Global trends from original research on COVID-19 and coinfection

Tendências globais de pesquisas originais sobre a COVID-19 e coinfecção

Tendencias globales de investigaciones originales sobre COVID-19 y coinfección

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ABSTRACT

Introduction: The clinical symptomatology of SARS-CoV-2 and the occurrence of coinfections can be masked by the similarity of the manifestations, thereby delaying the clinical diagnosis and therapeutic decision-making, favoring the worsening of the clinical condition and increasing the chances of death. **Aim:** to conduct a bibliometric analysis of the world's scientific production on COVID-19 and coinfection in general. **Outlining:** Bibliometric study with a quantitative approach. Two hundred eight articles were analyzed using the Bibliometrix R package and the Biblioshiny application. **Results:** The articles were published mainly in 2021 and 2022. The scientific journals that published the most were the Journal of Medical Virology and Cureus. The most cited was the Journal of Medical Virology. The articles were cited 2567 times and addressed the etiology of coinfections, which bacteria, other viruses, fungi, and vectors can cause. **Implications:** Through this bibliometric analysis, it was possible to identify global trends in research on COVID-19 and coinfection, which in the long term can support the development of new research and the elaboration of strategies aimed at preventing, controlling, and managing cases of coinfections, not only in the pandemic period but continuously.

DESCRIPTORS
SARS-CoV-2; Mixed Infection; Pandemic; Bibliometric Indicators.

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INTRODUCTION

COVID-19 was declared a new respiratory pandemic in March 2020 and has become a public health challenge for the entire world.[1] The disease caused by the SARS-CoV-2 virus is characterized by manifesting an acute flu-like condition that may be associated with fever, cough, headache, throat pain or irritation, dyspnea, diarrhea, myalgia, and vomiting.[2]

In addition, the disease can present a more severe condition with respiratory discomfort and saturation lower than 95%, characterizing Severe Acute Respiratory Syndrome (SARS).[3] As a result, before the creation and implementation of vaccines, a significant number of patients needed hospitalization in Intensive Care Units (ICU), as well as the use of Mechanical Ventilation, which favored the occurrence of coinfection.[4]

Associated with this picture, they can also favor coinfection, immunosuppression of patients, the existence of pathogens resistant to antimicrobials, submission of patients to invasive interventions, and the discontinuity of practices aimed at preventing and controlling infections. It should also be noted that coinfections assume a preponderant role because they demand new clinical conditions and additional care for patients, impacting evolution and prognosis.[5]

Thus, coinfection with other pathogens (viruses, bacteria, and fungi) is an essential factor that cannot be ignored. Data show that 19% of individuals hospitalized with COVID-19 had coinfection, which can increase the length of hospital stay and the mortality rate.[6]

In this context, According to a study in Wuhan, China, 50% of patients who died had a secondary infection, and 31% of intubated patients had Pneumonia Associated with Mechanical Ventilation (VAP).[4]

Therefore, coinfection with other pathogens associated with COVID-19 can significantly impact health systems, mainly due to the precariousness of care, lack of supplies, physical structure, and dimensioning of staffing. Above all, the clinical symptomatology of SARS-CoV-2 and the occurrence of coinfections can be masked by the similarity of the manifestations, thereby delaying the clinical diagnosis and therapeutic decision-making, favoring the worsening of the clinical condition and increasing the chances of death.[7]

Due to the importance of the theme, the objective was to carry out a bibliometric analysis of the world's scientific production on COVID-19 and coinfection in general.

METHOD

This research is descriptive and bibliometric with a quantitative approach guided by the five steps recommended in bibliometric research.[8]

The search for articles was performed on the Web of Science™ (WoS) on March 26, 2023, to select the articles to be analyzed. WoS was chosen because it is a selective, structured, and balanced database with full citation links and enhanced metadata that support multiple information purposes.[9] To formulate the search strategy, controlled and uncontrolled descriptors of Medical Subject Headings (MeSH), boolean operators, and wildcard characters were used.
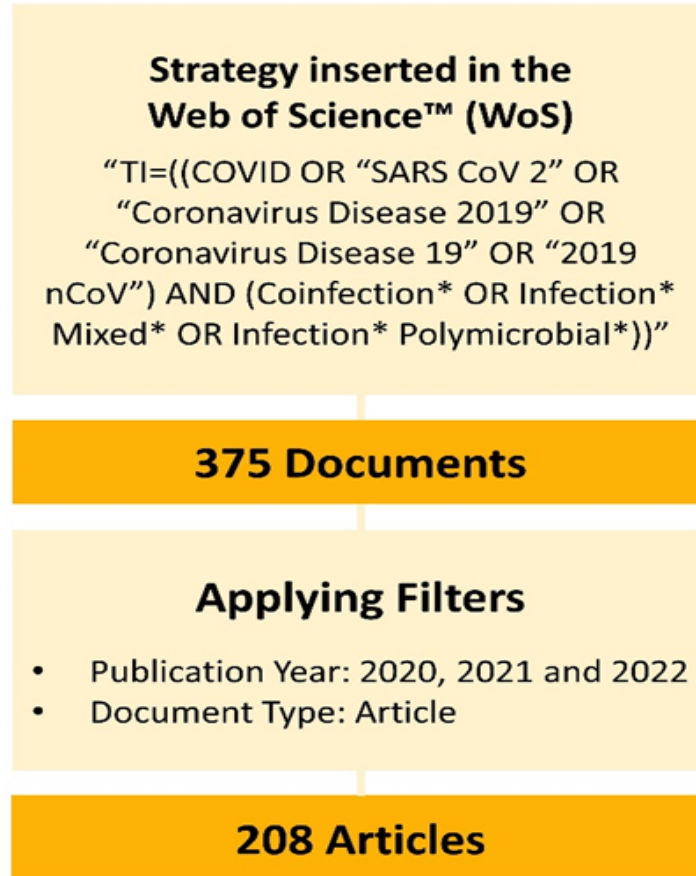
In order to increase precision and reduce false-positive results, this research used the advanced search by titles. The literature has already reported that specific searches by titles increase retrieval and specificity, generating a minimal loss of sensitivity compared to the search that includes all fields.[10-11]

For analysis, only original articles published until December 31, 2022, were included, excluding articles that deviated from the scope of the research, review articles, opinion articles, reflection articles, editorials, case studies, and articles with publication date de 2023. Thus, the search resulted in 375 documents. After filtering and applying the already

established criteria, 208 articles remained, whose information was downloaded in text file format for analysis. **Figure 1** summarizes how articles were selected for inclusion in this survey.

Figure 1 – Selection of articles for analysis. Teresina, Piauí, Brazil.

Strategy inserted in the Web of Science™ (WoS)

"TI=((COVID OR "SARS CoV 2" OR "Coronavirus Disease 2019" OR "Coronavirus Disease 19" OR "2019 nCoV") AND (Coinfection* OR Infection* Mixed* OR Infection* Polymicrobial*))"

375 Documents

Applying Filters
- Publication Year: 2020, 2021 and 2022
- Document Type: Article

208 Articles

Source: The authors.

The text file was imported into the RStudio Desktop Software (v.2023.03.0+386), linked to the R Software (v.4.2.3), and subsequently analyzed using the Bibliometrix R package (http://www.bibliometrix.org) and the application Biblioshiny.[12]

The analyzes made it possible to visualize the production of articles according to the year, the scientific journals that published the most compared to those that were most cited, the most productive countries according to the affiliations of the authors, and the collaborations carried out between the countries, the most cited articles and the focus of research according to the keywords of the authors.

RESULTS

Of the 208 articles evaluated, 42 were published in 2020, 82 in 2021, and 83 in 2022. That is, there was a growth rate of 95.2% from 2020 to 2021.

One hundred thirty-two different scientific journals were recognized, where 77% published only one article, 10% published two articles, 8% published three articles, and 5% published 4 to 12 articles. The Journal of Medical Virology, Cureus, and American Journal of Tropical Medicine And Hygiene were the ones that were published the most (Figure 2A).

In contrast, the scientific journals: Journal of Medical Virology and Clinical Infectious Disease had the highest number of citations (Figure 2B).

Figure 2 – Publications and citations of scientific journals. Teresina, Piauí, Brazil.
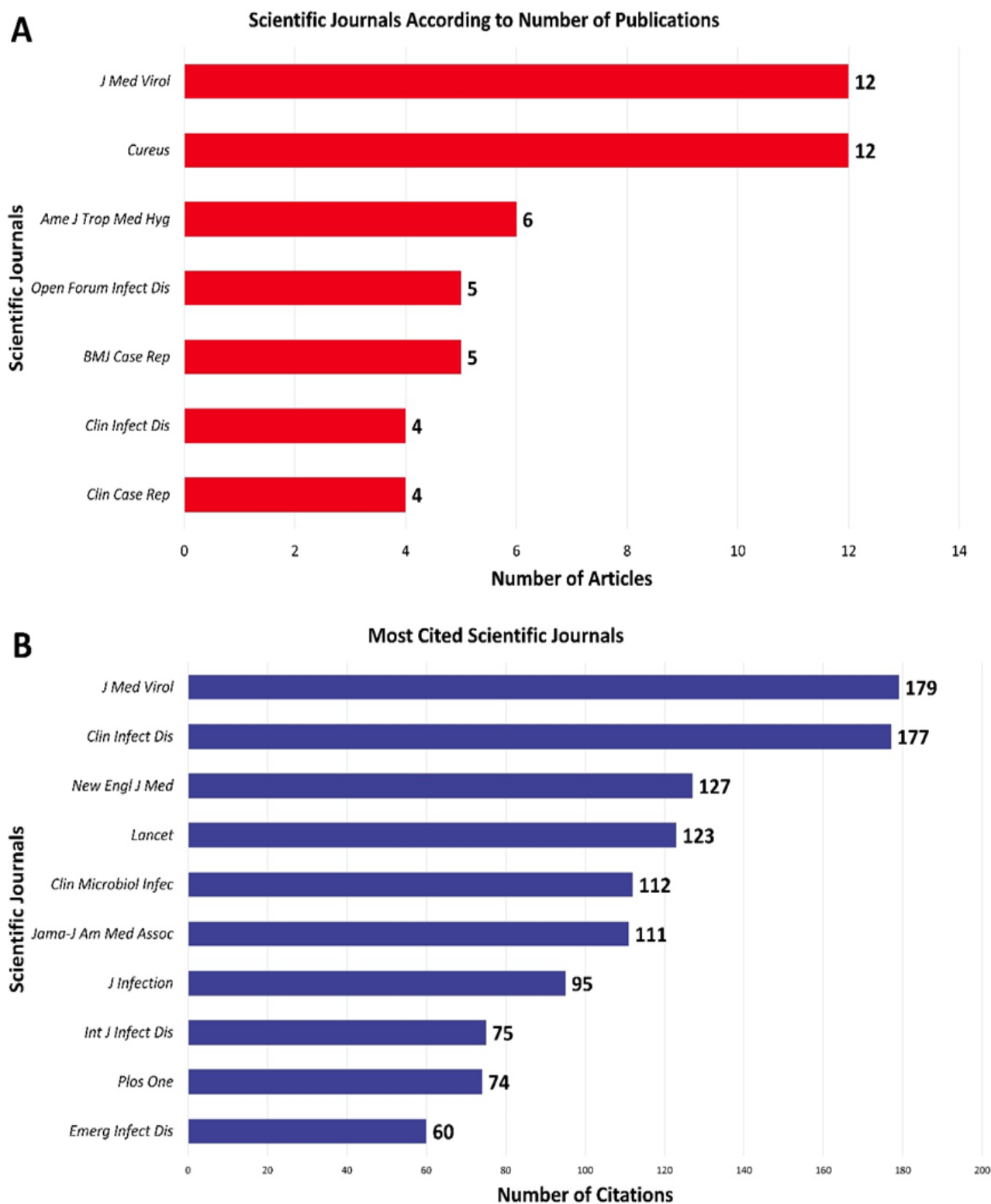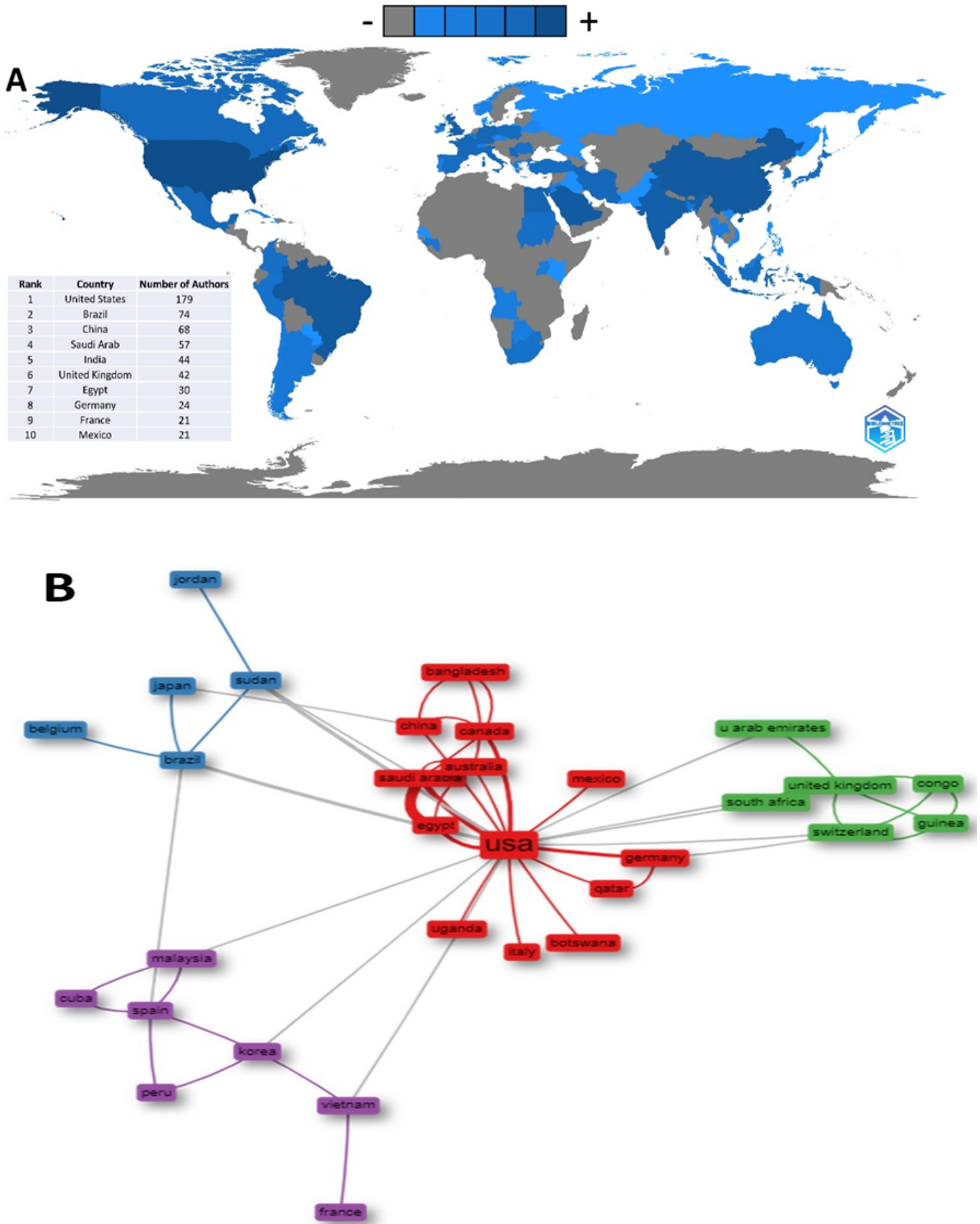

Source: Analysis with Bibliometrix R package.

The articles were produced by 1,660 authors from 58 countries. **Figure 3A** shows the countries that produced the most, considering the co-occurrence of these countries in the authors' affiliation. Therefore, as the figure shows, the researchers primarily resided in the United States (US).

Figure 3B, on the other hand, exposes the collaboration network (Leiden clustering algorithm[13]), where four distinct clusters were formed.

Figure 3 – Most productive countries and collaborations performed. Teresina, Piauí, Brazil.

Rank	Country	Number of Authors
1	United States	179
2	Brazil	74
3	China	68
4	Saudi Arab	57
5	India	44
6	United Kingdom	42
7	Egypt	30
8	Germany	24
9	France	21
10	Mexico	21

Legend: (A) Co-occurrence of countries according to authors' affiliations, with the gray color indicating the absence of local authors and the shades of blue – from lightest to darkest – indicating the increase of local authors. (B) Collaboration network, with the box size proportional to the number of times the country appears and the link width becoming more robust as the number of joint publications increases.
Source: Analysis with Bibliometrix R package.

The 208 articles were cited 2567 times, with an average of 12.3 citations per item. Citations of the top ten articles ranged from 319 to 52, as shown in Table 1. The most cited articles are from nine scientific journals, three published in 2020 and seven in 2021.

Table 1 – Ranking of the most cited articles on COVID-19 and coinfection. Teresina, Piauí, Brazil.

Rank	Author (Year), Scientific Journal	Title	Total Citations (TC)
01	Hughes S et al. (2020), Clin Microbiol Infect[14]	Bacterial and fungal coinfection among hospitalized patients with COVID-19: a retrospective cohort study in a UK secondary-care setting	319
02	Vaughn VM et al. (2021), Clin Infect Dis[15]	Empiric Antibacterial Therapy and Community-onset Bacterial Coinfection in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19): A Multi-hospital Cohort Study	192
03	Wu Q et al. (2020), Pediatrics[16]	Coinfection and Other Clinical Characteristics of COVID-19 in Children	140
04	Nori P et al. (2021), Infect Control Hosp Epidemiol[17]	Bacterial and fungal coinfections in COVID-19 patients hospitalized during the New York City pandemic surge	133
05	Bai L et al. (2021), Cell Res[18]	Coinfection with influenza A virus enhances SARS-CoV-2 infectivity	87
06	Zhao JJ et al (2020), Clin Infect Dis[19]	Early Virus Clearance and Delayed Antibody Response in a Case of Coronavirus Disease 2019 (COVID-19) With a History of Coinfection With Human Immunodeficiency Virus Type 1 and Hepatitis C Virus	62
07	Hashemi SA et al. (2021), J Med Virol[20]	High prevalence of SARS-CoV-2 and influenza A virus (H1N1) coinfection in dead patients in Northeastern Iran	59
08	Stowe J et al. (2021), Int J Epidemiol[21]	Interactions between SARS-CoV-2 and influenza, and the impact of coinfection on disease severity: a test-negative design	58
09	Zou XJ et al., (2021), Clin Gastroenterol Hepatol[22]	Characteristics of Liver Function in Patients With SARS-CoV-2 and Chronic HBV Coinfection	56
10	Riou C et al, (2021), J Clin Invest[23]	Relationship of SARS-CoV-2-specific CD4 response to COVID-19 severity and impact of HIV-1 and tuberculosis coinfection	52

Source: Analysis with Bibliometrix R package.

According to the literature, keywords can summarize the focus of articles and determine search trends.[24] In this article, the 50 keywords of the most frequent authors were used (**Figure 4**).

Figure 4 – Word cloud according to authors' keywords. Teresina, Piauí, Brazil.
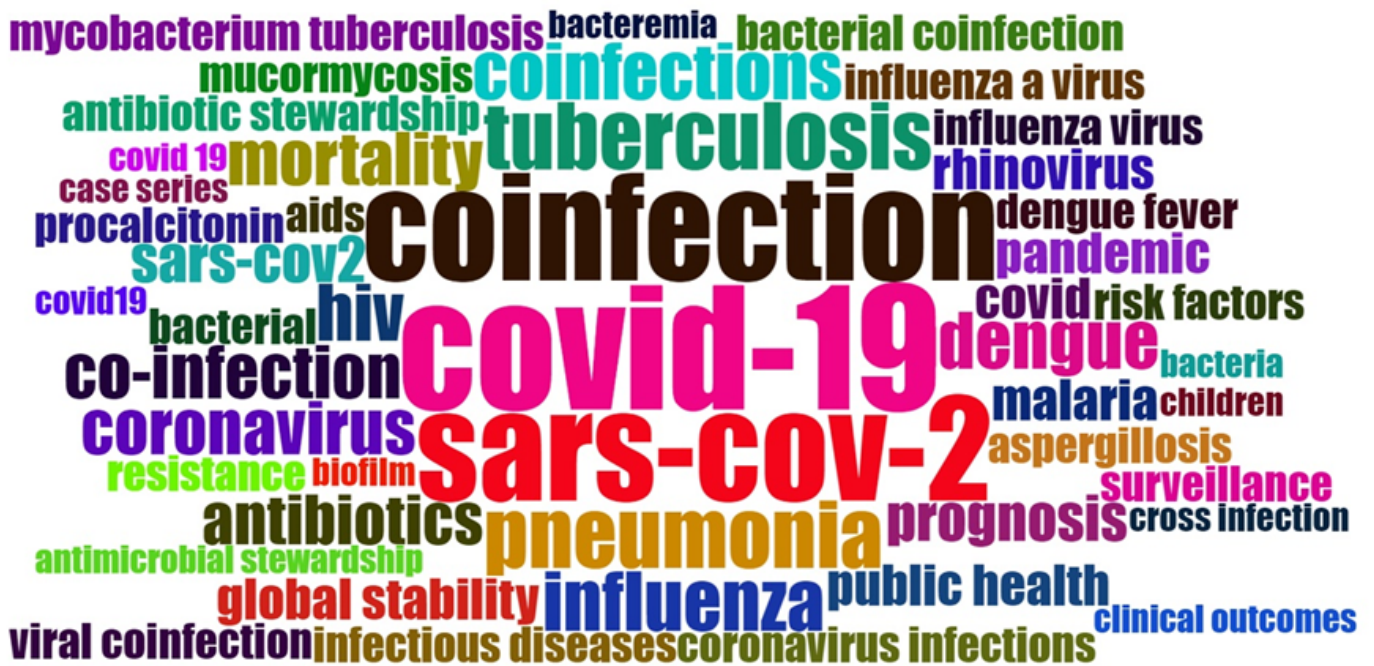
Source: Analysis with Bibliometrix R package.

DISCUSSION

This bibliometric analysis examined the global research trends on COVID-19 and general coinfection between 2020 and 2022. Thus, it was found that at the beginning of the pandemic, due to the high number of hospitalizations and deaths, the production on the subject showed a notorious growth (between 2020 and 2021). On the other hand, the creation of vaccines against COVID-19 and their subsequent implementation worldwide, which led to a decrease in severe cases and hospitalizations, may have favored the reduction in the production of articles on the subject, explaining the stagnation of publications between 2021 and 2022.[25-26]

When analyzing the number of publications on the subject in scientific journals, it is noted that two of these journals concentrated on the same number of articles (12). Namely, the Journal of Medical Virology publishes scientific articles about viruses that affect humans, and Cureus publishes in different medical specialties. Therefore, it is noted that the authors mainly chose scientific journals from virology, general medicine, microbiology, infectious diseases, and immunology.

On the other hand, the Journal of Medical Virology stood out when considering the most cited scientific journals, which causes reflection since only two of the scientific journals that produced the most on the subject are among the ten most cited.

Regarding the countries that produced the most, the results show that the United States, Brazil, and China are in the top positions. Such findings may be related to the fact that these countries have already conducted research on identifying, preventing, and controlling infections since before the COVID-19 pandemic.[27-29] In addition, they are countries where the COVID-19 pandemic has had an exacerbated impact.[30]

In Figure 3B, despite observing four distinct sets of collaboration, one can see mainly the collaborations carried out by the United States within the country itself and with other countries. This finding can be explained by the actions of the US Centers for Disease Control and Prevention, which is also part of the Global Infection Prevention Network (GIPC) of the World Health Organization.[31]

The most cited article evaluated bacterial and fungal coinfection among 836 hospitalized

patients with COVID-19 and identified a reduced rate of bacterial coinfection, which was laboratory confirmed in patients with COVID-19, isolating a few clinically significant pathogens. Thus, ventilator-associated *Klebsiella pneumoniae* and Enterobacter cloacae were attributed to infections of respiratory origin; *Candida albicans*, *Enterococcus* spp., and *Pseudomonas aeruginosa* to central catheter infection and *Escherichia coli* to a urinary catheter. Furthermore, all other bacteremia's had community-onset and were attributed to non-respiratory infections.[14]

The second most cited article sought to determine the prevalence and predictors of empirical antibacterial therapy and initially community-acquired bacterial coinfections in hospitalized patients with COVID-19. In this study, 1705 patients with COVID-19 were evaluated. It was identified that 56.6% received a prescription for early empirical antibacterial therapy, while only 3.5% had a confirmed community bacterial infection; the authors reinforce the discussion about the need to rationalize antimicrobials.[15]

Therefore, the third most cited article aimed to determine the epidemiological and clinical characteristics of 74 pediatric patients with COVID-19. The main result of this study was that pediatric patients with COVID-19 may have epidemiological, clinical, and radiological characteristics different from adult patients, and almost half of the infected children had coinfection with other common respiratory pathogens.[16]

In summary, when evaluating the content of the most cited articles, it was noted that they addressed the etiology and occurrence of coinfections of COVID-19 with other bacteria and fungi, [14,15,17] emphasizing coinfections of SARS-CoV-2 with the Influenza Virus.[16,18,20,21,10] Finally, some of the most cited articles addressed coinfection with the Acquired Immunodeficiency Virus (HIV), Hepatitis B, and C.[19,22,23]

When evaluating the keywords of the authors, it was clear that the articles generally approached

the disease in question and its causative virus, the occurrence of pneumonia, and coinfections caused by bacteria, other viruses, fungi, and those caused by vectors such as dengue and malaria.

In this study, it is necessary to discuss Health Care-Related Infections (HAI), which include bacterial, fungal, and viral infections, which can be multidrug-resistant and contribute to increased hospital mortality.[32] In addition, the literature demonstrates that COVID-19 outbreaks have strongly impacted hospital HAI rates, which demonstrates the need to routinely strengthen measures to prevent hospital infections aimed at preventing SARS-CoV-2 and other pathogens.[33]

The main limitation of the present study was the use of only one database. However, despite not including other databases, it is noteworthy that WoS is a comprehensive and reliable database for bibliometric analyses, which justifies its choice.[9]

Therefore, the growth trends in the number of global publications in the database above make it impossible to analyze them daily, which can also be a limitation. This way, it was decided to delimit the data collection period to proceed with its investigation and discussion. Finally, this study included articles published up to December 31, 2022, not including new publications from 2023.

CONCLUSION

Two hundred-eight articles were analyzed and published in 132 scientific journals; the Journal of Medical Virology and Cureus occupied the first publication positions on the subject, and the Journal of Medical Virology was the most cited. The United States reached the top of the article production ranking according to the authors' affiliations, being also the country that carried out the most collaborations. However, Brazil also stood out, as it was one of the countries most affected by the pandemic.

The published articles on COVID-19 and coinfection were cited 2567 times, with the most

cited addressing bacterial and fungal coinfection among 836 patients hospitalized with COVID-19. It was noted that the articles were focused on the etiology of coinfections, which bacteria, other viruses, fungi, and vectors can cause.

Finally, through this bibliometric analysis, it was possible to identify global trends in research on COVID-19 and coinfection, which in the long term can support the development of new research and the elaboration of strategies aimed at preventing, controlling, and managing cases of coinfections, not only in the pandemic period but continuously.

RESUMO

Introdução: A sintomatologia clínica do SARS-CoV-2 e das coinfecções podem ser mascaradas pela similaridade das manifestações e retardar o diagnóstico clínico, a tomada de decisões terapêuticas e agravar o quadro clínico, aumentando as chances de óbito. Nesse contexto, elencou-se como objetivo realizar uma análise bibliométrica da produção científica mundial sobre a COVID-19 e coinfecção de forma geral. **Delineamento:** Estudo bibliométrico com abordagem quantitativa. Foram analisados 208 artigos utilizando-se o pacote *Bibliometrix R* e sua interface web *Biblioshiny*. **Resultados**: Os artigos foram publicados principalmente em 2021 e 2022. As revistas científicas que mais publicaram foram o *Journal of Medical Virology e o Cureus*. O mais *citado foi o Journal of Medical Virology*. Os artigos foram citados 2567 vezes e estiveram voltados para a etiologia das coinfecções, que podem ser causadas por bactérias, outros vírus, fungos e por vetores. **Implicações:** Por meio dessa análise bibliométrica foi possível identificar as tendências globais de pesquisa sobre a COVID-19 e coinfecção, o que longo prazo pode subsidiar a realização de novas pesquisas e a elaboração de estratégias que visem tanto prevenção, controle e manejo de casos de coinfecções, não só no período pandêmico, mas de maneira contínua.

DESCRITORES

SARS-CoV-2; Infecção Mista; Pandemia; Indicadores Bibliométricos.

RESUMEN

Introducción: La sintomatología clínica del SARS-CoV-2 y las coinfecciones puede enmascararse por la similitud de manifestaciones y retrasar el diagnóstico clínico, la toma de decisiones terapéuticas y empeorar el cuadro clínico, aumentando las posibilidades de muerte. En este contexto, el objetivo fue realizar un análisis bibliométrico de la producción científica mundial sobre el COVID-19 y la coinfección en general. **Diseño:** Estudio bibliométrico con enfoque cuantitativo. Se analizaron 208 artículos utilizando el paquete Bibliometrix R y su interfaz web Biblioshiny. **Resultados:** Los artículos se publicaron principalmente en 2021 y 2022. Las revistas científicas que más publicaron fueron *Journal of Medical Virology* y *Cureus*. El más citado fue el *Journal of Medical Virology*. Los artículos fueron citados 2567 veces y se centraron en la etiología de las coinfecciones, que pueden ser causadas por bacterias, otros virus, hongos y vectores. **Implicaciones:** A través de este análisis bibliométrico, fue posible identificar tendencias globales en la investigación sobre COVID-19 y coinfección, que a largo plazo pueden apoyar el desarrollo de nuevas investigaciones y la elaboración de estrategias dirigidas a la prevención, control y manejo de casos de coinfecciones, no solo en el período pandémico, sino de forma continua.

DESCRIPTORES

SARS-CoV-2; Infección Mixta; Pandemia; Indicadores Bibliométricos.

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COLLABORATIONS

MEBM: substantial contributions in the research design, methodological and organizational structuring of the study and relevant critical review of the intellectual content. ARSN: Substantial contributions in data analysis with the Software and relevant critical review of intellectual content. REC, ARBC, NVGP and TAO: substantial contributions in the writing of the article and in the discussion of the data. ARMCV and DRJF: substantial contributions in the critical review of intellectual content. **All authors agree and are responsible for the content of this version of the manuscript to be published.**

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.