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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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EXPLORING THE INCIDENCE AND PREVALENCE OF NEW-ONSET AUTOIMMUNE DISEASE FOLLOWING COVID-19 PANDEMIC: A SYSTEMATIC REVIEW

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Abstract.

Background: The correlation between viral infections and the onset of autoimmune conditions has long attracted the scientific community. With the COVID-19 pandemic impacting the world like never before, we have a unique chance to better understand this complex disease and uncover its origin. In light of this, we performed a systematic review of the incidence and prevalence of newly diagnosed autoimmune diseases following the COVID-19 pandemic.

Methodology: We undertook an extensive literature review from 2012 to 2023, by using electronic databases such as Medline, Web of Science, PubMed, Cochrane Library, and supplementary sources like scholarly articles. Our review encompassed various types of studies, including trials, commentaries, and editorials. To evaluate bias, we adopted a recommended approach, employing a two-part tool to scrutinize five distinct domains: selection bias, performance bias, attrition bias, selective reporting, and other biases.

Results: In this review, a total of 14 studies were incorporated. On the basis of the findings of the present investigation, the average age of included patients was approximately 56.13 years, and the maximum were male. After the, meticulous examination we stated that there was a significant increase in inflammatory biomarkers, including ferritin, C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer and Interleukins IL-6. The majority of patients had an elevated level of CRP.

Conclusion: We conclude that there is a strong association between COVID-19 and a higher risk of various types of autoimmune diseases. In order to develop effective plans for the current pandemic as well as the post-pandemic period that follows, healthcare providers must recognize these autoimmune manifestations.

Key words. COVID-19, Inflammatory disease, auto-immune disease, Biomarkers, Post-COVID-19.

Introduction.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an (Ribonucleic acid) RNA virus, that is responsible for the COVID-19 infection. This illness is known as coronavirus disease 2019 [1]. According to a recent World Health Organization (WHO) report published on January 19, 2024, JN.1 is the most reported variant of interest (VOI) noted in approximately 71 countries worldwide at the time of writing [2]. Moreover, looking at the previous scenario, COVID-19 has evolved into a major health crisis all over the world. There were more than 768 million confirmed cases of COVID-19 reported, with 6.9 million deaths globally [3]. During the pandemic, both waves of COVID-19 infection, including the first and second waves of COVID-19 infections, have resulted in significant global losses in terms of morbidity, mortality, as well as GDP, and are probably to continue as newer variants emerge [4].

Emerging COVID-19 mutant strains pose ongoing challenges for healthcare systems. However, the immune response of the host cell to the coronavirus remains largely consistent across variants, characterized by an over expression of inflammatory markers. This reaction involves an over production of pro-inflammatory cytokines and chemokines, thereby exacerbating pulmonary inflammation [5]. As COVID-19 cases rise globally, we are learning more about the disease. Due to the global vaccination program, the mortality rate among individuals infected with COVID-19 is decreasing nowadays [6]. However, we are still witnessing significant morbidity, marked by rising rates of post-COVID-19 autoimmune and inflammatory diseases. It is yet unclear what processes underlie the link between viruses and autoimmunity.

According to reports, COVID-19 exhibits immunological characteristics akin to autoimmune disorders, including dysregulation of B and T cells, along with abnormal activation of mature natural killer cells including both i.e., CD8+ T cells [6,7]. Moreover, exposure to SARS-CoV-2 infection may lead to abnormal immune response or dysregulation and increased levels of inflammatory cytokines such as C-reactive protein (CRP), ferritin, lactate dehydrogenase (LDH), D-dimer, and Interleukins IL-6. Some investigations have described examples of autoimmune diseases that occurred after encountering SARS-CoV-2 [8,9].

Similarly, some other investigations revealed, the number of instances with Kawasaki-like disease, which is currently known as multisystem inflammatory syndrome in children (MIS-C), has significantly increased during the COVID-19 pandemic [1]. Several case reports have indicated the onset of Guillain-Barré syndrome following SARS-CoV-2 infection. Additionally, instances of psoriasis and systemic lupus erythematosus triggered by COVID-19 have been documented [10].

New information points to a possible connection between COVID-19 and a higher chance of autoimmune diseases. The objective of this systematic review is to investigate in detail the incidence and prevalence of newly identified autoimmune

disorders that occur after infection with COVID-19. Furthermore, we want to clarify any plausible underlying processes that could be involved in this correlation, with an emphasis on immune system dysregulation and the overproduction of inflammatory markers in particular.

The review's goal is to investigate not only the frequency of autoimmune disorders that have arisen after COVID-19 but also any potential underlying mechanisms that may be involved, such as immune system dysregulation and an excessive production of inflammatory markers.

Therefore, the present systematic review aims to meticulously analyse the existing literature to clarify the correlation between Covid-19 and autoimmune disorders. We attempt to determine whether Covid-19 possesses the potential to instigate autoimmune conditions, thereby shedding light on this complicated relationship.

Methodology.

The review technique was developed under the guidance of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) declaration. All modifications made to the protocol were duly recorded and documented.

Search strategy.

A thorough and comprehensive literature search was carried out across various databases, namely Google Scholar, PubMed, the Cochran library, Scopus, Web of Science, Embase, and Wiley. The process of selecting studies adhered to pre-established inclusion criteria, which were attained by carried out a search employing usual MeSH terms. The search parameters encompassed terms such as “COVID-19 infection’ “autoimmune disorder” “Inflammatory Response” “Multisystem Inflammatory Syndrome and Autoimmune Diseases” “post-acute sequelae of SARS-CoV-2 infection” “Sense the beginning of Cytokine Storm” “High risk of autoimmune diseases after COVID-19” and “Severity of the Disease and the Vaccination Status”.

Inclusion Criteria:

- Studies reporting on individuals with a history of COVID-19.
- Studies documenting the occurrence of new autoimmune diseases.

Exclusion Criteria:

- Studies lacking information on autoimmune diseases.
- Case reports or studies with small sample sizes.
- Studies not published in English.

Study Selection:

1. Using inclusion/exclusion criteria, evaluate the relevancy of titles and abstracts.
2. Retrieve full texts of potentially relevant studies for detailed evaluation.
3. Employ a systematic approach, involving at least two independent reviewers for study selection.

Statistical Analysis.

We first conducted a database search and then grouped the chosen articles into an Excel spreadsheet. Then, we removed any articles that were duplicates. Next, the full-text publications and abstracts were examined separately by two authors. Both authors meticulously reviewed each of the publication that were chosen for this study before deciding which ones to use. Additionally, we evaluated the included studies using Revman 5.4 to analyze risk of bias, study design, and methodological quality.

The asterisk (*) in the image probably serves as a cue that further information or explanations may be found in the legends or footnote sections of the picture. In academic writing, it is customary to use these symbols to direct the reader to further information about the figure.

This stage, which involves excluding 260 reports, is an essential component of the systematic review procedure. Upon doing a preliminary, comprehensive search across many databases and other sources, researchers often get a substantial quantity of possibly relevant papers. All of this research may not, however, fit the precise inclusion and exclusion criteria established for the review.

A total of 312 papers were evaluated for inclusion in our systematic review on the basis of their titles and abstracts. 260 of these reports were eliminated for a variety of reasons, such as:

1. study that did not fit the predefined review inclusion criteria, such as not reporting pertinent results, not addressing the study topic, or not including the target population.
2. Research that satisfied the criteria for exclusion, such as case studies, editorials, meta-analyses, or clinical recommendations, since they may not include primary data that is relevant to the review.
3. Research that overlapped or were duplicates of other included research, so as to prevent data double counting.
4. Research that did not meet the required language and availability standards, was not published in English, or was not available in full text.

Documenting the rationale behind each screening stage's exclusion of a study is a common procedure in systematic reviews. This openness reduces bias in research selection and guarantees the review process is repeatable.

Results.

In the present systematic review, 427 studies were primarily screened and reviewed on the basis of their title and abstract. Following this screening, 312 studies were excluded. Then, approximately a total of 52 full-text articles or studies were assessed for eligibility, leading to the exclusion of 38 articles. The exclusion criteria were applied based on article type, including studies lacking information on autoimmune diseases, case reports or studies with small sample sizes, letters to the editor, reviews, meta-analyses, and studies not published in English. Additionally, studies were excluded based on the population under study (cases not meeting the case definition for COVID-19 and other viruses).

After this thorough examination process, 14 studies were selected for the present systematic review on the basis of previously described inclusion and exclusion criteria, as represented in Figure 1. In this review, Table 1 provides comprehensive details regarding the study and patient characteristics of the included studies. The following Figures 2 and 3 offer a summarized assessment of the risk of bias for the prevalence of studies conducted.

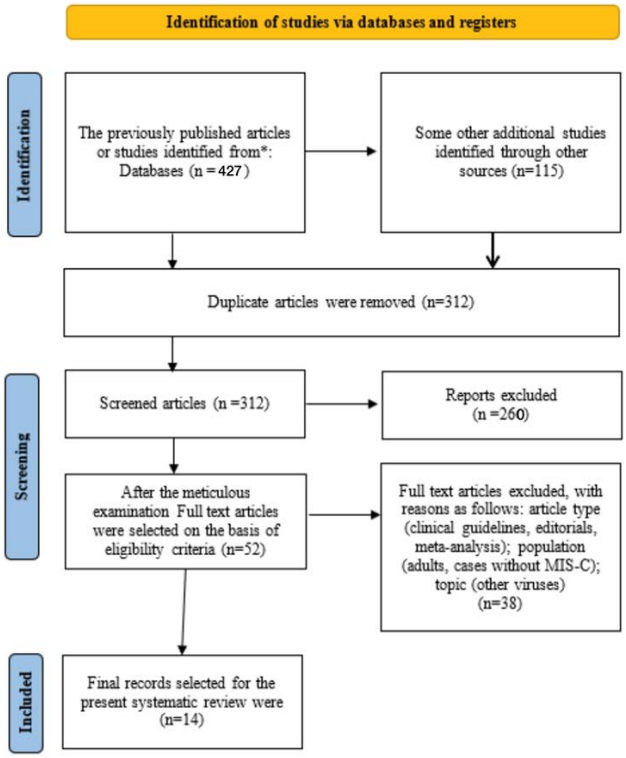

Figure 1. *PRISMA flowchart for the present systematic review.*

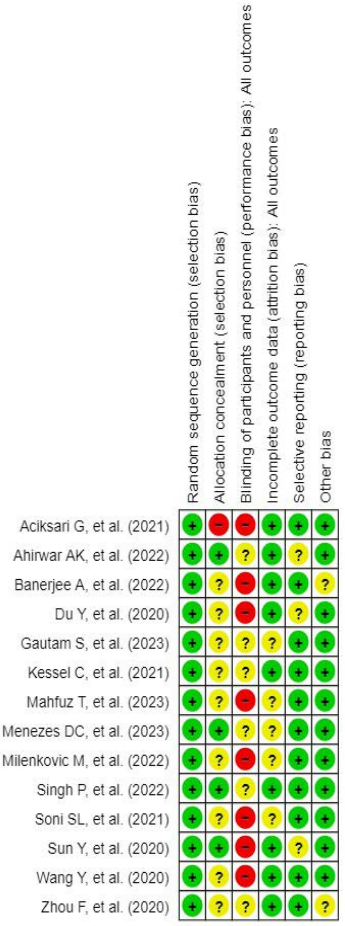

Figure 2. *Representing the risk of bias of included studies.*

In the present investigation, all the published articles were selected from the last 5 years, between 2019 to 2024. Among the selected studies as sample size, 5 studies were conducted in China [11-15]. Similarly, 5 studies were from the India, [16-20] 2 studies were conducted in the Seria [21, 22] and 1 each in Brazil and Turkey [23,24]. Overall, the studies included 5219 cases of COVID-19 infection.

Inflammatory Marker Levels in Patients with COVID-19:

The overproduction of inflammatory markers and immune system dysregulation are two suggested reasons for the possible development of autoimmune diseases after COVID-19. An overview of the inflammatory marker values reported in the included studies is provided in Table Interestingly, most studies found that COVID-19 patients had higher than normal levels of indicators such as ferritin, lactate dehydrogenase (LDH), D-dimer, interleukin-6 (IL-6), and C-reactive protein (CRP). These results provide context for the possible association between COVID-19 and an elevated risk of autoimmune illnesses and support the theory of immunological dysregulation."

Demographic features and laboratory outcomes:

On the basis of the findings of the present investigation, the mean age of study participants was 56.13 years, and the maximum were male. A total of 5239 research participants were examined in this analysis. Among the trials reporting gender information, 12 investigations were conducted exclusively on male subjects, with a total of 1603 participants. Similarly, 8 research studies, totalling 717 participants, specifically focused on female participants. However, within the context of this systematic review, one study included a distinctive cohort of 2919 children. Furthermore, the results of the routine laboratory investigation show in Table 1 that, there was a significant increase in inflammatory biomarkers, including ferritin, CRP, LDL, D-dimer, and interleukin-6 (IL-6). The majority of patients had an elevated level of CRP.

Interpretation of Table 1: Study Design and Inflammatory Markers with an emphasis on research design and the prevalence of inflammatory markers, Table 1 provides an overview of the salient features of the studies that are part of this systematic review.

Study Design: Every featured study is classified as either a cross-sectional, retrospective cohort, prospective cohort, or case-control study in the "Study Design" column. Readers may better grasp the approach used in each research study by using this categorization.

Cohort Studies: These studies track groups of people throughout time to find out when autoimmune disorders emerge. The subjects are either COVID-19 patients or healthy controls. While prospective studies gather data as the investigation moves forward, retrospective cohort studies examine data that has already been acquired.• Cross-sectional studies: These investigations look at a population at one particular moment in order to get a quick picture of the connection among inflammatory markers and COVID-19. They are unable to establish causal correlations, however.

Case-Control Studies: This research examines possible risk factors, such as a history of COVID-19 infection, by comparing people with a particular illness (autoimmune disease) to a

Table 1. *Representing the study characteristics and inflammatory biomarkers.*

Author	Patients (M/F)	Mean Age	Country	Symptoms	Inflammatory markers (mean value)					Comorbidities	Study Design
					IL-6 (pg/mL)	LDH (U/L)	CRP (mg/L)	Ferritin (ng/mL)	D-dimer (ng/mL)		
Du Y, et al. (2020) [11]	85 (62/23)	65.8	China	fever, coughing, or shortness of breath	-	-	107.259 ± 117.215	-	5.159 ± 4.679	-	Retrospective cohort study
Sun Y, et al. (2020) [12]	63 (0)	47	China	fever, coughing, or shortness of breath, Dizziness, Sore throat, headache	18.50 ± 20.03	-	19.53 ± 35.94	2.45 ± 2.48	1.97 ± 1.83	-	Retrospective cohort study
Zhou F, et al. (2020) [13]	191 (119/72)	56.0	China	fever, cough, and dyspnea	7.4 (5.3–10.8)	-	-	722.0 (377.2–1435.3)	1.96 (0.52–7.43)	Coronary heart disease, Chronic obstructive lung disease, Carcinoma, Hypertension	Retrospective cohort study
Wang Y, et al. (2020) [14]	344 (0)	64	China	Fever, cough, Fatigue, Diarrhea, Dyspnea, Anorexia	27.2 (5.9–60.1)	338 (237–491)	55 (14–106)	-	1.3 (0.5–5.0)	-	Retrospective cohort study
Açıksarı G, et al. (2021) [15]	223 (118/105)	59.70 ± 19.01	China	-	-	-	5.2 (1.3-10)	-	-	-	Retrospective cohort study
Soni SL, et al. (2021) [16]	114 (66/48)	33.5 yr	India	fever, cough, sore throat, nasal congestion, malaise and headache	-	-	2.1 (0.8-5.4)	90 (40.5-200.5)	-	Hypertension, diabetes, elevated levels of inflammatory markers including CRP, ferritin and LDH, renal dysfunction and high creatine	Cross-sectional study
Gautam S, et al. (2023) [17]	100 (0)	55.6 ± 15.3 years	India	Fever, Cough with Expectoration, Vomiting, Body ache, Loss of taste, loss of smell	33.22 ± 55.35	361.20 ± 109.63	49.56 ± 53.58	499.98 ± 305.63	854.65 ± 770.20	Hypertension, DM, Coronary Artery Disease, Chronic Kidney Disease (ACD), Chronic Obstructive, Pulmonary Disease (PD), Chronic Liver Disease (CLD)	Prospective cohort study
Banerjee A, et al. (2022) [18]	(n=94) (51/43) (Non-severe 77)	58.79 ± 12.95	India	fever, cough, myalgia	-	-	75.17 ± 70.31	567.95 ± 370.95	578.59 ± 440.36	-	Retrospective cohort study
	17 (severe)	64.82 ± 14.07			-	-	129.67 ± 92.06	890.62 ± 365.03	1010.79 ± 733.61	-	
Singh P, et al. (2022) [19]	2919 (Children) (0)	62.5 (16.25, 120) 72.73 ± 57.68 (Months)	India	fever, cough and fast breathing, gastrointestinal symptoms	-	-	41.5 (5–145.75)	579 (335–1128)	1032 (542–1050)	Tuberculosis, hematological malignancy and malnutrition	Cross-sectional study
Ahirwar AK, et al. (2022) [20]	Survivor (n=382) (236/146)	42 ± 17	India	-	10, 3–30 (n=35)	-	4, 1–20 (n=140)	-	0.1, 0–0.12 (n=381)	-	Retrospective cohort study
	Non-survivor (n=18) (15/5)	65.7 ± 13			95, 51–190 (n=18)	-	150, 93–1,755 (n=17)	-	2,940, 548–3,935 (n=18)	-	
Kessel C, et al. (2021) [21]	86	62 (50–67)	Serbia	hypoxia and pneumonia, fever, cough, dyspnea, rapid breathing	-	-	-	-	-	-	Cross-sectional study

Milenkovic M, et al. (2022) [22]	318 (219/99)	69 (60-77)	Serbia	-	110.8 (44.1-399.6)	-	88 (53.8-191.5)	822 (415.5-1478)	829 (497-2759.5)	-	Retrospective cohort study
Menezes DC, et al. (2023) [23]	215 (77/138)	49.6 ± 12.7	Brazil	fatigue, dyspnea, and muscle weakness and abnormal metabolic profile	-	-	27 (12.5)	176.5 ± 159	-	Hypertension, obesity	Cross-sectional study
Mahfuz T, et al. (2023) [24]	COVID-19 group (n=45) (25/20)	52 (33–63)	Turkey	-	-	-	63.6 (31.7–137)	396.7 (240.8–975.3)	1.65 (0.84–2.72)	-	Case-control study
	Healthy group (n=40) (22/18)	50 (32–64)			-	-	3 (2.42–3.7)	179.9 (134.9–205.4)	0.17 (0.12–0.25)	-	

Footnote: *C-reactive protein (CRP), ferritin, lactate dehydrogenase (LDH), D-dimer, and Interleukins IL-6, Chronic Kidney Disease (ACD), Diabetes mellitus (DM), Pulmonary Disease (PD), Chronic Liver Disease (CLD), coronavirus disease 2019.*

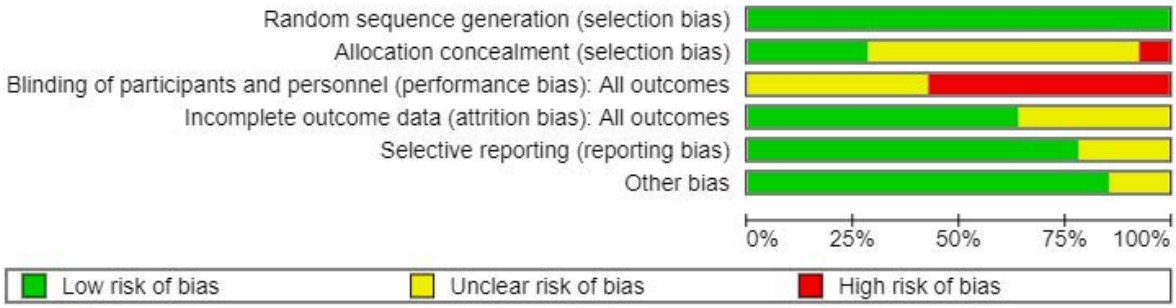

Figure 3. *Representing the percentage of risk of bias.*

control group who does not have the condition. Inflammatory Markers: Each of the inflammatory markers, including IL-6, LDH, CRP, ferritin, and D-dimer, has a column in the table with its corresponding unit (pg/mL, U/L, mg/L, ng/mL). The inflammatory response of the body is indicated by these markers. Readers may evaluate if COVID-19 individuals have inflammation and how severe it could be based on the provided results from the included research.

Consolidated Interpretation: It may be easier to comprehend the data by taking into account the inflammatory marker levels as well as the research design. A retrospective cohort study, for instance, that showed considerably higher levels of IL-6 in COVID-19 patients than in healthy controls (with units supplied) raises the possibility of a link between COVID-19 and an increased inflammatory response. Yet, there may be difficulties in adjusting for confounding factors due to the retrospective nature of the research design.

Outcomes of risk of bias:

RevMan software version 5.4 was used to analyse the risk of bias in the present study. With regard to selection bias (creation of a random sequence), performance bias (blinding of cases and staff), attrition bias (incomplete results data), selective reporting (reporting bias), and other biases, we evaluated individual studies according to various domains as well as criteria and classified them as having low, unclear, or high risk. The overall risk valuation for each of the 11 included research studies was represented as low risk (+), high risk (-), or unclear risk (?), as depicted in Figure 2. We provided a comprehensive overview of the risk of bias. Importantly, we identified serious methodological inadequacies in at least one bias domain across all the studies. Among the most concerning issues were the inadequacy or absence of randomization (resulting in a high risk of 9/84 = 10.71% of the trials), low-risk blinding of outcome assessors (noted as a low risk of 50/84 = 59.52% of the trials), and an unclear risk of 29.76% (unclear risk of 25/84 = 29.76% of the trials) as illustrated in Figure 3.

Discussion.

The main purpose of the systematic review was to examine the potential connection between COVID-19 and the heightened susceptibility to autoimmune diseases. Although the incidence and severity of newly identified autoimmune illnesses after COVID-19 were the main emphasis, it is crucial to comprehend the underlying processes that might be involved in this connection.

"This systematic review did not do a meta-analysis of inflammatory marker levels; nevertheless, Table 1 provides an extensive overview of the reported levels of markers, including CRP, ferritin, LDH, D-dimer, and IL-6, in the included studies. Numerous studies have shown that COVID-19 patients have higher levels of these markers, which may indicate immunological dysregulation and the ensuing inflammatory response. These results provide credence to the theory explaining the higher risk of autoimmune diseases that follows COVID-19 infection."

Make it clear that the study's innovation is in its thorough investigation of the relationship between COVID-19 and the elevated risk of autoimmune diseases, including data on prevalence as well as possible underlying processes, such as the function of inflammatory markers.

This systematic study is interesting since it thoroughly examines the relationship between COVID-19 and a higher risk of autoimmune illnesses. This review offers a comprehensive understanding of this complex relationship by combining data on the prevalence of newly diagnosed autoimmune diseases after COVID-19 with insights into the potential underlying mechanisms, such as immune system dysregulation and the overproduction of inflammatory markers. Inflammatory marker levels have been found in COVID-19 patients, which supports the suggested mechanistic relationship and emphasises the need for identifying and treating these immune-related symptoms in the clinical care of COVID-19.

While inflammatory markers were not the subject of a meta-analysis, Table 1's presentation of these markers provides a descriptive analysis of the included studies, emphasising the increased levels seen in COVID-19 patients.

One of the theories is that autoimmune disorders might arise as a result of immune system dysregulation and excessive production of inflammatory markers. Our goal in providing the inflammatory marker levels in COVID-19 patients was to lay the groundwork for comprehending the relationship between COVID-19 and autoimmune illnesses by offering data in favour of this plausible mechanism.

In addition, a thorough literature search and assessment of several studies, particularly those that reported inflammatory marker levels in COVID-19 patients, were part of the review process. Although these indicators were not the subject of a particular meta-analysis, Table 1's presentation of the data from the included studies provides a descriptive overview that emphasises the heightened levels of inflammatory markers seen in COVID-19 patients.

In the present systematic review, we investigated the prognostic value of over production of inflammatory markers such as ferritin, LDH, IL-6, D-dimer, and CRP in COVID-19 cases and their association with autoimmune disorders. The activation or overexpression of these inflammatory markers is referred to as “cytokine storm” or “cytokine release syndrome,” which results in autoimmune disorders. COVID-19 infection can lead to a range of immune-related complications affecting different organs, including the spinal cord, nerves, and skin. Additionally, it can trigger systemic immune dysfunction or inflammation, leading to conditions such as hemophagocytic lymphohistiocytosis (HLH), vasculitis, or Guillain-Barré syndrome [25,26]. Therefore, the results of this review showed that, the above-mentioned inflammatory markers were significantly associated with the survival of patients in severe cases of COVID-19. Our study specifically highlights that, a raised level of inflammatory markers investigated during admission could predict the severity of the disease, which plays a vital role in the management of SARS-CoV-2.

In this current investigation, we have conducted a comprehensive review of the existing published literature to thoroughly examine the clinical features and management strategies associated with COVID-19. Our analysis has yielded noteworthy findings, which are succinctly summarized as follows:

1) The average age of affected individuals was determined to be 56.13 years.

2) The majority of the cases were male, and the majority of the symptoms were fever, cough, shortness of breath, dyspnea, sore throat, vomiting, gastrointestinal symptoms and an abnormal metabolic profile.

3) The inflammatory markers, including D-dimer, IL-6, LDL, ferritin, and CRP, were significantly elevated with autoimmune disorder or organ dysfunction. These routine laboratory investigations are consistent with previous research work done by Jain P, et al. [27], Wang D, et al. [28], Saluja M, et al., [29] and Tjendra Y, et al [30].

According to a study performed by Saeed GA et al. [31] higher levels of inflammatory markers, including CRP, procalcitonin, IL-6, and D-dimer levels, have been associated with mortality and poor outcomes among COVID-19 cases. These results were similar with a study reported by Sun Y et al. [12] according to them, raised the level of IL-6, indicating the presence of a hyperimmune inflammatory disorder that leads to mortality or morbidity among COVID-19 cases. Further discoveries from their investigation revealed significant predictors of disease severity. According to their analysis using a binary logistic regression model, three factors stood out: C-reactive protein level (odds ratio [OR] 1.073, with a CI ranging from 1.013 to 1.136; $p = 0.017$), CD8 T lymphocyte counts (OR 0.989, CI 0.979–1.000; $p = 0.043$), and D-dimer levels (OR 5.313, CI 0.325–86.816; $p = 0.241$). These findings suggested that variations in these biomarkers could independently forecast the severity of the disease. On the other hand, an additional investigation by Liu et al., [32] concluded that organ failure in COVID-19 is mostly linked to immune-mediated processes, which are comparable to those in autoimmune illness, after comparing the immunological response in both conditions. According to Table 1, it was stated that, COVID-19 was associated with increased risks of all autoimmune diseases, and it was also associated with a higher fatality rate among infected patients. According to the recent study conducted by Verdoni L, et al. [33] and Salah NB, [34] et al., the incidence of Kawasaki-like disease, in modern terms referred to as MIS-C, has been observed to increase during the COVID-19 pandemic. Similarly, Bonometti R., et al. [35] also reported that, autoimmune diseases such as systemic lupus erythematosus and psoriasis have also been observed among COVID-19 patients.

We proposed that, in COVID-19, prolonged inflammation might encourage the production of antibodies by the immune system against self-antigen-like viral antigens. A cross-reactive response against both self- and non-self-antigens could result from this. Furthermore, immunological dysregulation and hyperstimulation carried on by COVID-19 variant may exacerbate disruptions in the environment and might result in illness in individuals who are at risk. A study done by Canas CA. [36] suggests that COVID-19 may cause autoimmune diseases by unexpectedly affecting both acquired and innate immunity, which can result in a loss of self-tolerance, as well as

by inducing an improper reconstitution of the immune system in people who are already prone to autoimmunity. Therefore, it is essential to recognize the overexpression of the inflammatory response, especially in COVID-19 patients. Thus, we suggested that anti-inflammatory therapy must be needed at the right time to reduce forthcoming complications.

Conclusion.

In summary, our initial findings strongly indicate a substantial link between COVID-19 and a higher risk of different autoimmune diseases. Recognizing these autoimmune manifestations is imperative for healthcare professionals to mount effective responses during the current pandemic and in the extended post-pandemic period. As we navigate these challenges, it becomes increasingly crucial to delve into the potential impact of vaccination on the incidence of autoimmune diseases, which suggests the way for comprehensive studies in the future.

Limitations.

1. The limited number of sample sizes and most of the comparative studies having limited follow-up periods, therefore we fail to provide long-term clinical outcomes for the study participants.
2. The present review was limited to articles published only in English language.

Conflict of interest:

The authors declare that there is no conflict of interests.

REFERENCES

1. Sharma C, Bayry J. High risk of autoimmune diseases after COVID-19. Nat Rev Rheumatol. 2023;19:399-400.
2. World health organization report. 2024. https://www.who.int/publications/m/item/covid-19-epidemiological-update---19-january-2024
3. World Health Organization WHO coronavirus (COVID-19) dashboard. 2023 https://covid19.who.int/
4. Bakhtar N, Bakhtar N, Pandey K, et al. Sensing the Smell of Beginning of Cytokine Storm: A Report on Study of Early Markers of the Complications. J Health Commun. 2021;6:21.
5. Jin Y, Yang H, Ji W, et al. Virology, Epidemiology, Pathogenesis, and Control of COVID-19. Viruses. 2020;12:372.
6. Moghadas MS, Vilches TN, Zhang K, et al. The impact of vaccination on COVID-19 outbreaks in the United States. Preprint. medRxiv. 2021;2020.11.27.20240051.
7. Mansourabadi AH, Aghamajidi A, Dorfaki M, et al. B lymphocytes in COVID-19: a tale of harmony and discordance. Arch Virol. 2023;168:148.
8. Hosseini P, Fallahi MS, Erabi G, et al. Multisystem Inflammatory Syndrome and Autoimmune Diseases Following COVID-19: Molecular Mechanisms and Therapeutic Opportunities. Front Mol Biosci. 2022;9:804109.
9. Trofin F, Nastase EV, Roșu MF, et al. Inflammatory Response in COVID-19 Depending on the Severity of the Disease and the Vaccination Status. Int J Mol Sci. 2023;24:8550.
10. Gracia-Ramos AE, Martin-Nares E, Hernández-Molina G. New Onset of Autoimmune Diseases Following COVID-19 Diagnosis. Cells. 2021;10:3592.
11. Du Y, Tu L, Zhu P, et al. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan. A Retrospective Observational Study. Am J Respir Crit Care Med. 2020;201:1372-1379.
12. Sun Y, Dong Y, Wang L, et al. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience. J Autoimmun. 2020;112:102473.
13. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-62.
14. Wang Y, Lu X, Li Y, et al. Clinical Course and Outcomes of 344 Intensive Care Patients with COVID-19. Am J Respir Crit Care Med. 2020;201:1430-1434.
15. Açıksarı G, Koçak M, Çağ Y, et al. Prognostic Value of Inflammatory Biomarkers in Patients with Severe COVID-19: A Single-Center Retrospective Study. Biomark Insights. 2021;16:11772719211027022.
16. Soni SL, Kajal K, Yaddanapudi LN, et al. Demographic & clinical profile of patients with COVID-19 at a tertiary care hospital in north India. Indian J Med Res. 2021;153:115-125.
17. Gautam S, Kumar R, Bhadoria DP, et al. Clinical profile of hospitalized moderate category COVID-19 patients: Short study from a Tertiary Care Centre in Delhi. J Family Med Prim Care. 2023;12:1644-1653.
18. Banerjee A, Banerjee J, Mazumdar M, et al. Impact of various hematological and biochemical parameters in severe and nonsevere COVID-19 patients: A retrospective single-center study. Mustansiriya Med J. 2022;21:178-83.
19. Singh P, Attri K, Mahto D, et al. Clinical Profile of COVID-19 Illness in Children-Experience from a Tertiary Care Hospital. Indian J Pediatr. 2022;89:45-51.
20. Ahirwar AK, Takhelmayum R, Sakarde A, et al. The study of serum hsCRP, ferritin, IL-6 and plasma D-dimer in COVID-19: a retrospective study. Horm Mol Biol Clin Investig. 2022;43:337-344.
21. Kessel C, Vollenberg R, Masjosthusmann K, et al. Discrimination of COVID-19 From Inflammation-Induced Cytokine Storm Syndromes Using Disease-Related Blood Biomarkers. Arthritis & Rheumatology. 2021;73:1791-1799.
22. Milenkovic M, Hadzibegovic A, Kovac M, et al. D-dimer, CRP, PCT, and IL-6 Levels at Admission to ICU Can Predict In-Hospital Mortality in Patients with COVID-19 Pneumonia. Oxid Med Cell Longev. 2022;2022:8997709.
23. Menezes DC, Lima PDL, Lima IC, et al. Metabolic Profile of Patients with Long COVID: A Cross-Sectional Study. Nutrients. 2023;15:1197.
24. Mahfuz T, Alp HH, Yildiz H, et al. Blood prestin levels in COVID-19 patients. J Chin Med Assoc. 2023;86:571-576.
25. Zacharias H, Dubey S, Koduri G, et al. Rheumatological complications of Covid 19. Autoimmun Rev. 2021;20:102883.
26. Ramos-Casals M, Brito-Zerón P, Mariette X. Systemic and organ-specific immune-related manifestations of COVID-19. Nat Rev Rheumatol. 2021;17:315-332.
27. Jain P, Sinha N, Prasad M, et al. Clinical and laboratory profile of COVID-19 patients admitted at a tertiary care center in New Delhi and assessment of factors predicting disease severity. Indian Journal of Medical Specialities. 2021;12:59-63.

28. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323:1061-1069.
29. Saluja M, Pillai D, Jeliya S, et al. COVID 19- Clinical Profile, Radiological Presentation, Prognostic Predictors, Complications and Outcome: A Perspective from the Indian Subcontinent. J Assoc Physicians India. 2020;68:13-18.
30. Tjendra Y, Al Mana AF, Espejo AP, et al. Predicting Disease Severity and Outcome in COVID-19 Patients: A Review of Multiple Biomarkers. Arch Pathol Lab Med. 2020;144:1465-1474.
31. Saeed GA, Gaba W, Shah A, et al. Correlation between Chest CT Severity Scores and the Clinical Parameters of Adult Patients with COVID-19 Pneumonia. Radiol Res Pract. 2021;2021:6697677.
32. Liu A, Hammond R, Chan K, et al. Comparison of Lymphocyte–CRP Ratio to Conventional Inflammatory Markers for Predicting Clinical Outcomes in COVID-19. J. Pers. Med. 2023;13:909.
33. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020;395:1771-1778.
34. Salah NB, Lahouel I, Mariem CB, et al. Multisystem inflammatory syndrome in children associated with erythema multiforme-like eruption following COVID-19. Int J Rheum Dis. 2022;25:375-377.
35. Bonometti R, Sacchi MC, Stobbione P, et al. The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection. Eur Rev Med Pharmacol Sci. 2020;24:9695-9697.
36. Cañas CA. The triggering of post-COVID-19 autoimmunity phenomena could be associated with both transient immunosuppression and an inappropriate form of immune reconstitution in susceptible individuals. Med Hypotheses. 2020;145:110345.