Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Research Article

COVID-19 pharmacological research trends: a bibliometric analysis

Yanyan Shi 1,#, Yahan Song 2,#, Zhijun Guo 3,#, Wei Yu 4, Huiling Zheng 3, Shigang Ding 3,#, Siyan Zhan 1,#

1 Research Center of Clinical Epidemiology, Peking University Third Hospital, Beijing 100191, China
2 Library of Peking University Third Hospital, Beijing 100191, China
3 Department of Gastroenterology, Peking University Third Hospital, Beijing 100191, China
4 Department of Gastroenterology, Affiliated Hospital of Jining Medical University, Jining, Shandong 272007, China

ARTICLE INFO

Keywords:
- Bibliometric analysis
- COVID-19
- Pharmacological interventions
- Vaccine
- SARS-CoV-2

ABSTRACT

Background The coronavirus disease 2019 (COVID-19) pandemic is ravaging the world. Many therapies have been explored to treat COVID-19. This report aimed to assess the global research trends for the development of COVID-19 therapies.

Methods We searched the relevant articles on COVID-19 therapies published from January 1, 2020, to May 25, 2022, in the Web of Science Core Collection Database (WOSCC). VOSviewer 1.6.18 software was used to assess data on the countries, institutions, authors, collaborations, keywords, and journals that were most implicated in COVID-19 pharmacological research. The latest research and changing trends in COVID-19-relevant pharmacological research were analyzed.

Results After manually eliminating articles that do not meet the requirements, a total of 5,289 studies authored by 32,932 researchers were eventually included in the analyses, which comprised 95 randomized controlled trials. 3,044 (57.6%) studies were published in 2021. The USA conducted the greatest number of studies, followed by China and India. The primary USA collaborators were China and England. The topics covered in the publications included: the general characteristics, the impact on pharmacists’ work, the pharmacological research, broad-spectrum antiviral drug therapy and research, and promising targets or preventive measures, such as vaccine. The temporal diagram revealed that the current research hotspots focused on the vaccine, molecular docking, Mpro, and drug delivery keywords.

Conclusion Comprehensive bibliometric analysis could aid the rapid identification of the principal research topics, potential collaborators, and the direction of future research. Pharmacological research is critical for the development of therapeutic and preventive COVID-19-associated measures. This study may therefore provide valuable information for eradicating COVID-19.

1. Introduction

The emergence and spread of coronavirus disease 2019 (COVID-19) was declared a global pandemic on March 11, 2020 by the World Health Organization (WHO), and has become a major health threat worldwide [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the coronavirus responsible for causing COVID-19. COVID-19 is characterized by such symptoms as viral pneumonia, fever, fatigue, dry cough, and lymphopenia. The most common manifestations of COVID-19 are a cough, fever, and fatigue, which are often accompanied by lung infection [2]. The number of confirmed new COVID-19 cases is increasing every day (at the time of writing). Consequently, hundreds of academic articles are being published every day that are closely related to various aspects of COVID-19, which include its epidemiology, pathology, and treatment. These COVID-19 studies emphasize the urgency of obtaining effective drugs [3].

The therapeutic efficacy of antimalarial drugs, antiviral drugs, monoclonal antibody therapy, and cell- and plasma-based therapies in the treatment of COVID-19 have been evaluated [4]. At the beginning of the outbreak, the mechanism employed by SARS-COV-2 to invade the human body was not clear. Thus, it was not possible to develop anti-SARS-COV-2 drugs based on the mechanism of viral infection. Instead, the principal strategy for guiding the emergency response against SARS-COV-2 was to utilize commercially available drugs based on studies of

* Corresponding authors: Siyan Zhan, Research Center of Clinical Epidemiology, Peking University Third Hospital, Beijing 100191, China (Email: siyanzhan@bjmu.edu.cn); Shigang Ding, Department of Gastroenterology, Peking University Third Hospital, Beijing 100191, China (Email: dingshigang222@163.com).
* These authors contributed equally to this work.

https://doi.org/10.1016/j.imed.2022.06.004
Received 29 April 2022; Received in revised form 7 June 2022; Accepted 24 June 2022
2667-1026/© 2022 The Authors. Published by Elsevier B.V. on behalf of Chinese Medical Association. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)
cellular and animal models. A series of in-depth studies on the infection mechanism of SARS-CoV-2 were later carried out, and on this basis, innovative drugs against SARS-CoV-2 were generated and evaluated for their specificity, safety, and efficacy. The development of novel indications for the treatment of COVID-19 and innovative drugs based on the mechanism of viral infection can ultimately achieve effective COVID-19 treatment. In this process, research teams have accumulated a wealth of expertise, which they have combined with the latest scientific and technological advances.

Bibliometric analysis is based on the unique publication parameters (such as information relating to country of origin, institution, and author identities) and uses a combination of mathematical and statistical methods to quantitatively assess the current status, research hotspots, and trends in science and technology. Researchers can subsequently use the information gathered for a particular purpose within their domains of interest (e.g., to identify active collaborative partners, landmark studies, research themes, and other useful information). As would be expected, COVID-19-drug-related research is booming. In this paper, we have summarized the latest COVID-19 pharmacological research and therapeutics advances in this field, with the aim of presenting systematic data to combat the COVID-19 pandemic. In addition, we envisage that this paper will provide a valuable reference for the development of new drugs to treat COVID-19.

2. Material and methods

We searched the Web of Science Core Collection (WOSCC) database on May 25, 2022, using the search strategy: TS = (COVID OR COVID19 OR COVID-19 OR COVID 19 OR coronavirus OR coronavirus disease 2019 OR SARS CoV 2 OR SARS coronavirus 2 OR severe acute respiratory syndrome coronavirus 2 OR 2019-nCoV) AND 2022 or 2021 or 2020 (Publication Years) AND (Pharmacology Pharmacy (Research Areas) OR Pharmacology Pharmacy (Web of Science Categories)) AND DT = (Article). Research articles published from January 2020 onwards were selected. We scanned the abstracts, manually deleted the records unrelated to COVID-19 pharmacology. Additionally, we selected works describing randomized controlled trials (RCTs) for a further separate analysis.

Excel 2010 (Microsoft Corporation, Redmond, WA, USA) was used to collect the extracted data and perform statistical analysis. VOSviewer 1.6.18 (Centre for Science and Technology Studies, Leiden University, Leiden, The Netherlands), a freely available computer program that was developed in 2009 for constructing and viewing bibliometric maps [5], was used to map research outputs and plot (Figures 1-7). VOSviewer is specifically designed for the graphical representation of bibliometric maps, which are being increasingly widely used to perform bibliometric analysis. In this study, VOSviewer 1.6.18 was used to assess and graph data on the countries, institutions, authors, collaborations, keywords, and journals that were most implicated in COVID-19 pharmacological research [6]. The size of the node is correlated with the occurrence frequency of the relevant parameter, while the thickness of the connection between nodes represents the degree of association, and different colors represent the different modules in the visualization map.

3. Results

3.1. Publication outputs

Between January 1, 2020, and May 25, 2022, a total of 5,523 articles were identified from the WOSCC database. However, some of them (n = 234) were unrelated to COVID-19 pharmacology. Therefore, we analyzed 5,289 regular articles and 95 manuscripts reporting RCTs. This process was shown in Supplementary Figure 1. Of the articles included in our analysis, 1,408 (26.6%), 3,044 (57.6%), and 837 (15.8%) were published or preprinted in 2020, 2021, and 2022, respectively (Supplementary Figure 2).

3.2. Co-authorship analysis; most active countries or regions, institutions, authors, and journals

The top ten countries or regions, institutions, and authors with the most publications are listed in Tables 1-3. Seventy-nine countries or regions published no less than five documents during the assessment pe-
The highest number of studies was conducted in the USA (1,088 records), followed by China (810), India (561), Italy (454), and Saudi Arabia (314). Seven clusters were obtained based on this information (Figure 1a). The USA had 68 collaborative partners and a total link strength (TLS) of 786. TLS is a measure used to describe the total strength between one unit and others, in this case the total strength of the co-authorship links between one researcher and other researchers.

USA’s primary collaborators were China (link strength = 61), the England (link strength = 58), India (link strength = 50), and Italy (link strength = 50).

The 5,289 studies involved 7,797 institutions, 117 of which each published at least 15 studies. The clustering of the institutions is shown in Figure 1b. The top publishing institution was King Saud University, which was responsible for 67 research outputs on the pharmacology of COVID-19. The main collaborators of this University were the Ministry of Health and the Prince Sattam Bin Abdulaziz University (link strength = 6). Tehran University of Medical Sciences (60 publication records), Huazhong University of Science and Technology (58 publication records), and the Chinese Academy of Sciences (56 publication records) were also among the top contributors of COVID-19 publications.

A total of 32,932 authors published research articles on the relevant topic; 230 of whom had each published five or more papers. Prof. Gupta BM from India had published the greatest number of documents during the study period (n = 19). Among the 230 authors, 64 had a connection with each other; the relevant cluster is shown in Figure 1c and d.

Table 4 shows the top ten most active journals, which published the largest articles on COVID-19 pharmacology; the top three were European Review for Medical and Pharmacological Sciences, International Journal of Clinical Practice, and Frontiers in Pharmacology.

3.3. Keyword co-occurrence analysis

Before constructing the cluster map, we manually standardized the keywords by merging and replacing similar keywords. A total of 207 keywords were considered in the analysis (occurrence ≥ 20). As described above, the TLS is used to describe the total strength of links between one unit and other units. The three most common keywords were “COVID-19” (TLS = 9,743; occurrences = 3,153), “SARS-CoV-2” (TLS = 7,134; occurrences = 1,819), and “coronavirus” (TLS = 3,575; occurrences = 798). To show the other keywords more clearly, the above most common three keywords were omitted from the figure. Five clusters were obtained from the analysis (Figure 2). Cluster 1 (shown in red) comprised 58 items that represented general terms related to COVID-19 and included keywords such as infection, pneumonia, inflammation, mortality, disease, cytokine storm, mechanism, expression, cells, and activation. Cluster 2 (shown in green) contained 50 items that represented the impact of COVID-19 and included keywords such as pandemic, risk, impact, outbreak, Wuhan, epidemiology, management, pharmacist, health, and anxiety. Cluster 3 (shown in blue) included 47 items that were associated with pharmacological research on COVID-19 and comprised keywords such as inhibition, molecular docking, antiviral, drugs, in-vitro, identification, drug repurposing, replication, Mpro (the main SARS-CoV-2 protease), design,
traditional Chinese medicine, discovery, molecular dynamics, and 3CL protease. Cluster 4 (shown in yellow) comprised 28 items relating to broad-spectrum antiviral drug therapy and COVID-19 research and included keywords such as hydroxychloroquine/chloroquine, remdesivir, pharmacokinetics, efficacy, antiviral drugs, safety, lopinavir/ritonavir, favipiravir, azithromycin, and clinical trials. Cluster 5 (shown in purple) included 21 items associated with promising COVID-19 drug targets or preventive measures, and keywords such as ACE2 (angiotensin-converting enzyme 2), viral infection, vaccine, spike protein, receptor, influenza, and immunity. We next constructed a temporal diagram (Figure 3), which showed that at the beginning of the COVID-19 pandemic research focused on topics such as chloroquine/hydroxychloroquine, pneumonia, respiratory syndrome coronavirus, epidemiology, traditional Chinese medicine, receptor, replication, cytokine storm, antiviral, efficacy, ACE2, remdesivir, spike protein, inflammation, and drug repurposing. However, most recent research hotspots were associated with keywords such as impact, molecular docking, Mpro, activation, vaccine, and drug delivery. The density visualizations shown in Figures 4 and 5 indicate the density of term frequency. In Figure 4, the items occurring with more frequency were redder in color, while less frequently occurring items were bluer. Similarly, the size of items in Figure 5 is related to density, and the color key is the same as used in Figure 2.

3.4. RCT analysis

Among the 95 RCT publications, Iran (n = 30), USA (n = 23), China (n = 18), and the England (n = 14) produced the greatest number of outputs. Institutions like Tehran University of Medical Sciences (n = 13) from Iran, Shahid Beheshti University of Medical Sciences (n = 10) from Iran, the University of Liverpool (n = 9) from the England, and Mazandaran University of Medical Sciences (n = 8) from Iran, were the most prolific at reporting clinical trials. Out of all the researchers, Prof. Andrew Hill (n = 6) and Prof. Hannah Wentzel (n = 5) from the England were most actively involved in designing RCTs.

The keywords pharmacokinetics, traditional Chinese medicine, viral infection, lopinavir/ritonavir, and favipiravir appeared more frequently in publications reporting RCTs (occurrences > 4). Keywords with an occurrence greater than two (other than “COVID-19” and “SARS-Cov-2”), which were omitted from the analysis, are presented in Figure 6.

3.5. Analysis of the top 100 most highly cited articles

We further analyzed the top 100 most highly cited articles within the WOSCC. China (n = 31) and the USA (n = 22) were responsible for over half of the most cited articles published during our study period. Aix-Marseille University (n = 7), IHU Mediterranee Infection (n = 4),
Figure 3. Co-word (keyword co-occurrence) bibliometric analysis: temporal trends of overlay visualization. The color of the nodes, changing from blue to yellow, represents the average publication year of the keywords.

Figure 4. Co-word (keyword co-occurrence) bibliometric analysis: item density visualization.

and Monash University (n = 4) each published more than three top-cited works. We also found that the research groups publishing the most cited papers were led by Prof. Didier Raoult (n = 4) in France and by Prof. Po-Ren Hsueh (n = 3) in China.

As shown in Figure 7, the keywords that appeared in the most highly cited literature were mainly focused on the mechanism of viral infection (i.e., spike protein, ACE2, 3CL protease, Mpro, and receptor) and antiviral drugs and their activity (i.e., chloroquine/hydroxychloroquine, remdesivir, ribavirin, molecular docking, and RNA-polymerase).

4. Discussion

During the global COVID-19 pandemic, increasing attention was focused on pharmacological research. Our bibliometric analysis of COVID-19-associated pharmacological research trends showed that publications were more numerous in 2021 versus 2020 (Supplementary Figure 2). We found that half of the original articles and reviews were published by three countries: the USA, China, and India. In addition, the USA and China outperformed all other countries in the number of publications.
and citations, especially in relation to the top 100 most highly cited articles. We observed that American COVID-19 research involved the highest number of international collaborations. The tightest academic collaborative partnerships were forged between USA and China, followed by USA and the England, Egypt and Saudi Arabia, USA and Italy, and USA and India. Certain institutions from Iran, Saudi Arabia, and China were highly prolific at generating research outputs (Figure 1). Five active journals, which are based in either Europe or Asia (listed in Table 4), published over 20% of the articles reporting COVID-19 pharmacological research. This finding demonstrates that certain periodicals preferentially publish scientific content relating to COVID-19 pharmacology. The 2020 impact factors for the top ten active publishers of COVID-19 pharmacological research were moderate, six of which were higher than 4.

Five clusters in the network visualization map hinted at the five categories of therapeutic research (Figure 2). We summarized the themes for each cluster as follows: (1) the general characteristics of SARS-COV-2 (red); (2) the impact of COVID-19 (green); (3) COVID-19 pharmacological research. This finding demonstrates that certain periodicals preferentially publish scientific content relating to COVID-19 pharmacology. The 2020 impact factors for the top ten active publishers of COVID-19 pharmacological research were moderate, six of which were higher than 4.

Five clusters in the network visualization map hinted at the five categories of therapeutic research (Figure 2). We summarized the themes for each cluster as follows: (1) the general characteristics of SARS-COV-2 (red); (2) the impact of COVID-19 (green); (3) COVID-19 pharmacological research. This finding demonstrates that certain periodicals preferentially publish scientific content relating to COVID-19 pharmacology. The 2020 impact factors for the top ten active publishers of COVID-19 pharmacological research were moderate, six of which were higher than 4.

Five clusters in the network visualization map hinted at the five categories of therapeutic research (Figure 2). We summarized the themes for each cluster as follows: (1) the general characteristics of SARS-COV-2 (red); (2) the impact of COVID-19 (green); (3) COVID-19 pharmacological research. This finding demonstrates that certain periodicals preferentially publish scientific content relating to COVID-19 pharmacology. The 2020 impact factors for the top ten active publishers of COVID-19 pharmacological research were moderate, six of which were higher than 4.

Five clusters in the network visualization map hinted at the five categories of therapeutic research (Figure 2). We summarized the themes for each cluster as follows: (1) the general characteristics of SARS-COV-2 (red); (2) the impact of COVID-19 (green); (3) COVID-19 pharmacological research. This finding demonstrates that certain periodicals preferentially publish scientific content relating to COVID-19 pharmacology. The 2020 impact factors for the top ten active publishers of COVID-19 pharmacological research were moderate, six of which were higher than 4.

Figure 5. Co-word (keyword co-occurrence) bibliometric analysis: cluster density visualization.

Figure 6. Co-word (keyword co-occurrence) bibliometric analyses of 95 RCTs.
logical research (blue); (4) broad-spectrum antiviral drug therapy and COVID-19 research (yellow); and (4) promising COVID-19 targets or preventive measures (purple). The mechanism seemed to be the foundation of pharmacologic research. The time trend of the overlay visualization map (Figure 3) revealed changes in research hotspots at different phases. In the early phase, COVID-19 pharmacological research focused on therapeutic schedule exploration for existing drugs such as antimalarial and antiviral drugs. In the latter phase, the research focus shifted to the impact on pharmacists' work and especially vaccine development.

Keyword analyses (Figures 2–5) visually demonstrated the burgeoning research hotspots and trends in COVID-19 pharmacology. Our result highlighted certain keywords that were highly associated with COVID-19 pharmacological research; they will be explored in more detail in this section.

First, 'ACE2' and the 'spike protein': the viral spike protein on SARS-CoV-2 binds to the cellular receptor ACE2 [7], which is widely distributed in various tissues and highly expressed in the lung and small intestine. This broad distribution of ACE2 may explain why COVID-19 can involve multiple organ systems [8]. The SARS-CoV-2 spike protein serves as a potential target for vaccine development, antibody-blocking therapy, and small molecule inhibitors [9]. The spikes can camouflage themselves to evade immunological surveillance [9], and, once mutations happen, the immune protection afforded by antibodies responding to infection or vaccination, is lost [10]. Besides, transplantation of ACE2 (-) mesenchymal stem cells may potentially improve the outcome for patients with COVID-19 [11].

Second, ‘vaccine’: vaccine development is a vital area of COVID-19 research. The COVID-19 vaccine is designed to attenuate the viral load, therefore diminishing the risk of febrile symptoms and illness duration [12]. Several types of COVID-19 vaccine such as inactivated vaccines, vector-based vaccines, and nucleic acid-based vaccines, have entered phase 3 clinical trials [13]. Moreover, the effectiveness and safety of certain vaccine candidates have been verified in real-world studies [14].

Third, 'chloroquine' and 'hydroxychloroquine': chloroquine, an antimalarial drug, has shown efficacy and safety against SARS-CoV-2 in Chinese multicenter clinical trials [15]. On the one hand, hydroxychloroquine and chloroquine are able to bind to the ACE2 receptor and prevent the viral S protein from binding to the plasma membrane [16]. On the other hand, chloroquine has been proven to inhibit the production and release of interleukin (IL)-6 and tumor necrosis factor (TNF) [17], curbing the cytokine storm, and thus effectively limiting viral replication \textit{in-vitro} [18]. However, some systematic reviews have shown that HCQ has little or no effect on the risk of death and progression in comparison to mechanical ventilation [19].

Forth, 'cytokine storm' and 'immunity': the dysregulation and excessive release of proinflammatory cytokines (e.g., IL-1β, IL-6, and TNF) [17] is a potential mechanism leading to severe COVID-19 manifestations. The decrease in CD4+ T cell, CD8+ T cell, and regulatory T cell (Treg) counts may aggravate inflammation and the cytokine storm and cause extensive tissue damage [20]. Hence, immunomodulators and cytokine antagonists such as the IL-6 receptor antagonist, tocilizumab, may represent promising drugs for the treatment of patients with severe COVID-19 [17,21].

Fifth, ‘traditional Chinese medicine’: traditional Chinese medicine formulations were successfully used in Wuhan to treat COVID-19, which provides reliable evidence for conducting follow-up research on this topic. Clinical trials have been conducted using Lianhua Qingwen capsules, Shuang Huang Lian Oral Liquid, and ShuFeng Jiedu capsules, among others [22–23]. 3-chymotrypsin-like protease (3CLpro), the SARS-CoV helicase protein nsP13, repressing virus-induced gene expression of IL-6, IL-8, TNF, interferon gamma-induced protein (IP-10), and monocyte chemoattractant protein-1 (MCP-1) may be relevant to the potential pharmacological mechanisms of traditional Chinese medicine [24].

Collectively, these five groups of keywords showed that during the COVID-19 pandemic, identification of the main viral target proteins and pathogenic mechanisms are important for conducting pharmacological research. Furthermore, drug repurposing and development should be performed to achieve effective viral eradication [25]. In the early phase of the pandemic, prior pharmacological research provided clues for therapeutic schedule exploration. Meanwhile, in the latter phase, novel pharmacological evidence was used to develop preventative regimens, such as vaccines. In summary, pharmacology was critical throughout the duration of the COVID-19 pandemic.
In addition to the factors already mentioned, our study highlighted other important COVID-19-associated factors, such as ‘convalescent plasma’, ‘diet’, and ‘mental health’.

Researchers have explored the feasibility of convalescent plasma transfer to treat severe COVID-19 cases [26]. Well-tolerated convalescent plasma therapy may potentially improve clinical outcomes via the transfer of neutralizing antibodies, achieving viral neutralization in patients with severe COVID-19 without severe adverse effects [27–28]. Accordingly, testing the efficacy and safety of convalescent plasma transfusion in SARS-CoV-2-infected individuals should be pursued [29].

Diet and mental health status should also be monitored during the COVID-19 pandemic. Numerous surveys had declared that COVID-19-imposed lockdowns had a negative effect on diet [30] and mental health [31]. Conversely, unhealthy lifestyle factors such as unreasonable diet structure [32] are related to a higher risk of COVID-19 hospitalization. Optimal nutritional status may reinforce immune function [33], and nutrient supplementation like vitamin D could be an additional measure to reduce the morbidity of COVID-19 [34].

RCTs, as the gold standard of research design, can rigorously verify the efficacy and safety of drugs. The RCT designs included in our study focused on the pharmacokinetics of antiviral drugs such as favipiravir and lopinavir/ritonavir, and traditional Chinese medicines such as curcumin. Based on ethical requirements, favipiravir and lopinavir/ritonavir were often used as a background treatment. Lopinavir/ritonavir was the national regimen adopted by Iran (which was also used in combination with interferon and hydroxychloroquine). Traditional Chinese medicine, as an empirical therapy approach, required other evidence-based forms of treatment to validate its efficacy. Therefore, the keywords with moderate occurrences (>2), such as the IL-6 receptor-blocking monoclonal antibody tocilizumab, azithromycin, and antiparasitic drug ivermectin, denoted pharmacological research hotspots.

However, our study inevitably had some limitations. Firstly, we only searched the WOSCC database. Other databases such as SCOPUS could also be considered in future studies. Secondly, although we had already excluded authors with the same name from the top ten active authors list, we could not artificially distinguish between all forms of name duplication on account of the huge author data set. Last, this study merely scanned and refined part of key points among the evolution of pharmacological research hotspots. Online tools are now available to monitor these trends. For instance, ‘evolving reviews’ provide updates on a particular area of research [4,35], and collaborations like the CORONA Project track and review the latest pharmacological research trends [36].

5. Conclusion

In conclusion, comprehensive bibliometric analysis can help us understand the current status and trends relating to a given research field, additionally highlighting areas of particular research interest. This approach represents an effective way of studying the literature that can provide a useful reference for researchers. Pharmacology research is critical for therapeutic and vaccine development. To the best of our knowledge, a bibliometric analysis of this sort has not been previously performed for COVID-19 pharmacological research. Thus, our study confirms that the field of pharmacology could make a valuable contribution to the bioprospecting of novel COVID-19 drugs and vaccines.

Conflicts of interest statement

The authors have no competing interests to declare that are relevant to the content of this article.

Funding

This work was supported by the special fund of Beijing Key Clinical Specialty Construction Project, and the Hospital Library Committee of Library Society of China (Grant No. YX2021Y05).

Author contributions

Yanyan Shi participated in project design, data collection, and manuscript writing. Yahan Song took part in data collection and data analyses. Zhijun Guo drafted the manuscript. Wei Yu performed data collection, and Huiling Zheng undertook the literature search. Shigang Ding and Siyan Zhan contributed to the project design and manuscript revision and provided study support. All authors read and approved the final manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imed.2022.06.004.

References

[1] Mahase E. Covid-19: WHO declares pandemic because of ‘alarming levels’ of spread, severity, and infection. BMJ 2020;368:m1036. doi:10.1136/bmj.m1036..
[2] Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med 2020;288(2):192–206. doi:10.1111/joim.13091.
[3] Sachs JD, Karim SA, Akinl, et al. Priorities for the COVID-19 pandemic at the start of 2021: statement of the Lancet COVID-19 Commission. Lancet 2021;397(10278):947–50. doi:10.1016/S0140-6736(21)00388-3.
[4] Randu Halie M, Wellhausen N, et al. Identification and development of therapeutics for COVID-19. mSystems 2021;6(6):e00233. doi:10.1128/mSystems.00233-21.
[5] van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics 2010;84(2):523–38. doi:10.1007/s11192-009-0146-3.
[6] Donthu N, Kumar S, Mukherjee D, et al. How to conduct a bibliometric analysis: an overview and guidelines. J Bus Res 2021;133:285–96. doi:10.1016/j.jbusres.2021.04.070.
[7] Bourgonje AR, Abdulle AE, Timens W, et al. Angiotensin-converting enzyme 2 (ACE2), SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19). J Pathol 2020;251(3):228–48. doi:10.1002/path.5471.
[8] Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endothelitis in COVID-19. Lancet 2020;395(10234):1417–18. doi:10.1016/S0140-6736(20)30937-5.
[9] Watanabe Y, Allen JD, Wrapp D, et al. Site-specific glycan analysis of the SARS-CoV-2 spike. Science 2020;369(6501):330–3. doi:10.1126/science.abb9983.
[10] Wang YC, Zhang L, Qi QQ, et al. The significant immune escape of pseudotyped SARS-CoV-2 variant Omicron. Emerg Microbes Infect 2022;11(1):1–5. doi:10.1080/22221751.2021.197757.
[11] Leng ZK, Zhu RJ, Hou W, et al. Transplantation of ACE2(-) mesenchymal stem cells improves the outcome of patients with COVID-19 pneumonia. Aging Dis 2020;11(2):216–28. doi:10.14336/ad.2020.0228.
[12] Thompson MG, Burgess JL, Naleway AL, et al. Prevention and attenuation of COVID-19 with the BNT162b2 mRNA vaccine. N Engl J Med 2021;385(4):320–9. doi:10.1056/NEJMa2107058.
[13] Anand U, Jakkola S, Induri O, et al. Potential therapeutic targets and vaccine development for SARS-CoV-2/COVID-19 pandemic management: a review on the recent update. Front Immunol 2021;12: doi:10.3389/fimmu.2021.658519.
[14] Sharma O, Sultan AA, Ding H, et al. A review of the progress and challenges of developing a vaccine for COVID-19. Front Immunol 2020;11:2413. doi:10.3389/fimmu.2020.5819.
[15] Gao J, Tian Z, Yang X, Brethrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19-associated pneumonia in clinical studies. Biosci Trends 2020;14(1):23–7. doi:10.5582/bst.2020.01047.
[16] McKinnon JE, Wang DD, Zervos M, et al. Safety and tolerability of hydroxychloroquine in health care workers and first responders for the prevention of COVID-19: WHIP COVID-19 study. Int J Infect Dis 2022;116:167–73. doi:10.1016/j.ijid.2021.12.243.
[17] Ye Q, Wang BL, Mao JH. The pathogenesis and treatment of the ‘cytokine Storm’ in COVID-19. J Infect 2020;80(6):607–13. doi:10.1016/j.jinf.2020.03.037.
[18] Cortigiani A, Ingoglia G, Ippolito M, et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. J Crit Care 2020;57:279–83. doi:10.1016/j.jcrc.2020.03.005.
[19] Singh B, Ryan H, Kredo T, et al. Chloroquine or hydroxychloroquine for prevention and treatment of COVID-19. Cochrane Database Syst Rev 2020(2):95. doi:10.1002/14651858.CD013587.pub2.

[20] Qin C, Zhou LQ, HuZW, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis 2020;71(15):762-8. doi:10.1093/cid/ciaa248.

[21] Zhang C, Wu Z, Li JW, et al. Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. Int J Antimicrob Agents 2020;55(5):6. doi:10.1016/j.ijantimicag.2020.105954.

[22] Lee DYW, Li QY, Liu J, et al. Traditional Chinese herbal medicine at the forefront battle against COVID-19: clinical experience and scientific basis. Phytomedicine 2021;80. doi:10.1016/j.phymed.2020.153337.

[23] Li RF, Hou YL, Huang JC, et al. Lianhuangqingwen exerts antiviral and anti-inflammatory activity against novel coronavirus (SARS-CoV-2). Pharmacol Res 2020;156. doi:10.1016/j.phrs.2020.104761.

[24] Yang Y, Islam MS, Wang J, et al. Traditional Chinese medicine in the treatment of patients infected with 2019 new coronavirus (SARS-CoV-2): a review and perspective. Int J Biol Sci 2020;16(10):1708–17. doi:10.7150/ijbs.45538.

[25] Rando HM, Wellhausen N, Ghosh S, et al. Identification and development of therapeutics for COVID-19. ArXiv 2021.

[26] Shen CG, Wang ZQ, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA-J Am Med Assoc 2020;323(16):1582–9. doi:10.1001/jama.2020.4783.

[27] Duan K, Liu BD, Li CS, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci USA 2020;117(17):9490–6. doi:10.1073/pnas.2004168117.

[28] Rojas M, Rodriguez Y, Monsalve DM, et al. Convalescent plasma in Covid-19: possible mechanisms of action. Autoimmun Rev 2020;19(7):9. doi:10.1016/j.autrev.2020.102554.

[29] Chen X, Xiong J, Bao L, et al. Convalescent plasma as a potential therapy for COVID-19. Lancet Infect Dis 2020;20(4):398–400. doi:10.1016/s1473-3099(20)30141-9.

[30] Di Renzo L, Gualtieri P, Pivari F, et al. Eating habits and lifestyle changes during COVID-19 lockdown: an Italian survey. J Transl Med 2020;18(1). doi:10.1186/s12967-020-02399-5.

[31] Rossi R, Socci V, Talevi D, et al. COVID-19 pandemic and lockdown measures impact on mental health among the general population in Italy. Front Psychiatry 2020;11:790. doi:10.3389/fpsyt.2020.00790.

[32] Butler MJ, Barrientos RM. The impact of nutrition on COVID-19 susceptibility and long-term consequences. J Transl Med 2020;18:53–4. doi:10.1186/j.translmed.2020.04.040.

[33] Calder PC, Carr AC, Gambert AF, et al. Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. Nutrients 2020;12(4). doi:10.3390/nu12041181.

[34] Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients 2020;12(4). doi:10.3390/nu12040988.

[35] Halie M, Rando CSG, Michael P Robson, et al. SARS-CoV-2 and COVID-19: An Evolving Review of Diagnostics and Therapeutics. 2022. Available from: https://greenlab.github.io/covid19-review/. (Accessed on September 3, 2022).

[36] CORONA. CORONA project; 2022. Available from: https://cdcn.org/corona/.