

Bibliometric review: Main publications that associate SARS-CoV-2 with blood cell changes in the year 2020

Revisão bibliométrica: Principais publicações que associam SARS-CoV-2 com as alterações nas células sanguíneas no ano de 2020

Revisión bibliométrica: Principales publicaciones que asocian el SARS-CoV-2 con los cambios en las células sanguíneas en el año 2020

Received: 08/18/2022 | Revised: 09/25/2022 | Accepted: 01/05/2023 | Published: 01/07/2023

Allan Carlos da Silva Tiago

ORCID: <https://orcid.org/0000-0002-0041-4161>
Universidade do Estado do Pará, Brazil
E-mail: pharma.allan@gmail.com

Luana Joana Barreto Cabral

ORCID: <https://orcid.org/0000-0002-1060-9317>
Universidade do Estado do Pará, Brazil
E-mail: luanajbcabral@gmail.com

Juliane de Lima Cruz

ORCID: <https://orcid.org/0000-0002-8757-970X>
Universidade do Estado do Pará, Brazil
E-mail: Julianelimacruz@gmail.com

Daniela Pereira Lopes

ORCID: <https://orcid.org/0000-0002-2204-8270>
Universidade do Estado do Pará, Brazil
E-mail: danmee1997@gmail.com

Sandy Farias da Silva

ORCID: <https://orcid.org/0000-0002-3217-4908>
Universidade do Estado do Pará, Brazil
E-mail: sandyfarias80@gmail.com

Jacqueline da Silva Quintal

ORCID: <https://orcid.org/0000-0001-6595-7696>
Universidade do Estado do Pará, Brazil
E-mail: jacquelinequin@hotmail.com

Mariana Aguiar Buriti

ORCID: <https://orcid.org/0000-0003-2828-9179>
Universidade do Estado do Pará, Brazil
E-mail: marianaburiti@hotmail.com

Mariângela Aguiar Buriti

ORCID: <https://orcid.org/0000-0002-5893-8398>
Universidade do Estado do Pará, Brazil
E-mail: angelaburiti2009@hotmail.com

Leidson Frank Santana Cardoso

ORCID: <https://orcid.org/0000-0002-5893-8398>
Centro Universitário da Amazônia, Brazil
E-mail: frank_cardozoz@yahoo.com.br

Lacy Cardoso de Brito Junior

ORCID: <https://orcid.org/0000-0001-9102-5817>
Universidade Federal do Pará, Brazil
E-mail: lcdbrito2@gmail.com

Abstract

To investigate through bibliometric parameters the blood cell changes in patients infected with the SARS-CoV-2 virus, described in the literature in 2020. This study used the bibliometric parameters to carry out the research with the creation of a search key to carry out the selection of articles and, through this, analyze the scientific findings quantitatively. The selection of articles was performed in May 2022, without language and year of publication restrictions, in the Web of Science database (Clarivate Analytics, Philadelphia, PA, USA). The search strategy retrieved 26,896 articles in the cited database. A total of 678 articles were evaluated, and only 17 articles had the searched endpoint. The most cited article was: "Dysregulation of Immune Response in Patients with Coronavirus 2019 (COVID-19) in Wuhan, China", published in the journal *Clinical Infectious Diseases*. More than 70% of the studies were conducted in China and 100% of them exposed changes in platelet and/or white blood cell parameters. Despite the low rate of selected articles and the need for more robust studies on this topic, we have noticed increasing

rates of citations, renowned institutions, and scholars researching on the subject as well as in other countries besides China. Thus, this study developed some indicators to assist in future research on the subject.

Keywords: Bibliometric; COVID-19; Blood Cells; Leukocytes.

Resumo

Investigar através dos parâmetros bibliométricos as alterações celulares sanguíneas em pacientes infectados pelo vírus SARS-CoV-2, descritas na literatura em 2020. O referido estudo utilizou os parâmetros bibliométricos para realizar a pesquisa com a criação de uma chave de busca para realizar a seleção dos artigos e, mediante isso, analisar os achados científicos quantitativamente. A seleção dos artigos foi realizada em maio de 2022, sem restrição de idioma e ano de publicação, na base de dados *Web of Science (Clarivate Analytics, Philadelphia, PA, USA)*. A estratégia de busca recuperou 26 896 artigos na base de dados citada. Foram avaliados 678 artigos e apenas 17 artigos possuíam o desfecho pesquisado. O artigo mais citado foi o: “*Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China*”, publicado na revista *Clinical Infectious Diseases*. Mais de 70% dos estudos foram realizados na china e 100% dos mesmos expuseram alterações nos parâmetros plaquetários e/ou glóbulos brancos. Apesar do baixo índice de artigos selecionados e a necessidade de estudos mais robustos frente essa temática, notam-se crescentes índices de citações, instituições e estudiosos renomados pesquisando sobre o assunto bem como outros países além da China. Dessa forma, esse estudo elaborou alguns indicadores para auxiliar em pesquisas futuras sobre a temática.

Palavras-chave: Bibliométrica; COVID-19; Células Sanguíneas; Leucócitos.

Resumen

Investigar mediante parámetros bibliométricos las alteraciones de las células sanguíneas en pacientes infectados por el virus SARS-CoV-2, descritas en la literatura en 2020. El mencionado estudio utilizó los parámetros bibliométricos para llevar a cabo la investigación con la creación de una clave de búsqueda para realizar la selección de artículos y, a través de ella, analizar cuantitativamente los hallazgos científicos. La selección de artículos se realizó en mayo de 2022, sin restricción de idioma y año de publicación, en la base de datos *Web of Science (Clarivate Analytics, Philadelphia, PA, USA)*. La estrategia de búsqueda recuperó 26 896 artículos en la base de datos citada. Se evaluaron 678 artículos y sólo 17 tenían el resultado investigado. El artículo más citado fue: “*Dysregulation of Immune Response in Patients with Coronavirus 2019 (COVID-19) in Wuhan, China*”, publicado en la revista *Clinical Infectious Diseases*. Más del 70% de los estudios se realizaron en China y el 100% de ellos expusieron cambios en los parámetros de las plaquetas y/o los glóbulos blancos. A pesar del bajo índice de artículos seleccionados y de la necesidad de realizar estudios más sólidos sobre este tema, observamos un aumento de las citas, de las instituciones y de los académicos de renombre que investigan sobre el tema, así como de otros países más allá de China. Por lo tanto, este estudio desarrolló algunos indicadores para ayudar en futuras investigaciones sobre el tema.

Palabras-clave: Bibliométrico; COVID-19; Células de Sangre; Leucocitos.

1. Introduction

In late 2019, a zoonotic disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), identified in the city of Wuhan in China, became a global pandemic generating approximately 14.9 million deaths due to the great ability of the SARS-CoV-2 virus to mutate its Spike protein and thereby generate new variants. The disease caused by this virus has been renamed Coronavirus Disease 2019 (COVID-19) and has been associated with a complex range of clinical presentations (Crook et al., 2021; Juan Gérvasa, 2020).

In COVID-19, the clinical presentation can range from the common cold to systemic pictures characterized by severe acute respiratory syndrome associated with: systemic coagulopathies, neurological, dermatological, renal, and cardiological disorders. All this is due to the systemic inflammatory state caused by the virus that generates the so-called "cytokine storm", which is directly related to the immunopathology of the disease and eosinopenia and lymphopenia, besides the severe reduction of CD4+ and CD8+ T cells, B cells, and natural killer (NK) cells (Gajendra, 2022; Juan Gérvasa, 2020). However, concerning the critical stages of the disease, it is often associated with pre-existing comorbidities in these patients such as heart disease, diabetes, chronic renal failure, and hypertension, which increases the risk of death (Merad & Martin, 2020; Rodrigues et al., 2020).

In this sense, although we already know a lot about COVID-19 from the experience of these last three years, this pathology is still very recent in history, and there are still numerous daily discoveries that need to be consolidated. Within this

aspect, bibliometric analysis can be a useful tool to investigate these discoveries, which was a term coined by the scientist Eugene Garfield in the 1950s. This type of analysis consists of the joining of data from science and mathematical principles that allow measuring, in numerical form, the main information already available in the literature, clarifying and giving knowledge about what already exists in an area of knowledge (P. Ahmad et al., 2020).

One of the most used parameters in this type of analysis is the determination of the frequency with which other researchers mention an article, this being done by counting the number of times it is cited, which then determines its degree of importance and its clinical and scientific relevance in a given area of knowledge. Also used in this analysis are the main relevant collaborations of certain authors, institutions, countries, and journals within a specific scientific community. Thus, with these parameters, it is possible to find a classic study for a given event, and this is also one of the goals of the bibliometric study (P. Ahmad et al., 2019).

This study aimed to investigate, through bibliometric parameters, the blood cell changes in patients infected with the SARS-CoV-2 virus described in the literature in the year 2020, contributing to the main information already published regarding the topic.

2. Materials and Methods

2.1 Strategy of search

For this study, the bibliometric analysis method was used, which consists of selecting the most cited articles, since these may have a high impact on the scientific community (Bakkalbasi et al., 2006 and Falagas et al., 2008). This study was conducted in may 2022. A search was performed with the search strategy described in Table 1, with descriptors contained in the decs/mesh (Health Science Descriptors) database, and searched in the Web of Science - core collection (WOS - CC) database.

Table 1 - search engine used in the Web of Science - main collection database.

STRATEGY OF SEARCH
TS= ("Covid-19" OR "SARS-CoV-2" AND "2019nCoV" AND "symptoms" OR "laboratory diagnosis" OR "hematology" OR "anemia" OR "hemogram" OR Leukocytes OR "white series" OR "white blood cells" OR "white cells" OR "red blood cells" OR "lymphocytosis OR lymphopenia)

Source: Authors (2022).

2.2 Eligibility criteria

The articles retrieved by the proposed strategy were organized in descending order according to the number of citations. Two researchers independently evaluated and selected the most cited publications that were relevant to the theme, based on pre-defined eligibility criteria. In case of disagreement between the researchers, another specialist was called to clarify the doubts about the inclusion or exclusion of the article. If any doubts remained, the divergences were solved by consensus among the specialists.

The articles selected were those that presented any term from the search strategy in the title, abstract, or keywords, and that addressed similar language, year of publication, or methodology. Congress abstracts and articles that did not converge with the objectives of this study were excluded from this search.

2.3 Data mining

Seventeen articles were selected for this study and the following bibliometric parameters were extracted from them: authors' names, year of publication, city of origin of the study, DOI, country of affiliation of the corresponding author, number of citations of the article in Google Scholar and Scopus by other authors, citation density, study outcome, and keywords used.

2.4 Used Tools

Using descriptive statistical analysis from the extracted data, the citation index was used as the main variable. Two softwares were also used: MapChart to represent the distribution of articles by continent and countries (see Figure 4), and VOSviewer. VOSviewer allows the elaboration of graphs that indicate associations of authors, keywords, and quantities of publications, where their representativeness is performed through clustering using representative colors (see Figure 2). In it, the thickness of each circle is proportional to the total number of articles with authors from a given country (see Figure 3). The distance between two countries is inversely proportional to the number of cooperating articles from these two countries.

For the analysis of new trends, a fractional count cluster of keywords and authors was created, including keywords that were used in at least two or more articles. This cluster is important to visualize the scientific cooperation networks, which are represented in a color scale (usually blue, yellow, and red).

3. Results

The search strategy retrieved 26,896 articles from the Web of Science - Main Collection database. A total of 678 articles were evaluated and only 17 articles had the outcome that was the objective of this research (see Table 2)

Table 2 - The 17 most relevant articles from 2020 that presented hematological cellular changes in patients infected with SARS-CoV-2 in 2020.

Rank	Authors and publication year	Article Title	Study Results	WoS – CC	Citation density	Scopus	Google Scholar	DOI
1°	Tian, Dai-Shi et. al.; 2020.	Dysregulation of Immune Response in Patients with Coronavirus 2019 (COVID-19) in Wuhan, China	Severe cases tend to have lower lymphocyte counts, higher WBC counts, and NLR.	2585	2585	2422	4242	http://dx.doi.org/10.1093/cid/ciaa248
2°	Ning, Qin et al.; 2020.	Clinical and immunological features of severe and moderate coronavirus disease 2019	SARS-CoV-2 infection can primarily affect T lymphocytes, particularly CD4(+) and CD8(+) T cells, resulting in a decrease in numbers.	2265	2265	2367	3889	http://dx.doi.org/10.1172/JCI137244
3°	Gao, Ya-Dong et al.; 2020.	Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China	Decreased eosinophil and lymphocyte counts, the absolute lymphocyte counts, were lower in severely ill patients compared to non-severe patients.	1529	1529	1983	3655	http://dx.doi.org/10.1111/all.14238
4°	Merad, Miriam et. al.; 2020.	Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages	A significant expansion of CD14 + CD16 + IL-6-producing monocyte populations was also observed in the peripheral blood of ICU patients with COVID-19 compared to those patients who did not require ICU admission.	1077	1077	1069	1711	http://dx.doi.org/10.1038/s41577-020-0331-4
5°	Giamarellos-Bourboulis, Evangelos J et. al.; 2020.	Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure	Overproduction of pro-inflammatory cytokines by monocytes and dysregulation of lymphocytes characterized by CD4 lymphopenia and, subsequently, B-cell lymphopenia.	1015	1015	1013	1526	http://dx.doi.org/10.1016/j.chom.2020.04.009
6°	Zheng, Meijuan et al.; 2020.	Functional exhaustion of antiviral lymphocytes in COVID-19 patients	Normal or high cytokine production capacity and increased circulating cytokines (especially IL-6). On the other hand, defects in lymphoid function are associated with IL-6-mediated decrease in HLA-DR expression.	877	877	916	1406	http://dx.doi.org/10.1038/s41423-020-0402-2
7°	Terpos, Evangelos et al.; 2020.	Hematological findings and complications of COVID-19	Patients with severe disease and fatal outcomes have a decreased lymphocyte to white blood cell ratio, associated with thrombocytopenia.	819	819	826	1439	http://dx.doi.org/10.1002/ajh.25829
8°	Yang, Dongliang et al.; 2020.	Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients	Severe cases showed significant and sustained reductions in lymphocyte counts and increases in neutrophil counts.	781	781	802	1439	http://dx.doi.org/10.1016/j.ebiom.2020.102763
9°	Lippi, Giuseppe et al.; 2020.	Hematologic, biochemical, and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis	Patients with the severe and fatal disease had significantly increased WBC and decreased lymphocyte and platelet counts compared to non-severe disease and survivors.	778	778	822	1316	http://dx.doi.org/10.1515/cclm-2020-0369
10°	Mo, Pingzheng et. al.; 2020.	Characteristics of Peripheral Lymphocyte Subset Alteration in COVID-19 Pneumonia	Total lymphocytes, CD4+ T cells, CD8+ T cells, B cells, and NK cells decreased in patients with COVID-19, and	572	572	564	890	http://dx.doi.org/10.1093/infdis/ji

			severe cases had a lower level than mild cases.					aa150
11°	Yost, Christian et al.; 2020.	Neutrophil extracellular traps contribute to immunothrombosis in COVID-19 acute respiratory distress syndrome	COVID-19 neutrophils exhibited excessive neutrophil extracellular traps at baseline. Thus, NETs triggering immunothrombosis may in part explain the pro-thrombotic clinical presentations in COVID-19.	494	494	500	741	http://dx.doi.org/10.1182/blood.202007008
12°	Wang, Xiaowu et. al.; 2020.	Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19	They found low lymphocyte and WBC counts in most patients.	469	469	487	888	http://dx.doi.org/10.1002/jmv.25770
13°	Chen, Ling et. al.; 2020.	Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19	They reported that severe cases of COVID-19 were likely to have higher neutrophil counts but lower lymphocyte counts compared to non-severe patients, so the NLR tended to be higher in patients with severe infection.	455	455	499	738	http://dx.doi.org/10.1016/j.jinf.2020.04.002
14°	Wang, Xianbo et. al.; 2020.	Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage	The neutrophil to lymphocyte ratio was identified as an independent risk factor for critical illness in patients with COVID-19 infection.	455	455	346	549	http://dx.doi.org/10.1186/s12967-020-02374-0
15°	Yang, Li et. al.; 2020.	Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis	The presence of lymphopenia was associated with an almost three-fold increased risk of severe COVID-19.	208	208	375	706	http://dx.doi.org/10.1016/j.ijid.2020.04.086
16°	Hu, Yu et. al.; 2020	Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study	The incidence of thrombocytopenia in patients with critical illness was significantly higher than in those with severe or moderate illness. The number of lymphocytes and eosinophils was significantly lower in patients with critical illness than in those with severe or moderate illness.	199	199	192	29	http://dx.doi.org/10.1016/S2352-3026(20)30217-9
17°	Pan, Yong et al.; 2020	Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China	Patients with COVID-19 have lower WBC, lymphocyte, eosinophil, platelet, and hemoglobin counts, but have higher NLR and MLR. In severe ICU, patients have the lowest lymphocyte count, but the highest neutrophil count and NLR. Dynamic surveillance of the peripheral blood system, especially of eosinophils, is useful in predicting severe cases of COVID-19.	154	154	156	263	http://dx.doi.org/10.1016/j.cca.2020.04.024

Note: The table presents a ranking, in descending order, of the total citations collected in the databases (Scopus, Google Scholar, and Web of Science) and the citation density of the Web of Science data. All studies had more than three authors. *COVID-19: coronavirus year 2019; HLA: Human Leukocyte Antigen DR: Gene Region (HLA-DR); IL: Interleukin; MLR: Monocyte-Lymphocyte Ratio; NETs: The Neutrophil Extracellular Traps; NK: Natural killer (Natural Killer) cells; NLR: Neutrophil-Lymphocyte Ratio; ICU: Intensive Care Unit; WBC: White Blood Cell or WBC count; WoS-CC: Web of Science - Core Collection. Source: Authors (2022).

All 17 articles were published in different scientific journals in the year 2020 and totaled 14,732 citations. The average citation was 866 citations. The most cited article was "Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China," published in the journal *Clinical Infectious Diseases*, with the highest number of citations in the three investigated bases. It had 2,585 citations in WoS-CC, 2,422 in Scopus, and 4,242 in Google Scholar. The article with the lowest citation number was "Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China", published in the journal *Clinica Chimica Acta* with only 154 citations in WoS-CC.

All 17 scientific journals that published the studies that were the subject of this search are indexed in WoS-CC and had a relevant impact factor. The journal *Allergy* published the third highest ranking study (IF = 32.26), being the journal with the highest impact factor of the selected studies. The journal *Clinica Chimica Acta*, which published the seventeenth article in this study, had the lowest impact factor (IF = 5.85) and the lowest citation index (see Table 3).

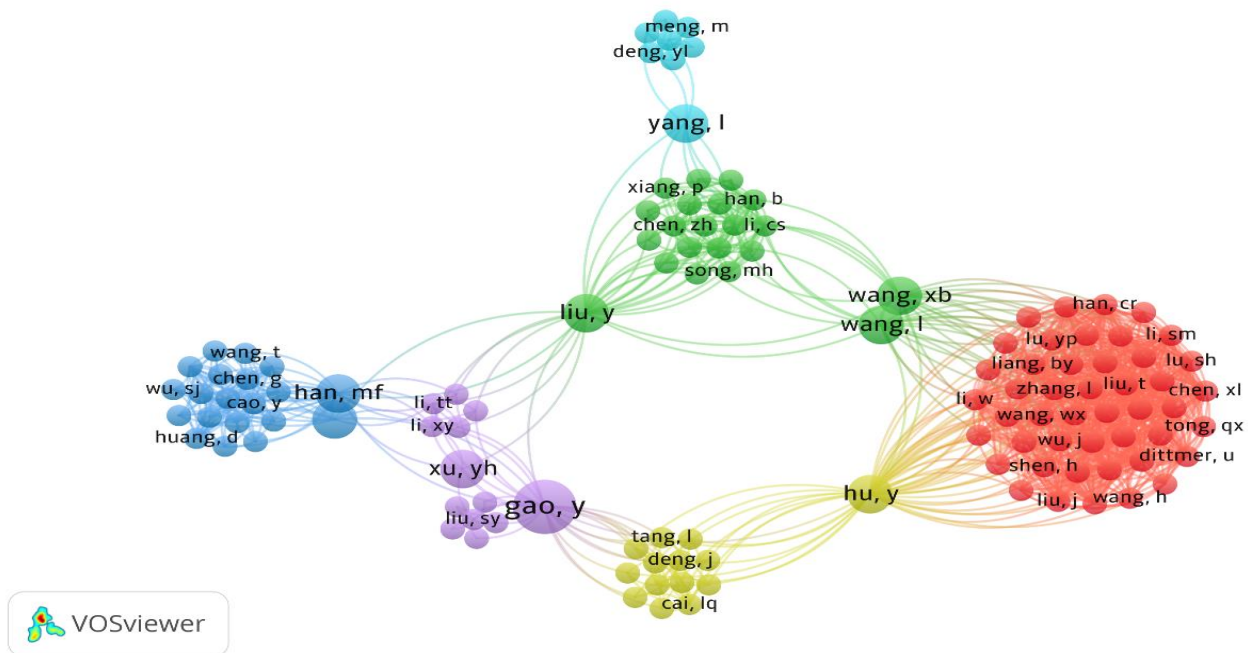
Table 3 - Impact Factor Index of each journal.

Rank	Journal	Impact Factor	Analysis Year
1	<i>Allergy</i>	32.26	2022
2	<i>Nature Reviews Immunology</i>	31.59	2022
3	<i>Cell Host & Microbe</i>	20.31	2022
4	<i>Journal of Medical Virology</i>	18.37	2022
5	<i>Journal of Infection</i>	18.06	2022
6	<i>Journal of Clinical Investigation</i>	14.15	2022
7	<i>Cellular & Molecular Immunology</i>	13.85	2022
8	<i>International Journal of Infectious Diseases</i>	10.68	2022
9	<i>Lancet Haematology</i>	9.91	2022
10	<i>Clinical Infectious Diseases</i>	9.75	2022
11	<i>Blood</i>	9.53	2022
12	<i>Ebiomedicine</i>	7.81	2022
13	<i>Journal of Translational Medicine</i>	7.71	2022
14	<i>American Journal of Hematology</i>	6.54	2022
15	<i>Clinica Chimica Acta</i>	5.85	2022
16	<i>Journal of Infectious Diseases</i>	5.60	2022
17	<i>Clinical Chemistry and Laboratory Medicine</i>	5.35	2022

Source: Google Scholar (2022).

The impact factor, co-authorship index, and the index of the most used keywords are very important tools for the outcome of the research. Our study presented 191 authors and the relationship between co-authorship and citation can be seen in Figure 1. Author Gao, y collaborated on three articles out of the 17 selected and totaled 1,546 citations. The authors: Han, mf; Liu, y; Wu, d; Xu, yh; Yang, l appeared in up to two selected studies, among them Han and Wu had the highest citation index, totaling 2 737 citations each. The other 184 authors were listed in only one study.

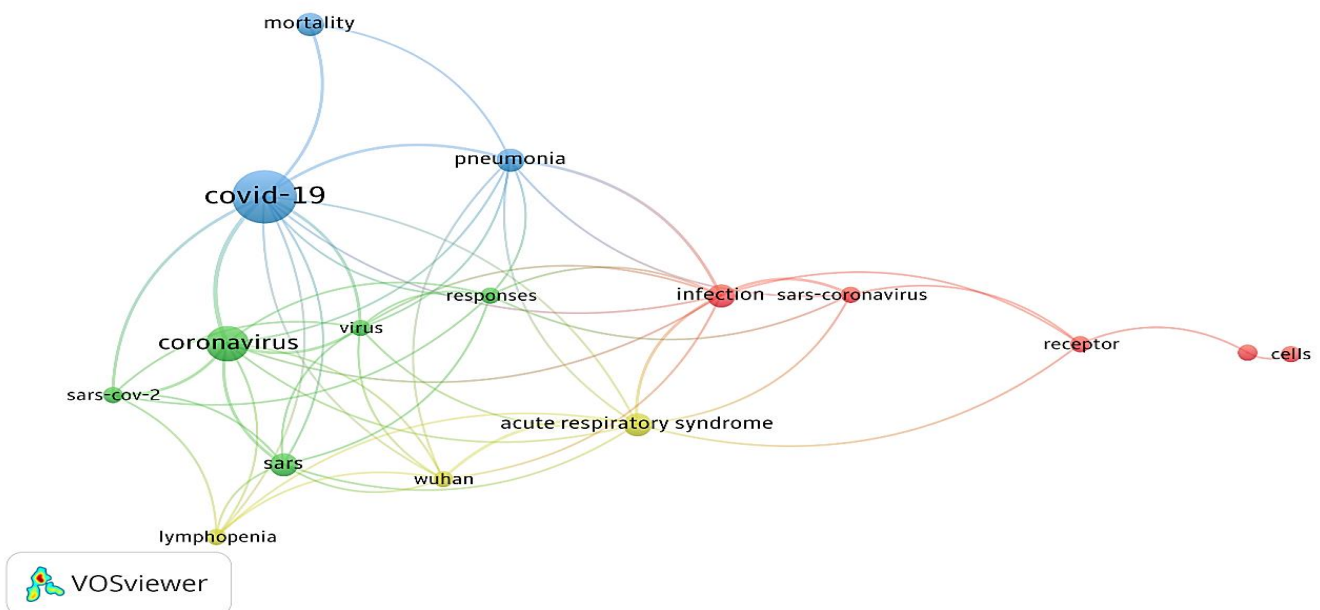
Figure 1 - Authors' co-authorship view network.



Note: The size of the intersection point represents the frequency of the co-authorship relationship. The points with the same colorings represent the same cluster, and the larger the node, the greater the co-authorship link, while the smaller the distance between the nodes, the greater the relative strength or closeness of the cooperativity. Source: WoS – CC (2022).

The study also presented 82 keywords and their interconnections. The keyword COVID-19 had the highest occurrence rate, being listed eight times. In second place was the keyword "coronavirus" listed five times, and in third place the most used keywords were "acute respiratory syndrome", "infection", "mortality", "pneumonia", "SARS", "SARS-CoV-2", "cells", "expression", "lymphopenia", "receptor", "responses", and "virus".

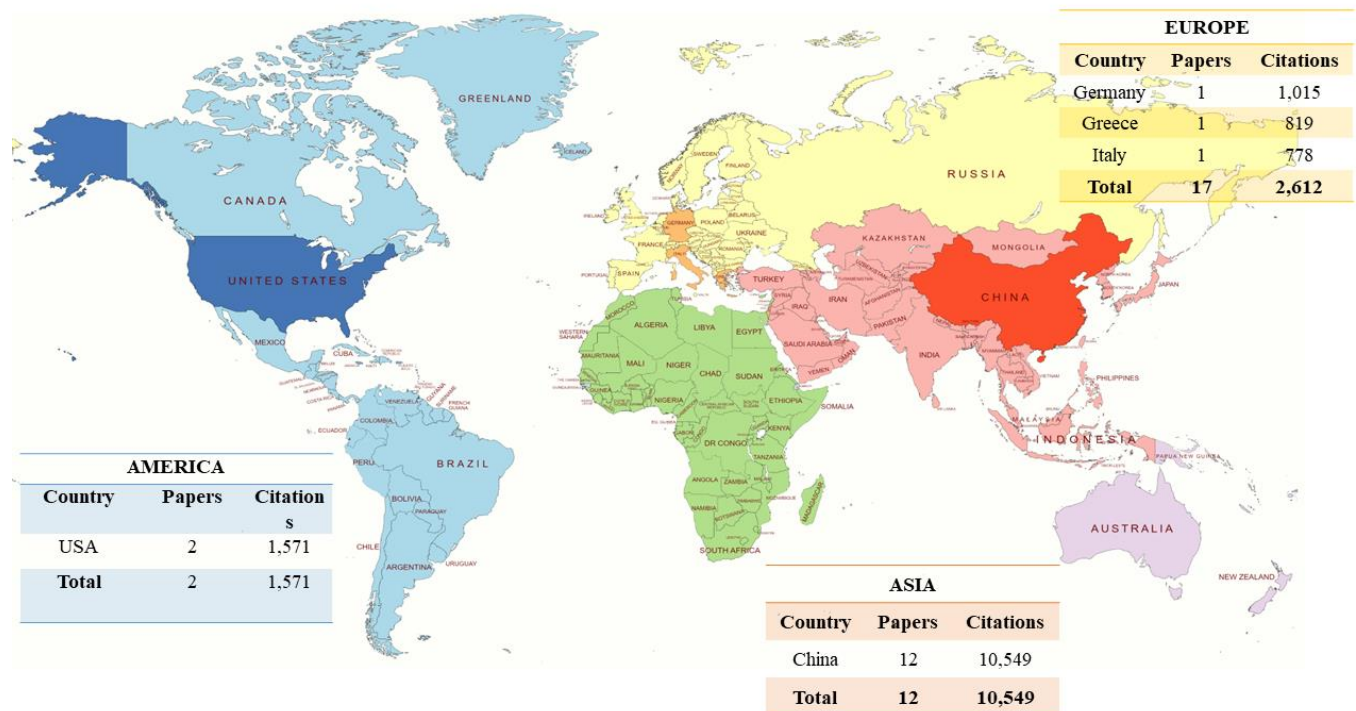
Figure 2 - Network for all keywords.



Source: WoS – CC (2022).

In addition to the relationships among authors, co-authors, and keywords, the bibliometric review makes it possible to show the distribution of studies by continent and country (see figure 2). Thus, in figure 3, the countries that have done the most research on the subject are represented with stronger coloring, where we observe a predominance in the Asian continent. China has 12 published studies, totaling 10,549 citations, followed by Europe and North America, which investigated possible cellular alterations in patients infected with the SARS-CoV-2 virus. The sum of the three publications found in Europe totaled 2,612 citations, and in the USA two studies were cited 1,571 times.

Figure 3 - Distribution of studies by continent and country.



Source: WoS – CC (2022).

4. Discussion

The choice of performing a bibliometric analysis, in the area of hematology, based on data from the Web of Science, occurred because, in addition to comprising an online citation index, identifying the citations and references of the scientific production, and also covering the largest number of studies indexed in it, it was possible to analyze the quality of the scientific production and the impact factor of each journal (Xavier et al., 2020; J. Zhang et al., 2010).

In this sense, the studies that fit the search criteria were all from the year 2020, the year of the pandemic milestone of COVID-19 when the first cases of death were reported in January of the same year in the Asian continent. And as previously mentioned, the massive investigation of this disease is still very recent in our environment, which justifies the importance of studies that bring a bibliographic framework to assist in the acquisition of knowledge and arouse interest in the subject addressed.

As already presented in our results, the most cited study in the period of this research analyzed the dysregulation of the immune response that patients infected with the SARS-CoV-2 virus developed. In this study, 452 patients were analyzed, of which 285 were critically ill patients. In the acute phase of these patients, the researchers observed that the WBC count, neutrophil-lymphocyte ratio (NLR), inflammatory biomarkers, and inflammatory cytokines were elevated, and the percentages

of monocytes, eosinophils, basophils, and T-cell quantity were significantly lower. In this study, the authors extolled lymphocytopenia in critically ill patients as the worst clinical outcome (Tang et al., 2020; H. Zhang et al., 2020).

Despite the numerical difference between the citation index of the first and last study in the selection rank, the results did not differ in their outcome. In the article with the lowest index, the authors observed lower counts of lymphocytes, eosinophils, platelets, hemoglobin, and WBCs, inferring that the neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR) were increased and could be of clinical importance for patient follow-up, corroborating with the article that had the highest number of citations in the rank. (Qin et al., 2020; Sun et al., 2020).

It is common for the virus to operate the machinery of immune system cells and trigger morphological changes in blood cells, often generating both an increase and decrease in some of these cells. The virus induces, for example, the following changes: the presence of reactive or atypical lymphocytes, hyposegmented neutrophils, monocytes with significant cytoplasmic vacuolization, and even mushroom-shaped RBCs. Regarding lymphocytes, these changes occur mainly in B lymphocytes activated in the fight against the invading virus through the production of antibodies (Chen & John Wherry, 2020).

Also, within the field of bibliometric analysis research, it is possible to observe that more and more studies are carried out collaboratively and no longer individually, which is why it is so important to analyze the connections between researchers and keywords. In this sense, the use of the VosViewer software allowed us to visualize the collaborations between several authors, such as between Professor Tian, Dai-Shi of Tongji Medical College, who has several publications related to immune system cells with other authors (Mortaz et al., 2020; Rodriguez et al., 2020).

In the bibliometric analysis study, we found that the keywords "COVID-19" and "coronavirus" were the most used in several studies and had a strong connection with two other keywords: "Lymphopenia" and "mortality". The keyword "COVID-19" was associated as the leading cause of death in Brazil, Northern Ireland, Scotland, Spain, Slovenia, and Sweden, and also among the countries with excess deaths during 2020. In this regard, by July 4, 2021, more than 183 million confirmed cases of COVID-19 had been recorded worldwide and 3.97 million deaths from the same cause (Crook et al., 2021; Yan & Wu, 2021).

As for the bibliometric analysis of the countries with the most publications on the topic, in the year 2020, more than 70% (12 articles) were from studies conducted in China, probably because the first cases appeared in that country and, it was noticed in all articles descriptions of relevant hematological changes.

5. Concluding Remarks

The scientific observations published about the SARS-CoV-2 virus and COVID-19, in the year 2020, formed the scientific basis for everything that is known today and still what will be discovered by the scientific community. As relevant data from this period, we highlight that patients infected by the SARS-CoV-2 virus presented main alterations in blood cells significant leukocyte counts, decreased lymphocyte, monocyte, eosinophil, basophil, and platelet counts, in addition to increased neutrophil and neutrophil/lymphocyte ratio in severe cases of COVID-19. And, although morphological changes in lymphocytes, neutrophils, monocytes, and RBCs associated with COVID-19 are already known, these are not pathognomonic effects of SARS-CoV-2 infection but could be further investigated.

Based on this, more robust studies are needed to investigate this issue. Despite the various studies on COVID-19, aspects still related to a gap with regard to the diagnosis and study of studies of advanced studies of studies relevant to a relevant diagnostic purpose significantly in helping early.

References

- Ahmad, P., Dummer, P. M. H., Chaudhry, A., Rashid, U., Saif, S., & Asif, J. A. (2019). A bibliometric study of the top 100 most-cited randomized controlled trials, systematic reviews, and meta-analyses published in endodontic journals. *International Endodontic Journal*, 52(9), 1297–1316. <https://doi.org/10.1111/iej.13131>.
- Ahmad, Paras, Vincent Abbott, P., Khursheed Alam, M., & Ahmed Asif, J. (2020). A bibliometric analysis of the top 50 most cited articles published in the Dental Traumatology. *Dental Traumatology*, 36(2), 89–99. <https://doi.org/10.1111/edt.12534>.
- Bakkalbasi, N., Bauer, K., Glover, J., & Wang, L. (2006). Three options for citation tracking: Google Scholar, Scopus and Web of Science. *Biomedical digital libraries*, 3(1), 1-8.
- Chen, Z., & John Wherry, E. (2020). T cell responses in patients with COVID-19. *Nature Reviews Immunology*, 20(9), 529–536. <https://doi.org/10.1038/s41577-020-0402-6>.
- Crook, H., Raza, S., Nowell, J., Young, M., & Edison, P. (2021). Long covid - Mechanisms, risk factors, and management. *The BMJ*, 374, 1–18. <https://doi.org/10.1136/bmj.n1648>.
- Falagas, M. E., Pitsouni, E. I., Malietzis, G. A., & Pappas, G. (2008). Comparison of PubMed, Scopus, web of science, and Google scholar: strengths and weaknesses. *The FASEB journal*, 22(2), 338-342.
- Gajendra, S. (2022). Spectrum of hematological changes in COVID-19. *American Journal of Blood Research*, 12(1), 43–53. <http://www.ncbi.nlm.nih.gov/pubmed/35291254%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC8918700>.
- Juan Gérvasa, y; M. P.-F. (2020). *E ditorial Morbilidad , mortalidad y sufrimiento ocultos. January*.
- Merad, M., & Martin, J. C. (2020). Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. *Nature Reviews Immunology*, 20(6), 355–362. <https://doi.org/10.1038/s41577-020-0331-4>.
- Mortaz, E., Tabarsi, P., Varahram, M., Folkerts, G., & Adcock, I. M. (2020). The Immune Response and Immunopathology of COVID-19. *Frontiers in Immunology*, 11(August), 1–9. <https://doi.org/10.3389/fimmu.2020.02037>.
- Qin, C., Zhou, L., Hu, Z., Zhang, S., Yang, S., Tao, Y., Xie, C., Ma, K., Shang, K., Wang, W., & Tian, D.-S. (2020). Dysregulation of Immune Response in Patients with COVID-19 in Wuhan, China. *SSRN Electronic Journal*. <https://doi.org/10.2139/ssrn.3541136>.
- Rodrigues, T. S., de Sá, K. S. G., Ishimoto, A. Y., Becerra, A., Oliveira, S., Almeida, L., Gonçalves, A. V., Perucello, D. B., Andrade, W. A., Castro, R., Veras, F. P., Toller-Kawahisa, J. E., Nascimento, D. C., de Lima, M. H. F., Silva, C. M. S., Caetite, D. B., Martins, R. B., Castro, I. A., Pontelli, M. C., ... Zamboni, D. S. (2020). Inflammasomes are activated in response to SARS-cov-2 infection and are associated with COVID-19 severity in patients. *Journal of Experimental Medicine*, 218(3). <https://doi.org/10.1084/JEM.20201707>.
- Rodriguez, L., Pekkarinen, P. T., Lakshmikanth, T., Tan, Z., Consiglio, C. R., Pou, C., Chen, Y., Mugabo, C. H., Nguyen, N. A., Nowlan, K., Strandin, T., Levanov, L., Mikes, J., Wang, J., Kantele, A., Hepojoki, J., Vapalahti, O., Heinonen, S., Kekäläinen, E., & Brodin, P. (2020). Systems-Level Immunomonitoring from Acute to Recovery Phase of Severe COVID-19. *Cell Reports Medicine*, 1(5). <https://doi.org/10.1016/j.xcrm.2020.100078>.
- Sun, S., Cai, X., Wang, H., He, G., Lin, Y., Lu, B., Chen, C., Pan, Y., & Hu, X. (2020). Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. *Clinica Chimica Acta*, 507(April), 174–180. <https://doi.org/10.1016/j.cca.2020.04.024>.
- Tang, N., Li, D., Wang, X., & Sun, Z. (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis*, 18(4), 844–847. <https://doi.org/10.1111/jth.14768>.
- Xavier, A. R., Silva, J. S., Almeida, J. P. C. L., Conceição, J. F. F., Lacerda, G. S., & Kanaan, S. (2020). COVID-19: Clinical and laboratory manifestations in novel coronavirus infection. *Jornal Brasileiro de Patologia e Medicina Laboratorial*, 56, 1–9. <https://doi.org/10.5935/1676-2444.20200049>.
- Yan, S., & Wu, G. (2021). Is lymphopenia different between SARS and COVID-19 patients? *FASEB Journal*, 35(2), 1–7. <https://doi.org/10.1096/fj.202002512>
- Zhang, H., Wang, C.-Y., Zhou, P., Yue, H., & Du, R. (2020). Histopathologic Changes and SARS-CoV-2 Immunostaining in the Lung of a Patient With COVID-19. *Annals of Internal Medicine*, 173(4), 324. <https://doi.org/10.7326/120-0895>.
- Zhang, J., Zhang, J., & Koutra, S. (2010). Bibliometric Analysis. *Handbook of Disease Burdens and Quality of Life Measures*, 4155–4155. https://doi.org/10.1007/978-0-387-78665-0_5187.