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Online first

Decoding the Landscape of Cytomegalovirus Research in Liver Transplantation: An In-Depth Analysis

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High Yield Medical Reviews

Introduction

Cytomegalovirus (CMV), a prevalent viral infection post-liver transplantation, significantly influences transplant outcomes. This bibliometric analysis explores the evolving landscape of CMV-related research in liver transplantation, emphasizing research output and key areas of interest.

Methods

Utilizing the Web of Science (WOS) database, we systematically searched for CMV and liver transplantation documents on October 16, 2023. R programming language, VOSviewer, and Microsoft Excel Office 365 were used for analysis.

Results

Analyzing 801 publications on CMV-related research in liver transplantation unveiled a variable publication pattern, peaking in 2010 and 2021. "Transplantation" stood out as the predominant journal. Leading contributors included the University of Pittsburgh, Mayo Clinic, and the University of Washington. The United States led in contributions, followed by Spain and the United Kingdom. The analysis highlighted substantial international collaboration, notably involving the United States, the United Kingdom, Canada, China, and Italy. Key themes revolved around recipients, prophylaxis, prevention, and antiviral therapies, with ganciclovir and valganciclovir as primary medications. Recently, there has been significant discussion regarding medications such as letermovir and maribavir.

Conclusion

This research highlights the dynamic landscape of CMV infection studies, focusing on emerging trends and new medications like 'letermovir' and' maribavir'. Given the persistent challenges in transplantation, leveraging these insights is crucial for collaborative efforts and innovative research initiatives. As the transplantation community grapples with the challenges of CMV infections, our paper aims to serve as a cornerstone among contributors, fostering collaboration among authors, centers, and countries. We hope this collaboration will significantly benefit patients and elevate healthcare standards.

INTRODUCTION

Cytomegalovirus (CMV) was first described in the early twentieth century after being isolated from salivary gland inclusions of infected patients, it is a ubiquitous herpesvirus, impacts a significant portion of the world's population.[1] CMV antibodies are present in more than 60% of adults globally, indicating a widespread and enduring viral infection .[2] Following the development of solid organ transplantation and the ensuing need for immunosuppres-

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sive treatments in subsequent years, CMV promptly evolved into the most prevalent infection following transplantation, being of particular concern in the first three months following transplant.[3,4] The infection can manifest as a de novo primary, reinfection by exogenous virus or as a reactivation infection.[3,4] Subsequent developments in molecular techniques and sophisticated diagnostic tools have enabled a more comprehensive understanding of the pathogenesis, epidemiology, and resistance patterns of CMV.[5,6] This progress has laid the foundation for the creation of targeted antiviral therapies and preventive measures.[5,6]

Given the notable progress in the field of CMV treatment and the consequential importance of this subject matter, there has been a considerable surge in scholarly output during the past two decades.[6,7] in spite of the advancements that have been made in preventative strategies, subset of patients may still encounter delayed onset CMV infection subsequent to the completion of their treatment.[8,9] In addition, some patients may encounter resistant or refractory CMV infection, necessitating the exploration into alternate therapeutic methods.[8-11]

The recent increase in research activity has stimulated numerous studies seeking to identify and validate potential alternative antiviral agents for the comprehensive management of CMV following liver transplantation.[10-14] Acknowledging the significance and depth of this research domain, our investigation will conduct a bibliometric examination of this extensive body of research, elucidating the primary contributors, patterns, and influential studies within the discipline.

The field of bibliometrics provides a quantitative framework for assessing the citations, authorship, and content of scholarly publications.[15] This framework helps to reveal the influence and impact of individual authors or studies within a particular research area.[15] These analyses provide researchers with the ability to identify current research trends, recognize emerging research areas, and facilitate potential collaborations.[15-17] To the best of our understanding, there is a lack of comprehensive bibliometric analyses that assess the literature on the prevention and treatment of CMV-related research in the field of liver transplantation. This research aims to address the existing knowledge gap by providing a bibliometric analysis of prominent contributors, emerging trends, and influential publications within this field.

2. METHODS

2.1. DATABASE SELECTION AND SEARCH STRATEGY

The Web of Science database (WOS), a widely recognized and frequently used database for bibliometric studies, provides bibliometric data, including titles, authors, countries, affiliations, abstracts, keywords, journals, and reference information, for download and further analysis. On October 16, 2023, WOS was utilized to conduct a systematic search of titles containing relevant keywords pertaining to CMV and liver transplantation. The appropriate use of '*' was employed to account for relevant variations of the keywords. The final advanced search query was ((TI=(CMV)) OR TI=(cytomegalovirus)) AND TI=(liver transplant*).

In order to ensure the inclusion of all pertinent documents, we refrained from excluding or imposing any limitations on the search query. All 801 relevant documents resulted from the previous search query were included. It is noteworthy to mention that the present study was granted exception from obtaining approval from the institutional review board due to its exclusive focus on bibliometric analysis and the absence of patient data extraction.

2.2. BIBLIOMETRIC ANALYSIS

After executing the prescribed search strategy, we proceeded with data extraction and bibliometric analysis. Descriptive analysis was carried out to examine the annual output, production from various countries, institutions, authors, and journals. Additionally, we explored co-authorship and collaborations among researchers, along with conducting a co-occurrence analysis of all keywords. Analyses of bibliometric indicators was done using "bibliometrix" package in the R programming language (version 4.2.2), VOSviewer (version 1.6.19) and Microsoft Excel Office 365.

2.3. VOSVIEWER VISUALIZATION INTERPRETATION

VOSviewer was developed in the Java programming language by Van Eck and Waltman from Leiden University in 2010.[18] Its proficiency lies in rendering intricate bibliometric networks more comprehensible through visually engaging maps.

In a VOSviewer visualization, terms are depicted as circles accompanied by their respective labels. The size of each circle is directly proportional to its weight (occurrence/citations), whereby larger circles denote greater weight. In certain instances, the label of an item may not be visibly presented, to prevent the occurrence of redundant labels. Clusters of related terms are differentiated based on their respective colours. The lines that connect the circles serve to denote the connections and co-citation relationships that exist between the terms. The proximity between two circles serves as an approximate measure of the degree of association, as determined by co-citation connections. When circles are closer in proximity, it implies a stronger level of interconnectedness. The network visualization effectively represents the interconnections among terms, their relative significance as indicated by their size, and their associations as demonstrated through proximity and links. The overlay visualization bears resemblance to network visualization, with the distinction that items are assigned distinct colours. This visualization employs colours to represent the publication years, includes a colour bar located in the bottom right corner, which serves to indicate the mapping of terms to specific colours.

RESULTS

Of the 801 publications found related to CMV post liver transplantation, 788 were in English, ten were in Spanish,

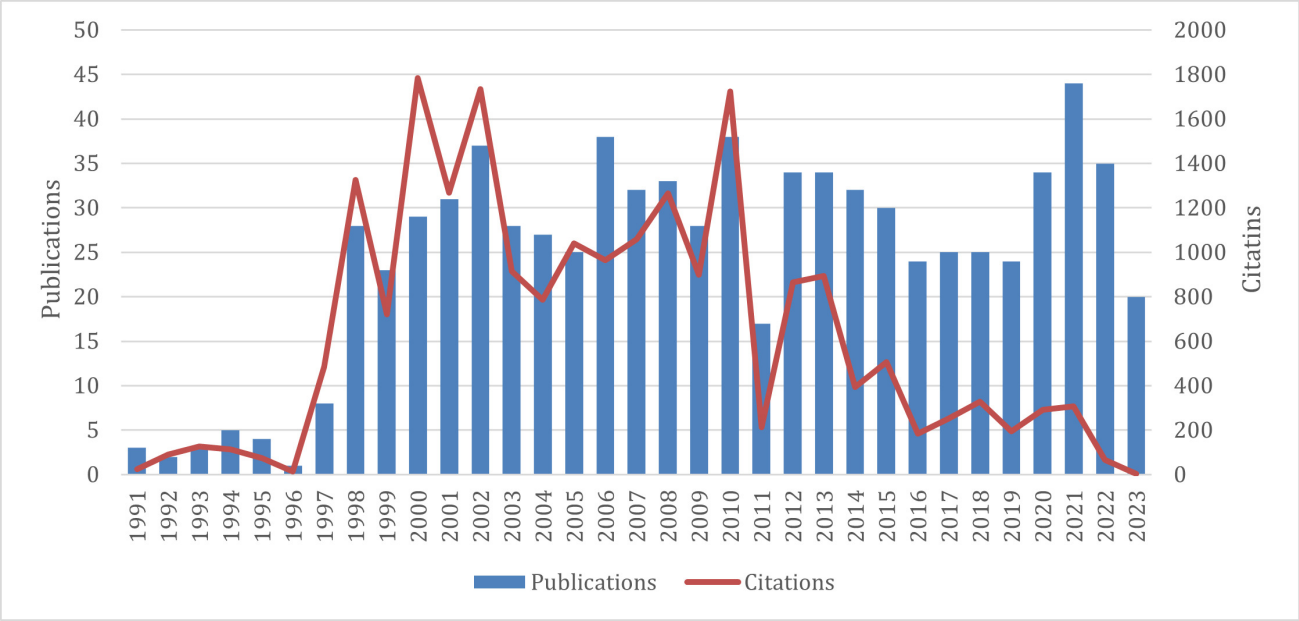

Figure 1. Annual Publications and Citations

one was in Turkish, and two were in French. There were 495 articles and 81 reviews. According to the WOS Categories, Transplantation category accounted for the highest number of publications (n=427), followed by Surgery (n=350), Immunology (n=272), Medicine (n=244), Gastroenterology and Hepatology (n=153), Infectious Diseases (n=124), Microbiology (n=82), Virology (n=44), Medicine General and Internal (n=44), and Pharmacology (n=33).

The leading funding agencies were: The National Institutes of Health (NIH) (US) (n=70), followed by the National Institute of Allergy and Infectious Disease (NIAID) (US) (n=20), the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) (n=16), and the Instituto de Salud Carlos III (Spain) (n=15).

PUBLICATION TRENDS

The number of publications showed a fluctuating pattern over the years, starting in 1991 and reaching its highest point in 2021 with 44 articles. Subsequently, there was a decline in the number of publications, with 35 articles being published in 2022. There was a prior peak in 2010 with 38 articles, and a decline to 24 articles in 2016 before rising up again. A total of 327 articles were published over the last decade, with a cumulative count of 3,423 citations. The year 2000 saw the highest number of citations, totaling 1,785. The average number of citations per year was 634, with a total of 20,900 since the year 1991. The average number of citations per publication was 26. See Figure 1.

TOP JOURNALS

"Transplantation" published the highest number of articles and was the most frequently cited journal, with a total of 4,180 citations across 84 articles, accounting for 10.5% of all publications. "Liver Transplantation" and "Transplantation Proceedings" followed closely with a total of 78 (9.7%) and 72 (9%) publications, respectively accounting for 2,503 and 671 citations, respectively.

TOP AUTHORS

This analysis examines the authors and their respective collaborations, identifying several researchers who have emerged as noteworthy contributors. Out of the total 801 documents, 50 were single-authored. On average, each document had 6.75 co-authors. International collaboration accounted for 10.49% of all co-authorships. The leading five authors in terms of publications were Nina Singh, who has contributed to 50 papers and received 1,542 citations; Irmeli Lautenschlager, with 29 publications and 701 citations; Marilyn M. Wagener, with 28 publications and 1,239 citations; Raymund R. Razonable, with 26 publications and 1,255 citations; and Ajit P. Limaye, with 25 publications and 868 citations.

TOP INSTITUTIONS

Several institutions have made significant contributions to this area of study in terms of publications. The top five contributing institutions were the University of Pittsburgh (US) (n=57), followed by Mayo Clinic and Mayo Foundation (US) (n=50), the University of Washington (US) (n=31), the University of Helsinki and Helsinki University Hospital (Finland) (n=22), and the Fred Hutchinson Cancer Research Center (n=11). Supplementary Table 1 presents the top ten contributed institutions in this field.

TOP COUNTRIES

An analysis of the contributions made by countries on the topic of CMV a liver transplant showed that the United States was the largest contributor with 328 publications and 10,643 citations, accounting for 41% of all publications.

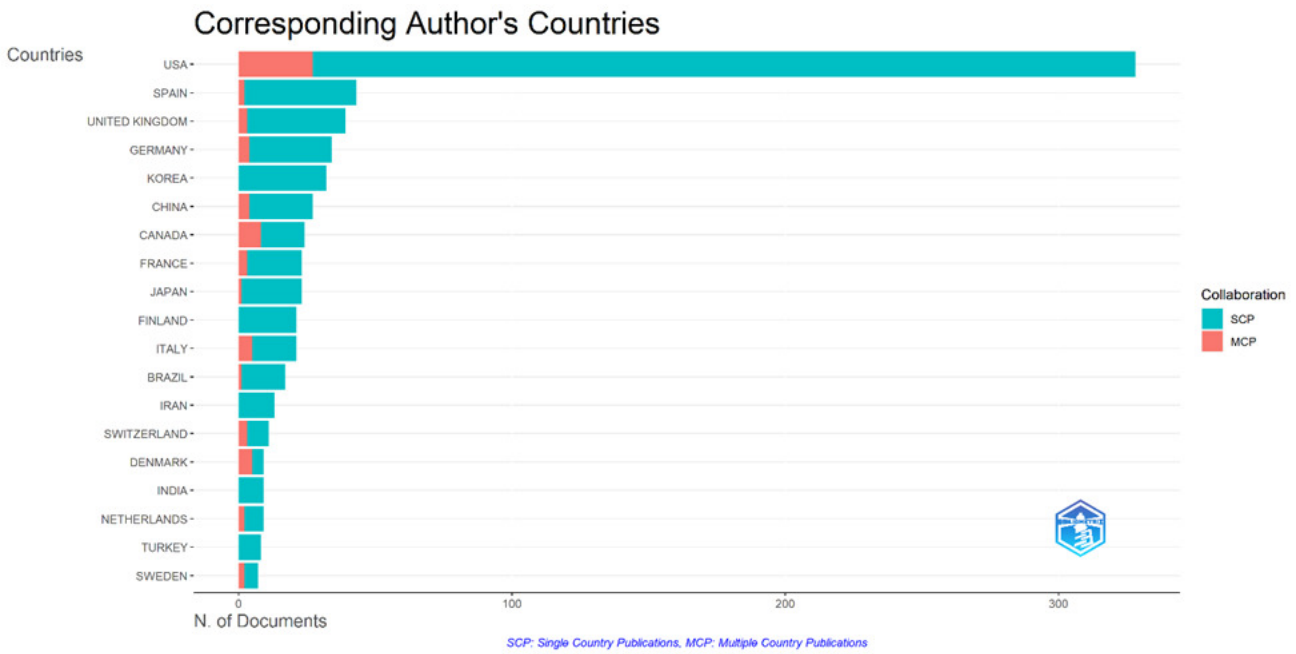

Figure 2A. Multiple (MCP) and single-country publications (SCP) of the top contributed countries.

Followed by Spain with 43 publications and 727 citations, United Kingdom with 39 publications and 1,471 citations, Germany with 34 publications and 589 citations, South Korea with 32 publications and 227 citations, China with 27 publications and 235 citations and Canada with 24 publications and 968 citations. The top 10 cited countries are represented in Supplementary Table 2.

Figure 2A present the number of multiple and single country publications. The Multiple Country Publication (MCP) ratio was computed in order to evaluate the degree of international collaboration present in our dataset. MCP ratio represents the proportion of articles in the dataset that involved collaborations between researchers from different countries. A higher MCP ratio indicates a higher prevalence of international collaboration in research publications. The US and Spain, as the leading contributors in this field, have exhibited a level of international cooperation, as seen by their respective MCP ratios of 8.2% and 4.2%. Certain nations, such as South Korea, Finland, and Iran, for instance, have an MCP ratio of 0, meaning that there was no international collaboration in their research projects. Figure 2B presents the countries network and collaboration map, most collaborations were between US and other countries including UK (n=11), Canada (n=10), China (n=10), and Italy (n=70).

TOP TEN CITED ARTICLES

The top ten most cited articles are represented in Supplementary Table 3. Kotton, CN et al article titled "International Consensus Guidelines on the Management of Cytomegalovirus in Solid Organ Transplantation", published in Transplantation in 2010, stands out with 429 citations. Followed by Pescovitz, MD et al article titled "Valganciclovir results in improved oral absorption of ganciclovir in liver transplant recipients", published in Antimicrobial Agents and Chemotherapy in 2000, with 244 citations and Limaye, AP et al article titled "Impact of cytomegalovirus in organ transplant recipients in the era of antiviral prophylaxis", published in Transplantation in 2006, with 180 citations.

TOP KEYWORDS

A total of 2,109 keywords were found on this topic. After excluding the nonspecific keywords such as "female," "male," "liver," "transplantation," and other redundant keywords. The keyword "recipients" appeared in 142 articles, followed by "prophylaxis" in 96 articles, "prevention" in 93 articles, "ganciclovir" in 85 articles, and "risk-factors" in 83 articles.

The analysis, depicted in Figure 3A, displays a network visualization that categorizes the top keywords into three separate clusters. The first cluster focuses on prevention and prophylactic therapy. The second cluster focuses on CMV infection and its diagnosis and management. The third cluster focuses on the risk factors and sequelae of CMV infection. Figure 3B displays an overlay network of the top occurred medications across the years in this field.

DISCUSSION

The prevention and management of CMV infection in liver transplant recipients continue to pose significant challenges within the transplantation field. This bibliometric analysis offers significant insights into the patterns, trends, and influential contributors in the field of research pertaining to CMV-related research in the field of liver transplantation.

Our study shows a variable pattern over time in the quantity of publications, characterized by discernible peaks

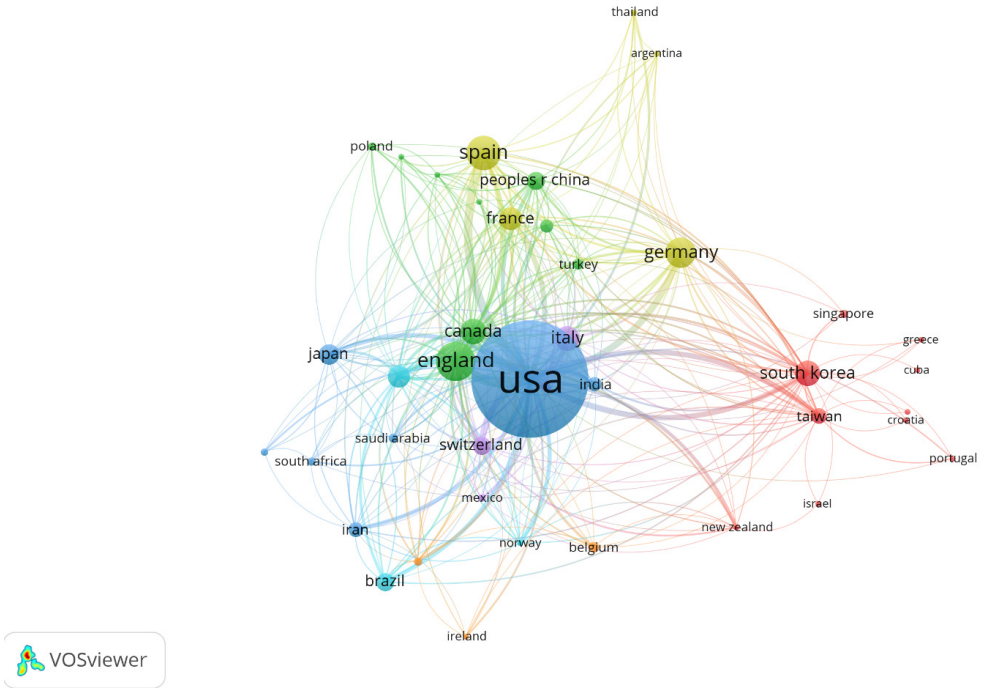

Figure 2B. Network visualization of the top-cited countries. Countries included in the same cluster are displayed in the same color. Larger circles indicate that the country had more citations. The distance between the two circles shows the degree of connection between two countries.

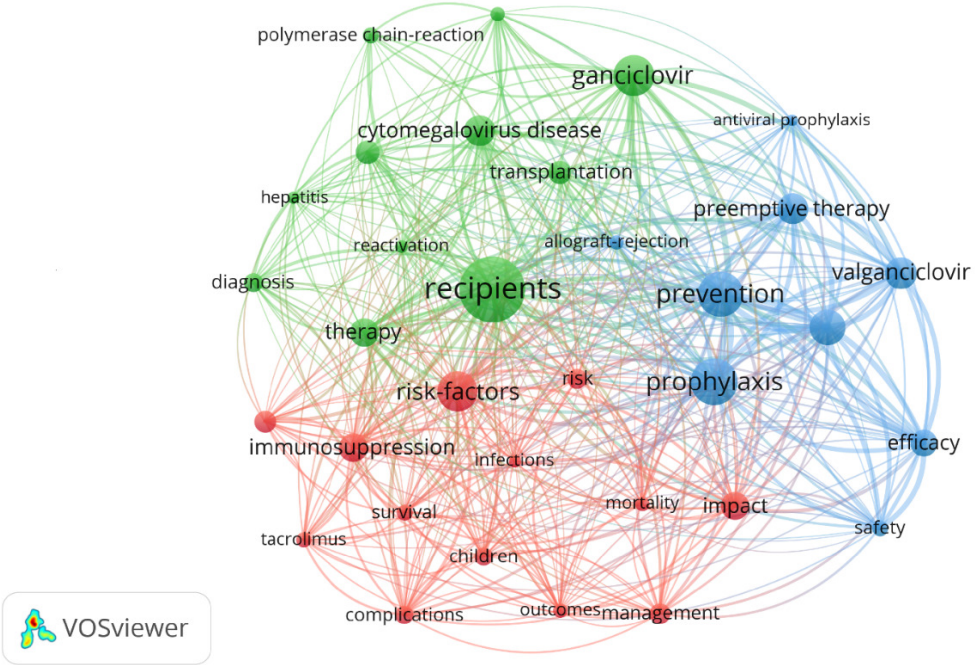

Figure 3A. Cluster visualization of the most occurring keywords and their interconnections grouped into three clusters. Each color represents a cluster of related items. Larger circles indicate that the keyword appears more frequently. The distance between two circles shows the degree of connection between two keywords.

in 2010 and 2021. The observed fluctuation may potentially signify the evolution of research interests, advancements in technology, or the introduction of novel antiviral medications.[7,11,19,20] In recent years, there has been significant development in the therapeutic field concerning CMV infection following liver transplantation. This progress has been driven by extensive research efforts and the introduction of innovative pharmaceuticals that specifically target different phases of the CMV replication process, moving away from conventional antiviral agents.[7,11,13,21,22] The in-

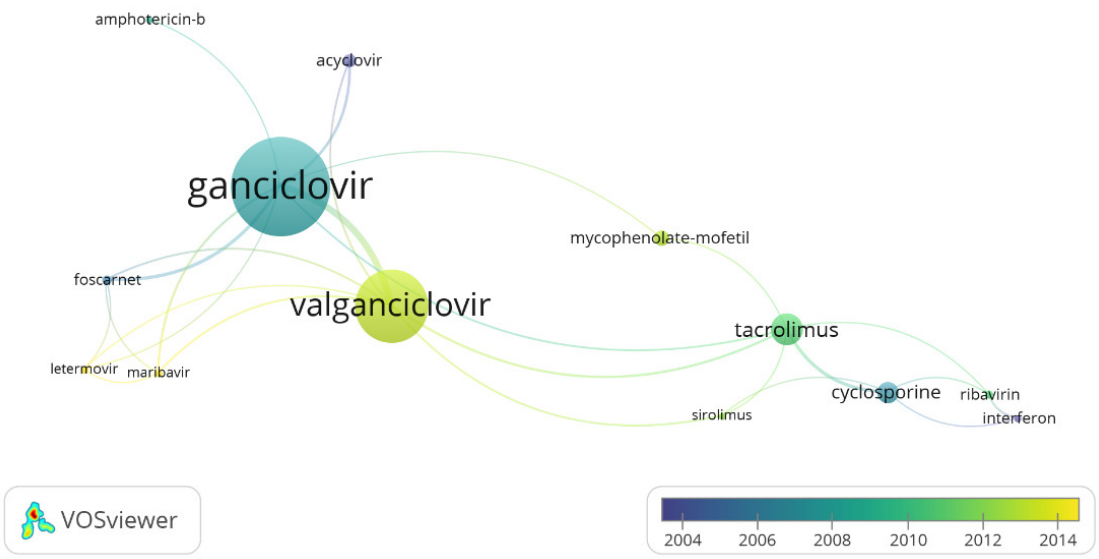

Figure 3B. Overlay presentation of the top occurring medications and their interconnections across the years. The color of a term indicates the average publication year. A color bar is shown in the bottom right corner of the visualization, which indicates the publication year range.

corporation of modern methodologies, accompanied by customized therapeutic strategies informed by pharmacogenomic knowledge, holds the potential to revolutionize the care of liver transplant recipients with CMV infection, enhance patient outcomes and reduce the occurrence of related complications.[6]

Given the critical importance of these interventions in clinical practice, it is not surprising that "prevention" and "prophylaxis" rank among the most frequently occurring keywords in the literature on this topic. The significance of the term "recipients" highlights research emphasis on prioritizing the well-being of patients, emphasizing the necessity of customized therapeutic approaches to improve patient outcomes.

Our bibliometric analysis provides valuable insights into the evolving discussion regarding the management of CMV in the field of liver transplantation, with a specific emphasis on key medications. Significantly, ganciclovir remains consistently prominent in research discussions. This ongoing focus draws attention to the continued significance of ganciclovir in the conversation about CMV management. Following that, there was a significant change, where valganciclovir becomes a central topic of conversation around 2012, indicating changing viewpoints on antiviral drugs at that time. The emergence of 'letermovir' and 'maribavir' as a treatment option signifies a shifting scenario, demonstrating a more extensive investigation of innovative drugs in the context of CMV and liver transplantation after 2014. The frequent occurrence of these medications in scholarly works suggests that there is ongoing discourse and investigation regarding their use in the field. Furthermore, it is expected that there will be notable progress in the prevention and treatment of CMV infection among individuals who have received liver transplants in the forthcoming years.[7] Figure 3B visually represents these patterns, providing insight into the changing conversation about medications and their perceived importance in addressing CMV-related challenges.

The results of our analysis demonstrated that the United States has established a prominent position in this research field. The United States has made substantial contributions in terms of both the number and impact of publications. The United States contributed significantly to the total number of publications, with 328 papers and 10,643 citations, representing 41% of all publications. Nevertheless, according to our analysis, research collaboration continues to be essential in order to obtain a comprehensive and worldwide perspective. International collaboration constitutes a relatively small portion (10.49%) of all co-authorships. Acknowledging the significance of collaborative endeavors, establishing partnerships among researchers, institutions, and countries can augment the variety of perspectives and approaches. These collaborations play a crucial role in addressing complex challenges in CMV research, facilitating the exchange of knowledge, and ultimately improving patient care in the field of liver transplantation.

Although this bibliometric analysis offers a comprehensive overview of the research landscape, it is important to acknowledge the presence of inherent limitations. Initially, the data was exclusively obtained from the WOS database, potentially excluding valuable contributions from alternative databases. This could potentially result in an inadequate portrayal of the research field. Furthermore, the investigation did not examine the clinical significance or

influence of the publications, and instead considered only the volume of articles and citations. This may have resulted in the oversight of influential works that have received less citations.

In conclusion, the bibliometric analysis presented in this study offers a thorough examination of the research landscape pertaining to the prevention and treatment of CMV-related research in the field of liver transplantation. The dynamic nature of this research domain is highlighted by the identified evolving trends, influential contributors, and key themes. As the transplantation community persists in addressing the complexities associated with CMV infections, it is imperative to utilize these understandings, cultivate partnerships, and promote pioneering research endeavors to maximize patient outcomes and improve the standard of healthcare.

DISCLOSURES

We declare that we have no competing interest to disclose. This research was not funded by any organization and we have no conflict of interest to report

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SUPPLEMENTARY MATERIALS

Supplementary material

Download: https://hymr.scholasticahq.com/article/94962-decoding-the-landscape-of-cytomegalovirus-research-in-liver-transplantation-an-in-depth-analysis/attachment/199618.docx?auth_token=Kv79yxa3gsvYvo-fyEkS