clinical records may affect data accuracy and completeness. Moreover, the generalizability of these findings to other populations should be approached with caution due to the unique characteristics of the Cusco region. Despite these limitations, the results provide valuable insights into the factors associated with COVID-19 reinfection and can serve as a foundation for future research and public health strategies.

## Conclusion.

This study confirms that male sex and residence in lower-altitude regions are key risk factors for COVID-19 reinfection in a high-altitude population. These findings highlight the need for tailored prevention and epidemiological surveillance strategies adapted to the unique characteristics of high-altitude regions, with a particular focus on high-risk groups, such as men and individuals with high interregional mobility. Additionally, further research is recommended to explore the biological and environmental mechanisms conferring protection in high-altitude populations and to assess the impact of emerging viral variants on reinfection dynamics.

## Author contribution statement.

**Walter Edgar Gomez-Gonzales:** Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation, Writing- Reviewing and Editing. **Juan Carlos Valencia Martínez:** Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation. **Luis Alberto Chihuantito-Abal:** Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation. **Jessika Corahua Ordoñez:** Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original

draft preparation. **Yeny Gutiérrez Acuña:** Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation. **Lidia Vargas Pancorbo:** Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation. **Maria Fatima Gómez-Livias:** Writing- Original draft preparation, Visualization, Visualization, Validation, Writing- Reviewing and Editing.

## Ethics statement.

The study was approved by the Ethics Committee of the Universidad Andina del Cusco, through report N°004-2023-CIEI-UAC, signed on December 1, 2023.The authors declare that the present study was conducted under the strictest ethical conditions.

## AI Statement:

During the preparation of this paper, the authors used ChatGPT in order to improve editing and proofreading. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.


## Financial support.

None.


## Conflict of interest.

The authors declare no conflicts of interest

## Availability of data.

The datasets generated and /or analyzed during current study available from the corresponding author on reasonable request.


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