



## A Quantitative Study of The Most Influential Articles on Cytomegalovirus in Solid Organ Transplantation

### Solid Organ Transplantasyonunda Sitomegalovirüs Üzerine En Etkili Makalelerin Nicel Bir Çalışması

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#### Abstract

**Aim** In this quantitative study, the previous literature on the topic of Cytomegalovirus (CMV) in solid organ transplant (SOT) recipients was analysed. Our overarching goal was to explore the publications in this field and to identify research hotspots.

**Material and Method** The Web of Science (WoS) database was utilized to research publications. The following terms were included in the search strategy syntax: "CMV" or "CMV infection" or "Cytomegalovirus" and "solid organ" or "hepatic" or "liver" or "pancreatic" or "lung" or "heart" or "transplantation" or "organ donation". Articles were selected as the document type. The complete text data of the included publications was retrieved from the WoS database. The VOSviewer (version 1.6.10, Leiden University, Netherlands) was used to do the bibliometric study in order to display the collaboration network, emphases, and future trends in the relevant topic.

**Results** 2432 results were reached from the WoS Core Collection. 1390 of them were articles. The USA was the top-ranked country (29.928%). Germany, Japan, England, and France (6.043%) were ranked in the first 5 countries. Turkey ranked 16th. 1351 (97.194%) of the publications were published in SCI-EXPANDED journals. The first article was published in the year 1971. 990 (71.87%) of the articles were published after 2000. The highest number of publications was in the year 2020 (4.892%). The H index of the articles was 100. There were a total of 45063 citations and an average of 32.42 per item. The number of citations and publications has increased over the last 30 years. The University of London was the top-ranked affiliation. Most of the articles (11.871%) were published in the journal "Transplantation Proceedings".

**Conclusion** The number of publications in this field is very low, especially for developing countries. The USA, Japan, and European countries are the countries with the highest number of publications.

**Keywords** Bibliometric, citation analysis, scientific publications, Cytomegalovirus, solid organ transplantation.

#### Özet

**Amaç** Bu nicel çalışmada, solid organ nakli (SOT) alıcılarında Sitomegalovirüs (CMV) konusunda önceki literatür analiz edildi. Kapsamlı hedefimiz, bu alandaki yayınları keşfetmek ve araştırma noktaları belirlemektir.

**Gereç ve Yöntem** Yayınları araştırmak için Web of Science (WoS) veritabanı kullanıldı. Arama stratejisi anahtar kelimeleri olarak şu terimler kullanıldı: "CMV" veya "CMV enfeksiyonu" veya "Sitomegalovirüs" ve "solid organ" veya "karaciğer" veya "hepatik" veya "pankreatik" veya "akciğer" veya "kalp" veya "nakil" veya "organ nakli". Belge türü olarak makaleler seçildi. Dahil edilen yayınların tam metin verileri WoS veri tabanından alındı. VOSviewer (versiyon 1.6.10, Leiden University, Hollanda), ilgili konudaki işbirliği ağı, vurguları ve gelecekteki eğilimleri görüntülemek için bibliyometrik çalışmayı yapmak için kullanıldı.

**Bulgular** WoS Core Collection'dan 2432 sonuca ulaşıldı. Bunların 1390'i makaleydi. ABD (%29.928) en üst sıralamadaki ülke idi. Almanya, Japonya, İngiltere ve Fransa (%6.043) ilk 5 ülkede yer aldı. Türkiye 16. sırada yer aldı. Yayınların 1351'i (%97.194) SCI-EXPANDED dergilerinde yayınlanmıştı. İlk makale 1971 yılında yayınlanmıştı. Makalelerin 990'i (%71.87) 2000 yılından sonra yayınlanmıştı. En fazla yayın (%4.892) 2020 yılında yayınlanmıştı. Makalelerin H indeksi 100 idi. Toplam 45063 atıf ve makale başına ortalama 32.42 atıf yapılmıştı. Son 30 yılda atıf ve yayın sayısı artmıştı. Londra Üniversitesi en üst sıralamada yer alan kurum idi. Makalelerin çoğu (%11.871) "Transplantation Proceedings" dergisinde yayınlanmıştı.

**Sonuç** Bu alandaki yayın sayısı özellikle gelişmekte olan ülkeler için oldukça düşüktür. ABD, Japonya ve Avrupa ülkeleri en fazla yayına sahip ülkelerdir.

**Anahtar Kelimeler** Bibliyometrik, atıf analizi, araştırma yayınları, Sitomegalovirüs, solid organ nakli.

## INTRODUCTION

Human Herpes virus 5, often known as cytomegalovirus (CMV), has the biggest genome of any known human virus (230 kb), with 200 genes encoding proteins. After solid organ transplantation (SOT) and hematopoietic cell transplantation (HCT), CMV is one of the most common infections, especially in seronegative receivers of seropositive donors (D+/R-) and seropositive recipients (R+). CMV infection is considered “high risk” in these people. CMV-seropositive SOT recipients have prior CMV-specific cell-mediated immunity and are thus at an intermediate risk for CMV infection, with D+/R+ recipients being at a higher risk than D-/R+ recipients due to the possibility of donor-derived virus superinfection.<sup>1,2</sup>

CMV infection develops in the majority of high-risk SOT patients without antiviral prophylaxis, resulting in viremia, CMV disease, and end-organ damage. Its immunomodulatory properties may hasten graft rejection and make patients more susceptible to opportunistic infections. While ganciclovir or valganciclovir have been the standard of therapy for high-risk SOT recipients for decades, these medicines are associated with higher costs, neutropenia, and a high incidence of postprophylaxis illness.<sup>2,3</sup> Prophylaxis and preemptive therapy are the two main approaches for CMV prevention. After SOT, prophylaxis effectively avoids CMV infection, although it is linked with high rates of neutropenia and delayed-onset postprophylaxis illness. Preventive treatment, on the other hand, has the advantage of lowering CMV illness rates and promoting robust humoral and T-cell responses. It's commonly used in hematopoietic cell transplant recipients, but it's less common following SOT due to logistical issues, which could be addressed by new approaches to monitor CMV viremia using self-testing platforms.<sup>3</sup>

Screening tests have advanced significantly in recent years, both in terms of type and quality, allowing for more precise and savvy treatment. Advances in diagnostics include the development of an international standard, which should

allow for comparison of results across different methodologies, as well as as assays for cellular immune function against CMV. Ganciclovir is the mainstay of treatment, but new evidence suggests that oral valganciclovir medication isn't inferior to intravenous ganciclovir therapy. Treatment of resistant viruses is still difficult, although the availability of a variety of new treatment medicines has made it easier.<sup>2</sup>

In this study, we conducted a bibliometric overview of the previous literature on the topic of CMV in SOT recipients. Our overarching goal was to explore the importance of publications in this field all over the globe and to identify research hotspots.

## METHODS

As this was a literature survey, there was no need for ethics committee approval. In most bibliometric investigations, no ethical approval is necessary because neither humans nor animals are involved.

The Web of Science (WoS) database (Clarivate Analytics, Philadelphia, PA, USA) was utilized to find CMV and SOT research publications. On March 25,2022, data for this study was retrieved from WoS. The following infection-related terms were included in the search strategy syntax: “CMV” or “CMV infection” or “Cytomegalovirus” and “solid organ” or “hepatic” or “liver” or “pancreatic” or “lung” or “heart” or “transplantation” or “organ donation”. The search language was chosen as English, which is the most dominant scientific language worldwide. For our search, articles were selected as the document type. To manage the downloaded findings and erase duplicate information, Microsoft Office Excel was used.

We accessed the information through the online library and digital resources of the Çanakkale Onsekiz Mart University.

### Overview of the output from the WoS database

The publication year, location or nation, study category,

authorship, and citation counts of the retrieved publications were all identified using the WOS database. Only articles published between 1970 and 2022 were included in the timeframe. Since the most significant advancements in medicine have occurred in recent years, this study focused on publications published after the 1970s. In addition, the publications from Turkey were analysed for comparison with the global literature.

### Network analysis

The complete text data of the included publications was retrieved from the WoS database. The VOSviewer (version 1.6.10, Leiden University, Netherlands) was used to do the bibliometric study in order to display the collaboration network, emphases, and future trends in the relevant topic. The VOSviewer software was used to import the obtained data. The following information was extracted and analyzed: authorship, affiliation, citation, keywords, and theme words. Finally, bubble maps were created to display the results of the bibliometric analysis. Colors indicate item clusters in the bubble maps, while the distance and breadth of lines between two bubbles reflect co-occurrence frequency. The diameters of the bubbles under co-authorship, citations, keywords/theme words, and co-occurrence analysis, respectively, show the number of documents, citations, and occurrences.

### RESULTS

2432 results were reached from the Wos Core Collection. 1390 of them were articles. The USA was the top-ranked country with 416 (29.928%) published articles. Germany (10.216%), Japan (9.281%), England (7.122%), France (6.043%), Spain (5.468%), Italy (5.180%), Netherlands (4.964%), China (4.748%), South Korea (3.381%), Australia (3.022%), Switzerland (2.590%), Sweden (2.158%), Brazil (2.014%), Austria (1.727%), and Belgium (1.583%) ranked among the top 15. Turkey ranked 16th with 17 (1.223%) published articles. 484 of them were published as open access. 1330 (95.683%) of them were written in English. Furthermore, French (1.439%) and German (1.295%)

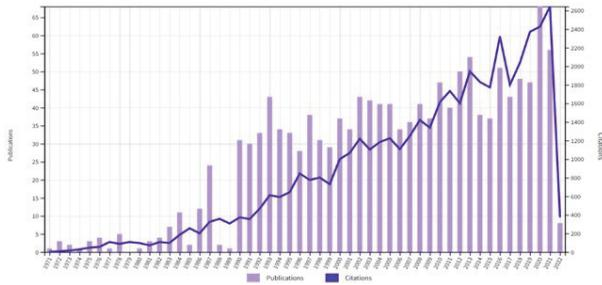
were the most preferred languages.

1351 (97.194%) of the publications were published in SCI-EXPANDED journals. The remains were published in the other indexes [CPCI-S: 177 (12.734%), ESCI: 34 (2.446%), BKCI-S: 5 (0.360%), and 4 (0.156%), SSSI: 2 (0.360%) indexed journals].

The first article was published in the year 1971. 990 (71.87%) of the articles were published after 2000. The highest number of publications was in the year 2020 (n = 68, 4.892%).

The H index of the articles was 100. There were a total of 45063 citations and an average of 32.42 per item. The number of citations and publications has increased over 30 years (Graphic 1). The articles were mostly (46.906%) from the Transplantation area (Table 1).

Table 1. Research areas.		
Web of Science Categories	Record Count	% of 1.390
Transplantation	652	46.906
Immunology	646	46.475
Surgery	413	29.712
Hematology	313	22.518
Infectious Diseases	225	16.187
Microbiology	120	8.633
Oncology	108	7.770
Medicine General Internal	95	6.835
Biophysics	78	5.612
Virology	61	4.388
Respiratory System	47	3.381
Urology Nephrology	47	3.381
Gastroenterology Hepatology	39	2.806
Cardiac Cardiovascular Systems	37	2.662
Pediatrics	34	2.446
*Showing 15 out of 53 entries		



Graphic 1. Growing number of citations and publications since 1970.

Michael Boeckh from the USA was the top-ranked author (Table 2). 2.086% of the articles were published by group authors. Infectious Diseases Working Party Europe (n = 2, 0.144) was the most published group.

Table 2. Top ranked authors list.

Authors	Record Count	% of 1.390
Boeckh, Michael (USA)	33	2.374
Kanda, Yoshinobu (Japan)	27	1.942
Einsele, Hermann (Germany)	23	1.655
Razonable, Raymund R. (USA)	20	1.439
Griffiths, Paul D. (England)	17	1.223
Showing 5 out of 8.035 entries		

The University of London was the top ranked affiliation with 108 articles (Table 3).

Table 3. Top ranked affiliations.

Affiliations	Record Count	% of 1.390
University of London	108	7.77
University of Washington	98	6.15
Fred Hutchinson Cancer Center	56	4.029
Mayo Clinic	43	3.094
Assistance Publique Hopitaux Paris	34	2.446
Pennsylvania Commonwealth System of Higher Education	33	2.374
University of Pittsburgh	31	2.230
Harvard University	28	2.014
Showing 8 out of 1.346 entries, 8 record(s) (0.576%) do not contain data in the field being analyzed		

Most of the articles (n = 165, 11.871%) were published in the journal “Transplantation Proceedings” (Table 4).

Table 4. Journals mostly published the articles on CMV&SOT.

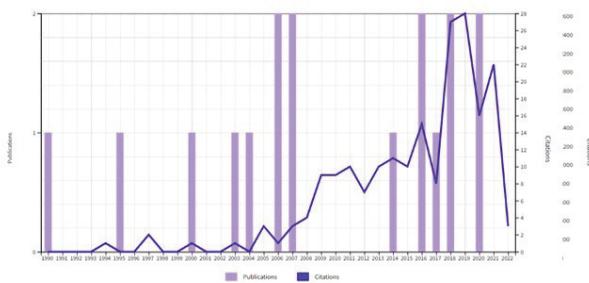
Journals	Record Count	% of 1.390
Transplantation Proceedings	165	11.871
Transplantation	105	7.554
Transplant Infectious Disease	88	6.331
Bone Marrow Transplantation	77	5.540
Biology of Blood And Marrow Transplantation	59	4.245
Blood	41	2.950
Journal of Infectious Diseases	38	2.734
Clinical Infectious Diseases	30	2.158
Clinical Transplantation	28	2.014
American Journal of Transplantation	27	1.942
Journal of Heart and Lung Transplantation	25	1.799
Journal of Medical Virology	23	1.655
International Journal of Hematology	19	1.367
British Journal of Haematology	18	1.295
Transplant International	18	1.295
Journal of Clinical Microbiology	17	1.223
Annals of Hematology	16	1.151
Liver Transplantation	13	0.935
Pediatric Transplantation	11	0.791
Transplantation and Cellular Therapy	11	0.791
Showing 20 out of 332 entries		

The United States Department of Health and Human Services funded most of the articles (11.799%) on this topic (Table 5).

Funding Agencies	Record Count	% of 1.390
United States Department of Health Human Services	164	11.799
National Institutes of Health Nih USA	161	11.583
Nih National Cancer Institute	89	6.403
Nih National Institute of Allergy Infectious Diseases Niaid	41	2.950
Nih National Heart Lung Blood Institute	39	2.806
European Commission	35	2.518
Nih National Institute Of Diabetes Digestive Kidney Diseases	29	2.086
National Natural Science Foundation of China	27	1.942
Instituto De Salud Carlos Iii	21	1.511
Merck Company	15	1.079
Showing 10 out of 529 entries, 943 record(s) (67.842%) do not contain data in the field being analyzed		

**Contribution of Turkey**

There were 17 articles from Turkey. The articles had 201 citations (11.82 per article) and the H index was 6. The number of publications and citations had an irregular distribution over the years (Graphic 2).



Graphic 2. Times cited and publications from Turkey since 1970.

Baskent University and Ankara University were the leading affiliations, with four articles each (Table 6).

Ranked	Affiliations	Record Count	% of 17
1	Baskent University	4	23.529
1	Ankara University	4	23.529
2	Ege University	3	17.647
2	Hacettepe University	3	17.647
3	Adana Numune Training Research Hospital	2	11.765
3	Akdeniz University	2	11.765
3	Antalya Training Research Hospital	2	11.765
3	Childrens Hospital	2	11.765
Showing 8 out of 35 entries			

**DISCUSSION**

Organ transplantation (OT) is one of contemporary medicine’s most effective innovations. Patients with end-stage disease often have no other option except to undergo transplantation. Even before the first transplant, it was evident that OT could only be successful if it was approached in a multidisciplinary manner.<sup>5</sup> In 1933, Ukrainian physician Voronoy, U.U. performed the first human-to-human transplant in the Soviet Union.<sup>5,6</sup>

The United Network of Organ Sharing (UNOS), which was founded in 1984, was the next significant step in the evolution of OT. This organization oversees all transplant activities in the United States, including the upkeep of a national transplant list for all forms of transplantation, data gathering, and educational activity coordination. A number of organizations with identical functions exist throughout Europe and Asia.<sup>5</sup> The Middle East Dialysis and Organ Foundation was founded in 1984, and has now evolved into the Middle East Society for Organ Transplantation (MESOT), a significant step forward for organ transplantation in the region and a member of the Transplant Society.<sup>7</sup> MESOT has managed to operate and hold international congresses despite worldwide turmoil in the

Middle East. Many issues linked to transplantation have been addressed by MESOT member countries in countries with similar sociocultural features.<sup>8</sup>

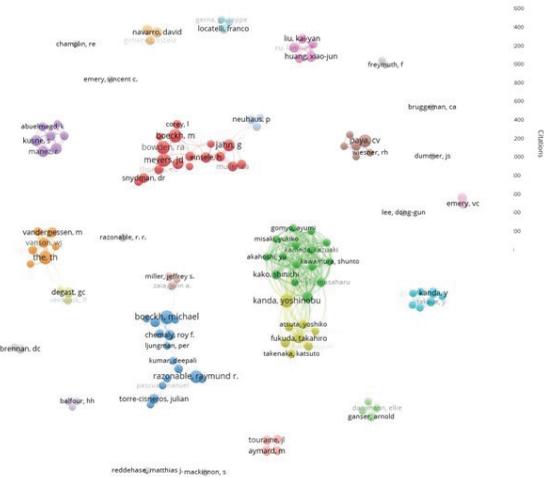


Figure 1. Citation visualization map among authors with a minimum of 5 publications and 1 citation.

\*\*Lines connecting countries are indicative of citation. Authors represented with larger circle size or font size had relatively more citation.

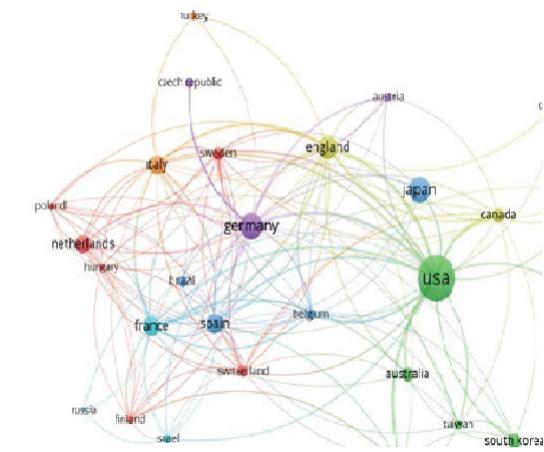


Figure 2. Network visualization map of co-authorship among countries.

\*\*Lines connecting countries are indicative of collaboration. Thicker lines indicate stronger collaborations. Countries represented with larger circle size or font size had relatively more international collaboration.

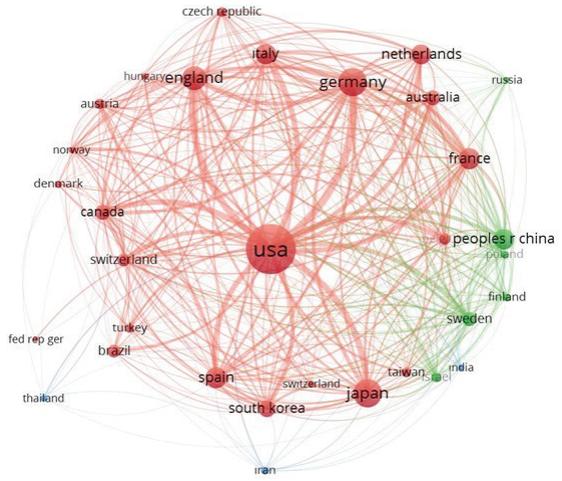


Figure 3. Network visualization map of citation map among countries.

\*\*Lines connecting countries are indicative of collaboration. Thicker lines indicate stronger collaborations. Countries represented with larger circle size or font size had relatively more international collaboration.

Along with the successful transplantation of an organ, the management of infections that may develop in the patient is one of the most important issues in organ transplantation, and infections are one of the main causes of death in these patients. CMV is one of the most important infectious agents in both SOT and HCT recipients.<sup>1-3</sup> Despite advances in molecular technologies for CMV detection and the introduction of extremely efficient preventative therapies, CMV continues to be a primary cause of morbidity and mortality in HCT recipients. Pneumonia, hepatitis, colitis, retinitis, and encephalitis are among the tissue-invasive diseases caused by CMV. HCT recipients with CMV illness have a mortality rate of up to 60%. CMV infection has been linked to an increased risk of secondary bacterial and fungal infections, graft-versus-host disease, and high non-relapse mortality rates after HCT.<sup>9</sup> The topic of CMV in transplantation seems to be becoming even more popular as the number of both HCT and SOT recipients is increasing globally.<sup>5-8</sup>

The scientometric or bibliometric analysis is used to map the scientific knowledge field objectively, while the critical evaluation is used to suggest research themes and difficulties based on the scientometric results<sup>10,11</sup>. Despite the fact that bibliometric analyses on transplantation have been found in the medical literature<sup>10-16</sup>, no similar study could be found in the available literature on CMV infection in SOT, which is one of the most important problems for posttransplant patients. Only Chen et al.<sup>17</sup> conducted a bibliometric study to research the status of CMV infection after hematopoietic stem cell transplantation.

Our research is the first to conduct a global bibliometric examination of current scholarly output on CMV and SOT. In addition, the publications from Turkey were analysed for comparison with the global literature. This bibliometric study will help researchers better understand the state of CMV research in SOT recipients and predict future trends. In the next few years, understanding risk factors for peritransplantation CMV infections and developing efficient therapies for infectious complications should be prioritized.

In this study, we evaluated 1390 articles in the WOS core collection based on the research topic of CMV and transplantation, using various statistical items like references and keywords in Vosviewer, and came to strong conclusions from the visualization analysis. Furthermore, by assessing the findings of our study, readers will be able to identify the biggest scientific communities in the field, as well as the most referenced academics and journals, which will aid them in their search for potential research collaborators.

According to a bibliometric analysis of the most cited articles in this field, the plurality of the top 100 most cited publications on transplantation were published mostly in the USA between 2000 and 2009. Most of the top 100 papers on transplantation were published in the New England Journal of Medicine, followed by Transplantation and

Nature journals.<sup>10</sup>

Chen et al.<sup>17</sup> conducted their study on the same database (WOS) on June 15, 2021, and they used CiteSpace V visualization software. They reported that a total of 1,476 documents were found to be relevant. The United States, Germany, Japan, China, and Italy ranked first through fifth in terms of the number of publications. The Fred Hutchinson Cancer Research Center, the University of Washington, the University of Minnesota, the Karolinska Institute, and Peking University were the top five institutions by number of publications. The Fred Hutchinson Cancer Research Center, Henri-Mondor Hospital, the National Cancer Center, Karolinska University Hospital, and the University of Pavia were the top four institutions for centrality scores. With a centrality score of 0.01, there were just 4 writers. The research was mostly published in prestigious hematological journals as well as immunization and transplantation journals. In our study, we found that since 2000, the number of articles on CMV and transplantation has steadily increased, with no noticeable spikes, indicating the field's constant development. 990 (71.87%) of the articles were published after 2000. The highest number of publications was in the year 2020 (n = 68, 4.892%). When looking at the literary sources, the USA, which is at the forefront of this research, has published over 400 pieces of literature (n = 416, 29.928%) in the past, and the USA is home to a plethora of vital agencies and reputable researchers. Furthermore, Germany (10.216%), Japan (9.281%), England (7.122%), France (6.043%), and Spain (5.468%) all play important roles in research. The most cited article was published in the journal *The Journal of Infectious Diseases*. Despite the fact that the University of London was the most mentioned and prolific country in the field of CMV and transplantation research, the USA was the most cited and productive country. This could be owing to the abundance of institutions and financial assistance in the USA.

In 1989, the Turkish Ministry of Health launched a national organ sharing program, and in 2001, National Co-

ordination Centers for dead donor organ distribution were established.<sup>18</sup> The World Transplantation Society (TTS) promoted the establishment of kidney and liver transplant programs in low- and middle-income nations. By accepting large numbers of fellows from each country, Baskent University has played a major role in the teaching and research of local health professionals.<sup>19</sup> There were a limited number of articles (17 articles) from Turkey on CMV and transplantation. Baskent University and Ankara University were the leading affiliations, with four articles each. The first article was published in 1990, and for some years, no documents were published.

This bibliometric study can help researchers better understand the state of CMV research in SOT recipients and predict future research trends. In the coming years, identifying risk factors for peritransplantation infections and developing effective therapies for infectious complications should be prioritized. The number of publications in this field is very low, especially for developing countries. The USA, Japan, and European countries are the countries with the highest number of publications. Although there has been an increase in the number of articles published in recent years, our scientific output results have shown that the numbers are not at the desired level. The number of publications should be increased, especially from the countries where SOT is performed, and these countries should be scientifically supported by governments and institutions.

#### **Limitations of the study**

The study's findings are based on literature screened from the WOS core collection, and efforts are being made to improve scientific and effective analytical results from the private document library. However, the quality and amount of articles will fluctuate depending on the source of literature and subjective criteria. Furthermore, changing Vosviewer parameter settings will alter the visualization analysis outcome. As a result, there are certain limitations to this research. In addition, the most cited articles were

not examined.

#### **Conflicts of Interest**

All authors have filled out the ICMJE uniform disclosure form. There are no potential conflicts of interest for the authors to disclose.

#### **Ethical Statement**

The authors are responsible for all aspects of the work, including ensuring that any questions about the work's accuracy or integrity are thoroughly examined and resolved.

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