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Analysis of scientific publications related to Hepatitis B prevention in the last decade: 2013-2023

Análise das publicações científicas relacionadas à prevenção da hepatite B na última década: 2013-2023

Análisis de publicaciones científicas relacionadas con la prevención de la Hepatitis B en la última década: 2013-2023

Anoucheka Julien¹ , Antonio Rosa de Sousa Neto² , Ana Raquel Batista de Carvalho² , Daniela Reis Joaquim de Freitas² , Luana Kelle Batista Moura^{3,4} , Maria Eliete Batista Moura² , Simone Maria Muniz da Silva Bezerra¹ , Rosilane de Lima Brito Magalhães² 

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¹ State University of Pernambuco (UPE), Postgraduate Program in Nursing. Recife, Pernambuco, Brazil

² Federal University of Piauí (UFPI), Postgraduate Program in Nursing. Teresina, Piauí, Brazil

³ University of Ribeirão Preto (UNAERP), Postgraduate Program in Dentistry. Ribeirão Preto, São Paulo, Brazil


⁴ Faculty of Technology of Teresina (CET). Teresina, Piauí, Brazil

ABSTRACT

Introduction: The World Health Organization estimates that chronic infection with the Hepatitis B Virus globally affects approximately 296 million individuals, with 1.5 million new infections yearly. Those affected often remain asymptomatic for extended periods but may inadvertently transmit Hepatitis B Virus to others. **Aim:** To analyze scientific publications related to the prevention of hepatitis B from 2013 to 2023. **Outlining:** A bibliometric study with a quantitative approach analyzing 333 articles using the Bibliometrix R package and its web interface Biblioshiny. **Results:** Articles were predominantly published in 2018 and 2019, with the Journal of Viral Hepatitis being the primary scientific journal. These articles were authored by 2,467 individuals from 810 institutions, emphasizing Udice - French Research Universities. Among the 81 countries identified, China figured prominently. The articles accumulated a total of 8,964 citations. The KeyWords Plus™ highlighted a focus on infection and its transmission pathways, notably vertical/perinatal, immunization against infection, and treatment using antiretrovirals. **Implications:** The need for new studies focused on educational interventions related to hepatitis B prevention was identified, including the creation, application, and evaluation of educational technologies.

DESCRIPTORS

Hepatitis B; Infectious Disease Transmission, Vertical; Sexually Transmitted Diseases; Communicable Disease Control.

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Corresponding Author:

Antonio Rosa de Sousa Neto
Address: Rua Dr. Epifânio Carvalho, 1391 - Ininga, Teresina, Piauí, Brazil.
ZIP Code: 72910-733 - 64049-760 - Teresina - PI, Brazil.
Phone: +55 (61) 99634-3678
E-mail: antonioneto@ufpi.edu.br

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INTRODUCTION

The World Health Organization (WHO) estimates that chronic Hepatitis B Virus (HBV) infection affects 296 million individuals globally, with 1.5 million new infections annually.¹ Those affected often remain asymptomatic for long periods but may inadvertently transmit HBV to others.²

In this context, it is noteworthy that transmission occurs mainly through direct contact with blood, contaminated body fluids, and mucous secretions from infected individuals. This can happen through the sharing of needles between injecting drug users, unprotected sexual intercourse, blood, and perinatal transfusions from the infected mother to the newborn during birth.²

Symptoms of hepatitis B include fatigue, lack of appetite, stomach pain, nausea, and jaundice. However, it can become a chronic infection, which in the long term can lead to serious and even fatal health problems such as liver disease or liver cancer.³

In the period from 2000 to 2022, Brazil registered 276,646 confirmed cases of hepatitis B. The highest incidence was observed in the Southeast region (34.2%), followed by the South (31.3%), North (14.5%) regions, Northeast (10.9%) and Central-West (9.1%). Between 2012 and 2019, there was a 16.0% reduction in hepatitis B detection rates in the country, from 8.1 to 6.7 cases per 100,000 inhabitants. In 2022, the detection rate decreased even further, reaching 4.3 cases per 100 thousand inhabitants.⁴

Considering the indices above, the prevention of hepatitis B is imperative, which includes not sharing needles, the use of condoms, and, mainly, vaccination. It is worth highlighting the importance of Brazil, which began introducing the vaccine in 1998 as part of the National Immunization Program (PNI) and expanded it to all age groups in 2016.⁵

As for the vaccine, it is recommended to administer three doses, which are capable of providing protective levels of antibodies in more than 90% of healthy adults and young people and in more

than 95% of infants, children, and adolescents.⁶ However, adherence to vaccination among the adult population is still limited, mainly due to the phenomenon known as vaccine hesitancy.⁷ Where vaccine hesitancy is responsible for the increase in the number of vaccine-preventable diseases in unvaccinated or under-vaccinated populations.⁸

Therefore, it is necessary to research the prevention of hepatitis B to significantly reduce the incidence of the disease and support intervention actions related to prevention, diagnosis, and treatment. These actions can significantly reduce public spending associated with monitoring those affected at different health care and assistance levels.⁷

Additionally, addressing this issue is crucial since the preventive sphere also encompasses the conduct of initiatives that induce the modification of risk behaviors, such as the practice of unprotected sexual relations, the practice of sexual relations with multiple partners, and the abusive consumption of alcohol and illicit substances.²

Thus, carrying out bibliometric studies can contribute to understanding what is being produced about preventing hepatitis B, aiming to support the implementation of preventive actions and the direction of future research. Therefore, this study aims to analyze scientific publications related to the prevention of hepatitis B from 2013-2023.

METHOD

This study constitutes a descriptive bibliometric analysis employing a quantitative approach based on the five steps for conducting bibliometric research.⁹ The selection of articles to be analyzed began with a search on Web of Science™ (WoS) on September 14, 2023.

For the formulation of the search strategy, the Medical Subject Headings (MeSH) were consulted for term selection. Terms were related using the boolean operator "AND" and the asterisk (*), representing any group of characters, including no

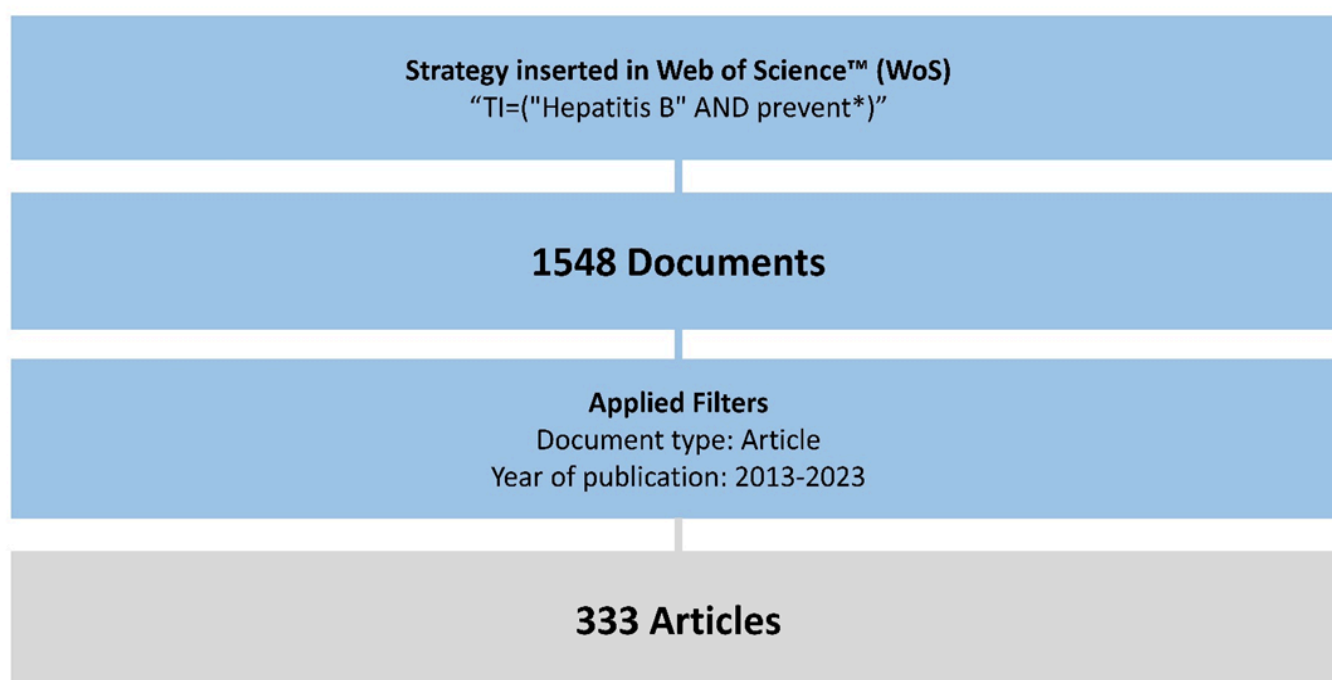
characters. The developed strategy was: "TI=("Hepatitis B" AND prevent)".

The search utilized advanced title search to enhance precision and minimize false-positive results. The literature has documented that specific title searches contribute to increased retrieval and specificity, reducing sensitivity loss compared to searches covering all fields.¹⁰⁻¹¹

The analysis included only original articles published from January 1, 2013, to September 14,

2023, excluding those not aligned with the research scope, as well as review articles, opinion pieces, reflections, editorials, and case studies. Thus, 333 articles were selected from the initially identified 1548 documents after filtering and applying predefined criteria. Information from these articles was downloaded in text file format for subsequent analysis. Figure 1 succinctly presents the process of article selection included in this study.

Figure 1 - Search strategy used to select included articles.



Source: The authors, 2023.

The text file was imported into RStudio Desktop Software (version 2023.06.2+561), integrated with R Software (version 4.3.1), and then subjected to analyses using the Bibliometrix R package (<http://www.bibliometrix.org>) and the Biblioshiny application.¹²⁻¹⁴

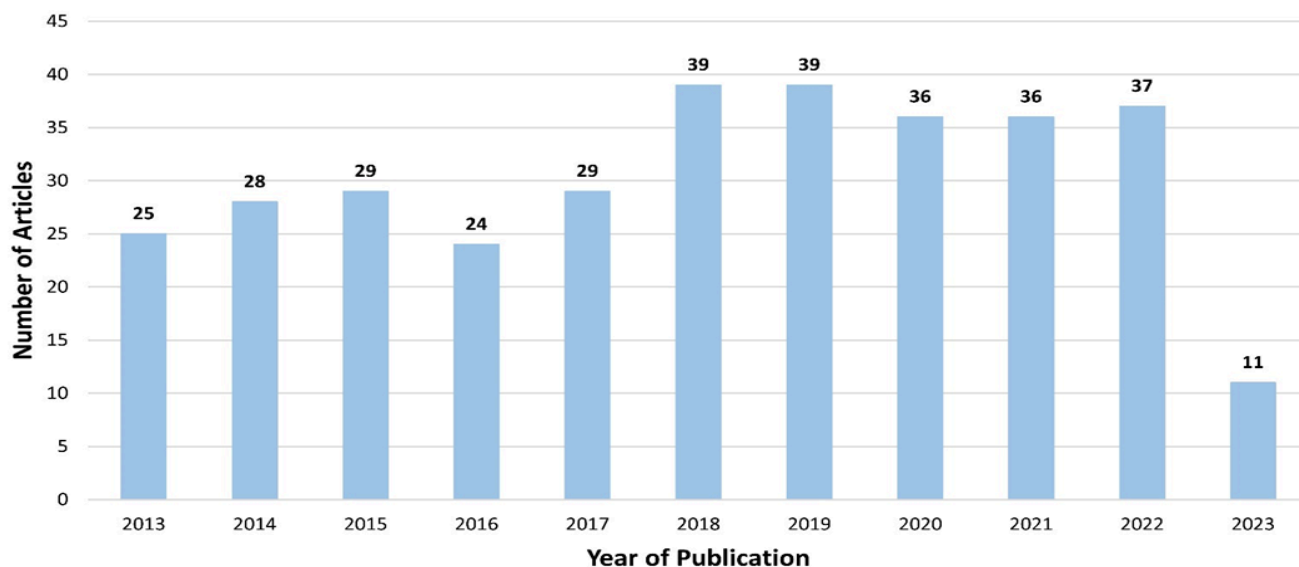
These analyses allowed for the visualization of article production by year, scientific journals by number of articles, leading authors by number of publications over time, the most productive countries by authors' affiliations, collaborations conducted

according to corresponding authors' affiliations, most cited articles, and conceptual structure using the most frequent KeyWords Plus™.

RESULTS

The number of articles published per year can be seen in Figure 2. In this figure, the annual number of articles published during the study period has fluctuated, reaching peaks in 2015, 2018, 2019, and 2022.

Figure 2 - Number of articles according to year of publication. (n=333)

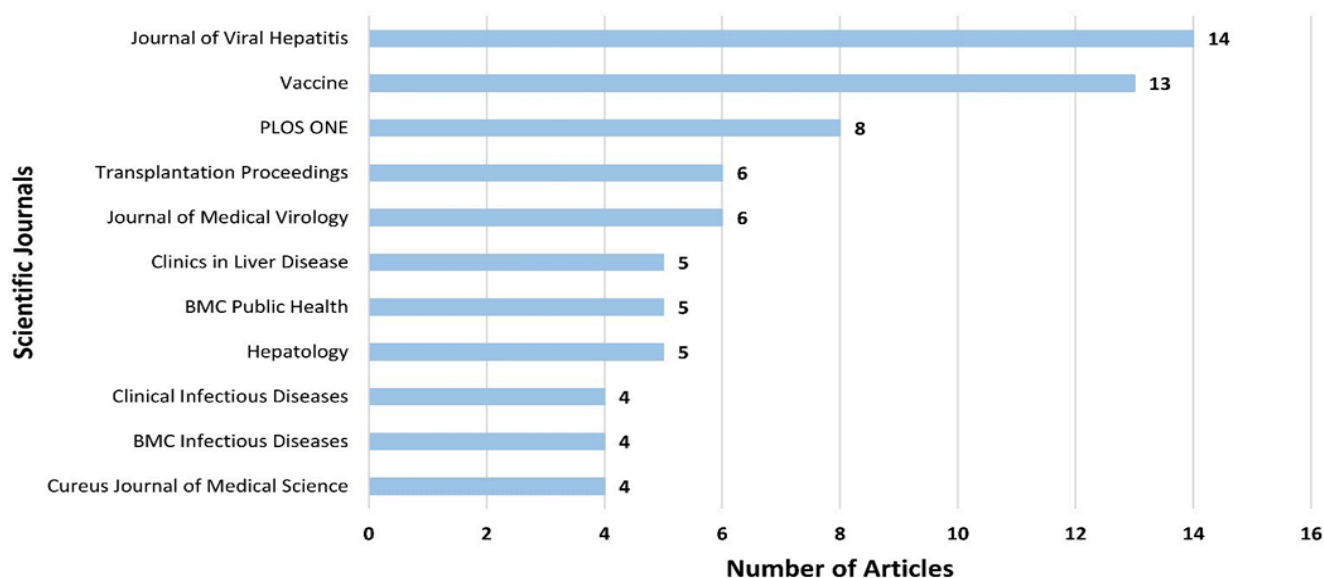


Source: WeB of Science™.

The evaluated articles were published in 215 different scientific journals, where the majority, 73.9%, published only one article, 21% published 2 to 3 articles, and 5.1% published four or more articles. The journals that published the most are displayed in

Figure 3, where the Journal of Viral Hepatitis stood out with 14 articles, followed by the Vaccine Journal and PLOS ONE, with 13 and eight articles, respectively.

Figure 3 - Main scientific journals according to the number of articles.



Source: WeB of Science™.

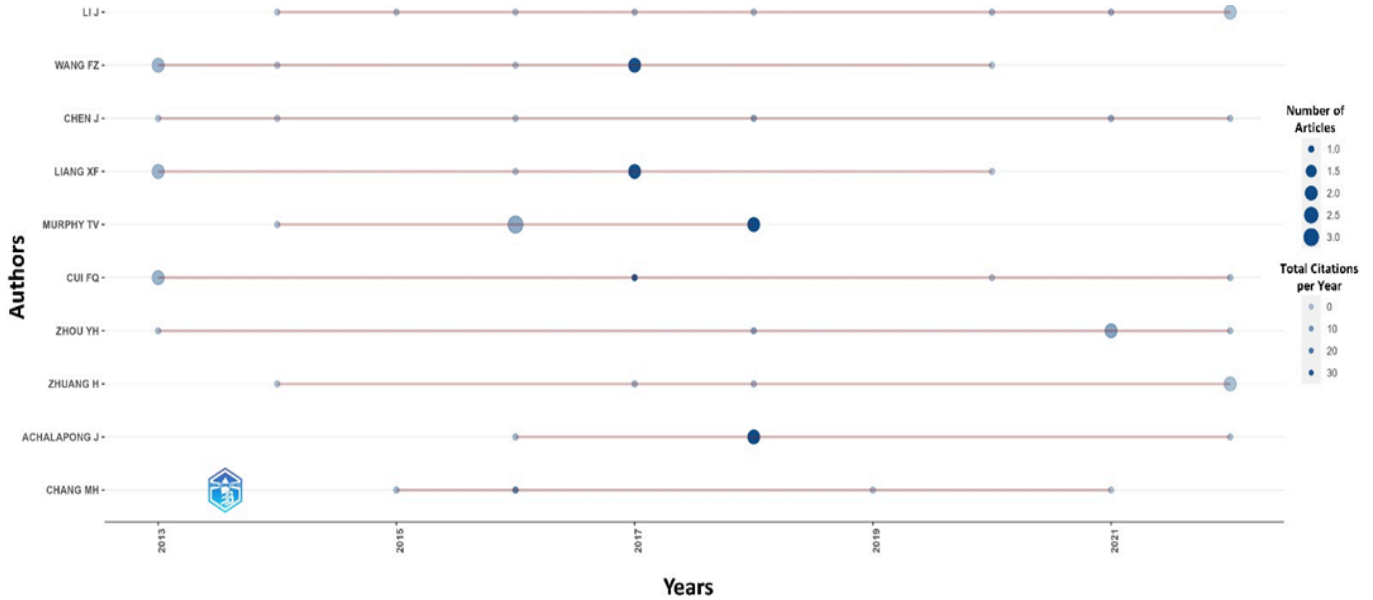
Two thousand four hundred sixty-seven different authors authored the articles. Figure 4 demonstrates the production of the main authors

over time, with the size of the bubbles being proportional to the number of published articles (giant bubbles represent a higher quantity of

articles). The shades of blue are proportional to the number of citations per year (darker blue bubbles represent more citations). Considering the number of articles published, Jie Li stood out (n=9), followed by

Fuzhen Wang (n=7), with Jie Chen, Xiao-Feng Liang, and Trudy V. Murphy tying (n=8), publishing the same number of articles each.

Figure 4 - Main authors according to the number of publications over time.

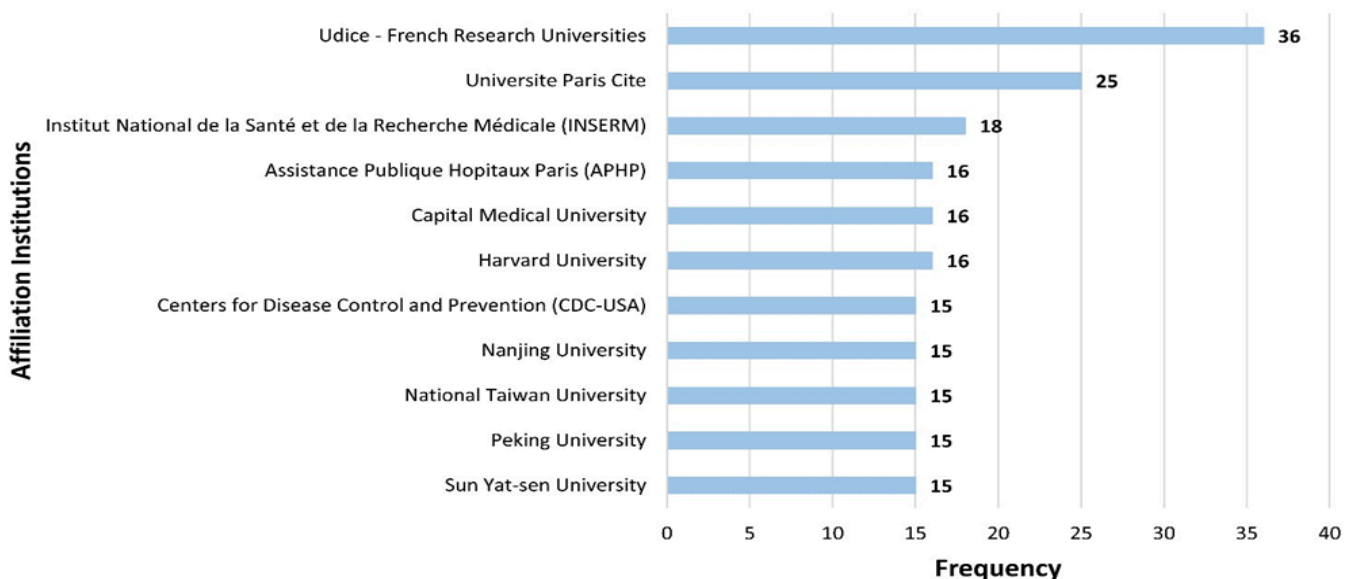


Source: *WeB of Science*™.

810 different institutions were identified in the authors' affiliations. The results showed that 61.2% of institutions appeared only once, 35.9% from 2 to 10 times, and 2.9% from 10 to 36 times. Figure 5 shows the main institutions according to the

co-occurrence analysis in authors' affiliations. Thus, authors from Udice-French Research Universities published the most, considering that the institution appeared 36 times.

Figure 5 - Main institutions according to co-occurrence in authors' affiliations.

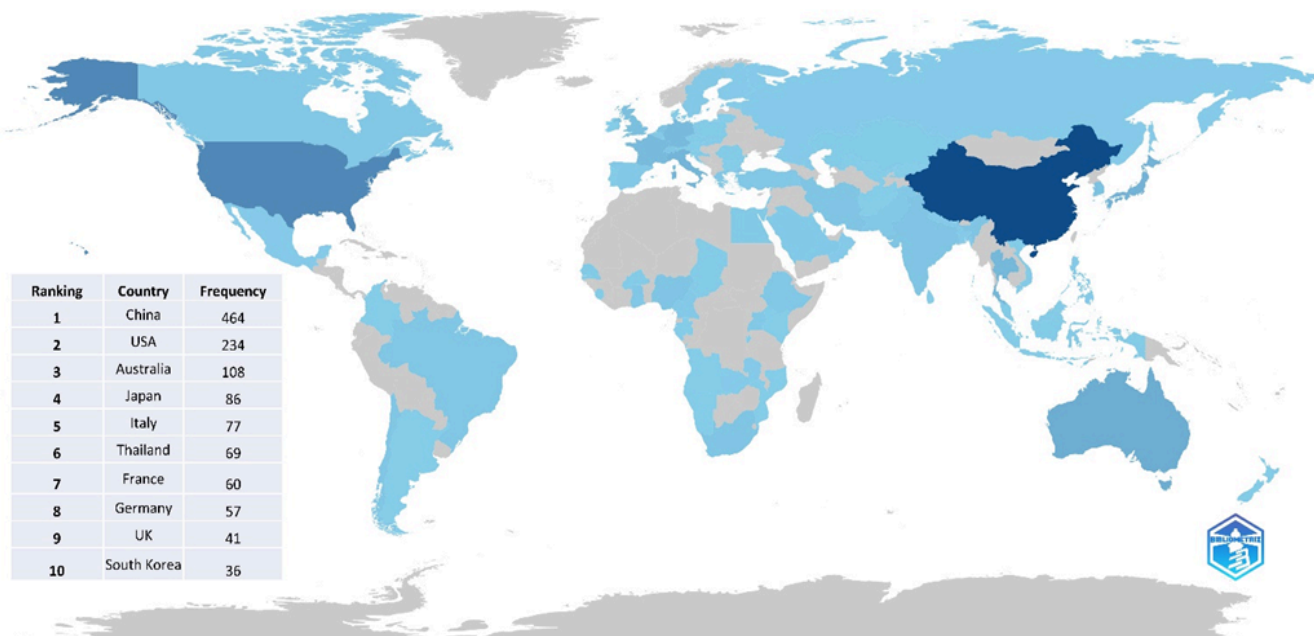


Source: *WeB of Science*™.

The authors of the analyzed articles came from 81 different countries. In Figure 6, constructed through the analysis of country co-occurrence in authors' affiliations, where shades of blue, from lightest to darkest, represent an increase in local

authors, while gray represents the absence of local authors, it can be seen that authors primarily resided in China (n=464), United States of America (USA) (n=234), and Australia (n=108).

Figure 6 - Main countries according to co-occurrence in authors' affiliations.

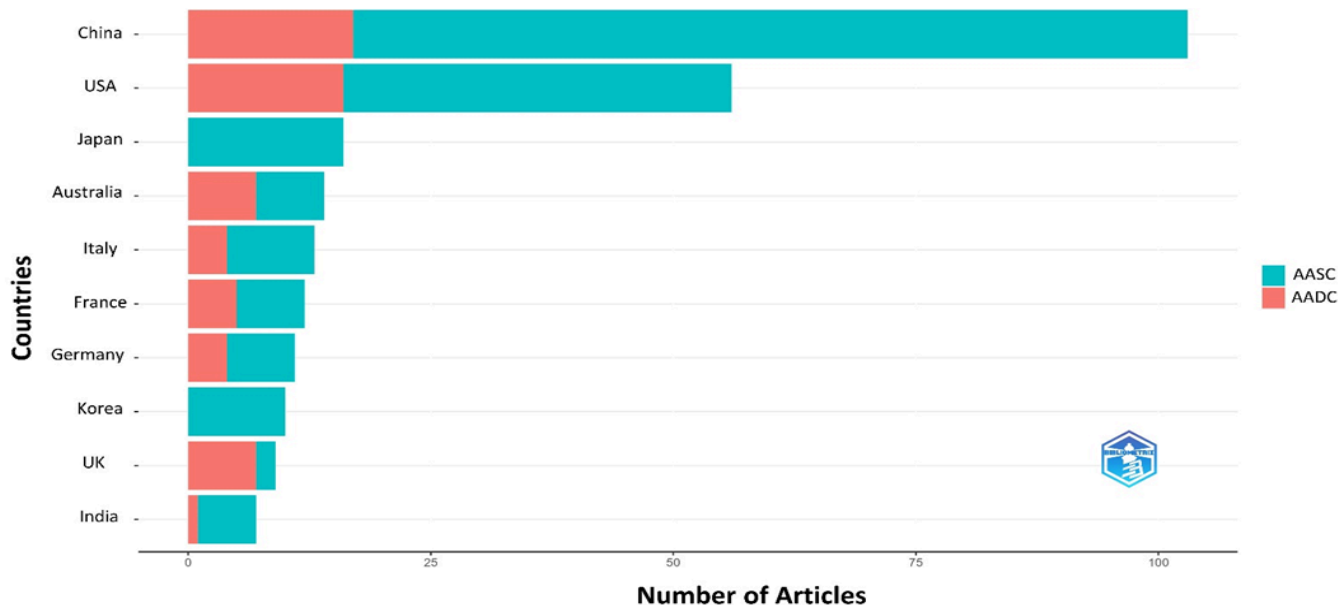


Source: WeB of Science™.

Consequently, when evaluating collaboration among countries according to the corresponding

author (Figure 7), it became evident that most were carried out between authors from the same country.

Figure 7 - Country collaboration according to the corresponding author's affiliation.



Legend: AASC: Article with Authors from a Single Country and AADC: Article with Authors from Different Countries.

Source: WeB of Science™.

The 333 articles were cited 8,964 times, averaging 26.9 citations per article. Consequently, the top 10 cited articles ranged from 1,382 to 139

citations, published in seven different scientific journals from 2014 to 2018, as shown in Table 1.

Table 1 - Ranking of the most cited articles related to hepatitis B prevention.

Ranking	Author (Year), Scientific Journal	Title	Total Citations (TC)
1	Terrault NA <i>et al.</i> (2018), Hepatology ²	Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance	1.382
2	Polaris Observatory Collaborators (2018), Lancet Gastroenterol Hepatol ¹⁵	Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study	834
3	Schillie S. <i>et al.</i> (2018), MMWR Recomm Rep ¹⁶	Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices	426
4	Reddy KR <i>et al.</i> (2015), Gastroenterology ¹⁷	American Gastroenterological Association Institute Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy	419
5	Pan CQ <i>et al.</i> (2016), N Engl J Med ¹⁸	Tenofovir to Prevent Hepatitis B Transmission in Mothers with High Viral Load	372
6	Perrillo RP <i>et al.</i> (2015), Gastroenterology ¹⁹	American Gastroenterological Association Institute Technical Review on Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy	362
7	Cui F <i>et al.</i> (2017), Emerg Infect Dis ²⁰	Prevention of Chronic Hepatitis B after 3 Decades of Escalating Vaccination Policy, China	203
8	Jourdain G <i>et al.</i> (2018), N Engl J Med ²¹	Tenofovir versus Placebo to Prevent Perinatal Transmission of Hepatitis B	194
9	Chang MH <i>et al.</i> (2016), Gastroenterology ²²	Long-term Effects of Hepatitis B Immunization of Infants in Preventing Liver Cancer	141
10	Huang H <i>et al.</i> (2014), JAMA ²³	Entecavir vs Lamivudine for Prevention of Hepatitis B Virus Reactivation Among Patients With Untreated Diffuse Large B-Cell Lymphoma Receiving R-CHOP Chemotherapy A Randomized Clinical Trial	139

Source: WeB of Science™.

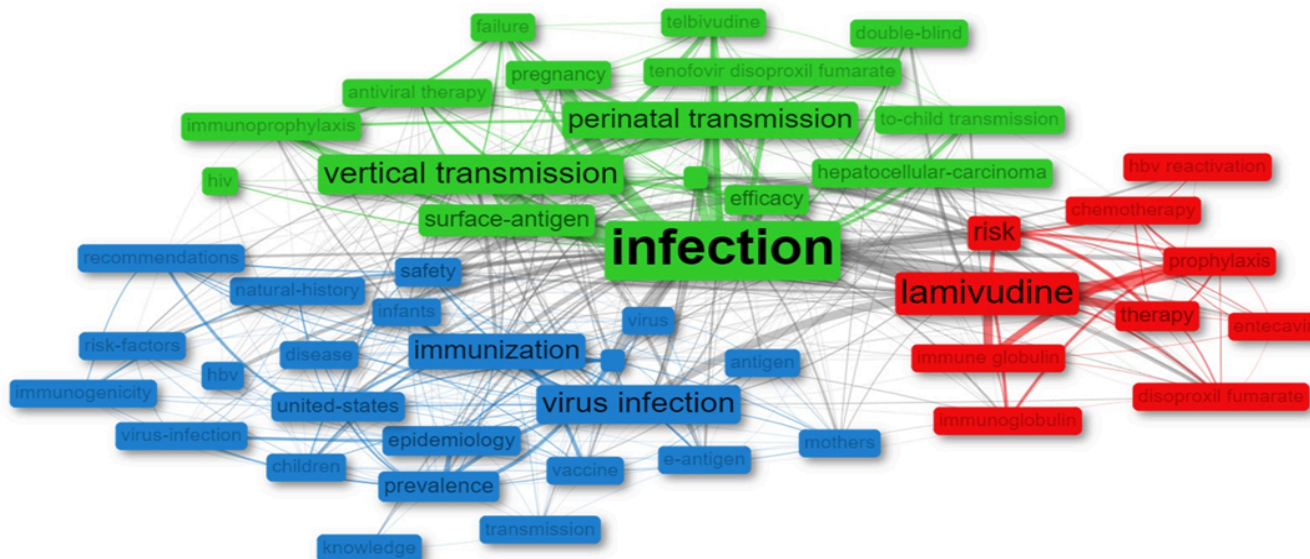
To elucidate the conceptual structure of the articles, the 50 most frequent KeyWords Plus™ were used to create Figure 8 (Automatic Network

Distribution, Walktrap clustering algorithm, adopting the box as node format). Thus, by observing the figure, it is possible to identify the formation of three

sets, demonstrating different focuses regarding hepatitis B prevention, with terms referring to infection and its transmission modes such as

vertical/perinatal (green); immunization against infection (blue); and treatment using antiretrovirals (red).

Figure 8 - Conceptual structure of articles related to hepatitis B prevention.



Source: WeB of Science™.

DISCUSSION

Considering the results of the present study, there was an observed increase in the number of articles related to the topic, notably starting in 2018. This can be explained by the publication of the "Update on Prevention, diagnosis, and Treatment of chronic hepatitis B" by the American Association for the Study of Liver Diseases (AASLD) in that year, which updated the AASLD 2016 Practical Guidelines for the Treatment of Chronic Hepatitis B and previous guidelines on HBV from 2009.^{2,24}

Additionally, this 2018 publication stood out as the most cited. This can be attributed to its updates on hepatitis B treatment (particularly the use of Tenofovir Alafenamide); guidance on screening, counseling, and prevention; specialized virological and serological testing; monitoring of untreated patients; and treatment of hepatitis B in special populations.²

Subsequently, publications were identified primarily in scientific journals focused on infectious diseases and medical virology (BMC Infectious

Diseases, Clinical Infectious Diseases, Journal of Medical Virology, and Journal of Viral Hepatitis) and scientific journals focused on hepatology and liver diseases (Hepatology, Clinics in Liver Disease, and Transplantation Proceedings). Other types of scientific journals included those focused on public health and epidemiology (BMC Public Health), general and multidisciplinary medicine (Cureus Journal of Medical Science and PLOS ONE), and immunization (Vaccine).

When considering the main authors over time, Jie Li and Fuzhen Wang stood out, with their latest articles respectively addressing a management algorithm for preventing vertical transmission of the hepatitis B virus and prophylaxis with Tenofovir to prevent mother-to-child transmission of the hepatitis B virus.²⁵⁻²⁶

Following with the authors, Jie Chein, Xiao-Feng Liang, and Trudy V. Murphy. These authors, in their recent works, published respectively on the Efficacy of the hepatitis B vaccine alone in preventing perinatal transmission of hepatitis B in babies born to

mothers with hepatitis B and negative antigen; Tenofovir prophylaxis to prevent mother-to-child transmission of the hepatitis B virus and Tenofovir exposure during pregnancy and postpartum in women receiving Tenofovir Disoproxil Fumarate for the prevention of mother-to-child transmission of the hepatitis B virus.²⁷⁻²⁹

Regarding institutions, these were primarily located in China (Sun Yat-sen University, Peking University; National Taiwan University, Nanjing University, and Capital Medical University); France (*Assistance Publique Hopitaux Paris, Institut National de la Santé et de la Recherche Médicale, Université Paris Cité, and Udice - French Research Universities*); and in United States (Centers for Disease Control and Prevention and Harvard University).

Consequently, China also stood out by being present in the affiliation of most authors, often even in the corresponding author's affiliation, demonstrating the intense pursuit of hepatitis B prevention by this country. This finding is possibly related to China's relationship with the World Health Organization (WHO), which established a global strategy, approved by all Member States, to reduce new hepatitis infections by 90% and deaths by 65% between 2016 and 2030.³⁰

Regarding the most cited articles, these covered updates and guidance on hepatitis B, regarding prevention, diagnosis, and treatment, also including guidance in case of hepatitis B virus reactivation during immunosuppressive drug therapy; epidemiology and modeling of hepatitis B; guidelines and recommendations in the United States; prophylaxis and prevention of perinatal transmission; vaccination policies in China; long-term impact of immunization; and prevention of HBV reactivation in cancer patients.²³

Thus, it is evident that these findings align with the three main research focuses. The first set (green) addressed transmission, mainly vertical and perinatal. More specifically, the studies addressed the relevance of surface antigen in assessing immune

protection efficacy; the importance of interventions, such as antiviral therapy, notably with Tenofovir Disoproxil Fumarate; the association of chronic HBV infection with hepatocellular carcinoma development, as well as therapy for mother-to-child transmission prevention and co-infection with Human Immunodeficiency Virus (HIV).

Moreover, the second set (blue) focused on the importance of vaccination and immunization in preventing the spread of HBV. Furthermore, it showed that comprehensive epidemiological investigation is also needed in immunization studies, such as investigation of infection prevalence, knowledge of HBV's natural history, risk factors, and safety practices, also focusing on immunization of infants and mothers.

Lastly, the third set (red) addressed HBV management by implementing antiviral therapy, using Lamivudine, Entecavir, and Tenofovir Disoproxil Fumarate, effective for chronic hepatitis B treatment. Furthermore, its terms refer to the need for HBV reactivation risk minimization, incorporating prophylactic therapies, such as administering Anti-Hepatitis B Immunoglobulin (by protocols), and considering specific conditions, such as patients on chemotherapy and immunosuppressive therapy.

To note, reducing mortality from HBV-infected individuals can be achieved through vaccination, diagnostic testing, medications, and educational campaigns. However, there is a clear need for new studies related to educational interventions, such as creating, applying, and testing educational technologies. Therefore, investing in research dedicated to health education assessment is imperative to optimize current preventive strategies and develop innovative and adaptable approaches that effectively meet the needs of hepatitis B prevention in diverse populations and contexts.³¹

CONCLUSION

Three hundred thirty-three articles were analyzed, predominantly published in 2018 and 2019,

and distributed across 215 distinct scientific journals. Notably, the Journal of Viral Hepatitis, Vaccine, and PLOS ONE stood out as the main publication outlets in the field. These articles were authored by 2467 authors, with Li Jie standing out by contributing nine articles. The authors' affiliations demonstrated a diversity of 810 institutions, with Udice - French Research Universities prominently featured. Among the 81 identified countries, China featured prominently and frequently cited in authors' affiliations, including those of corresponding authors.

Articles related to hepatitis B prevention accumulated a total of 8,964 citations. The most referenced publications covered updates and guidance on hepatitis B comprehensively and in cases of hepatitis B virus reactivation during

immunosuppressive drug therapy, as well as hepatitis B epidemiology and modeling, guidelines in the United States, prophylaxis, and prevention of perinatal transmission, vaccination policies in China, long-term impacts of immunization, and prevention of HBV reactivation in cancer patients.

The most frequent KeyWords Plus™ highlighted the diversity of approaches in hepatitis B prevention research, encompassing infection and its transmission routes, notably vertical/perinatal transmission, immunization against infection, and antiretroviral treatment. However, there was an identified urgent need for new studies focused on educational interventions, including the creation, implementation, and evaluation of educational technologies.

RESUMO

Introdução: A Organização Mundial da Saúde estima que a infecção crônica pelo Vírus da Hepatite B afeta globalmente entre 296 milhões de indivíduos, com 1,5 milhões de novas infecções por ano. Os afetados frequentemente permanecem assintomáticos por longos períodos, mas podem inadvertidamente transmitir o Vírus da Hepatite B para outras pessoas. **Objetivo:** analisar as publicações científicas relacionadas à prevenção da hepatite B no período de 2013-2023. **Delineamento:** Estudo bibliométrico com abordagem quantitativa de 333 artigos utilizando-se o pacote *Bibliometrix R* e sua interface web *Biblioshiny*. **Resultados:** Os artigos foram publicados principalmente em 2018 e 2019, o *Journal of Viral Hepatitis* foi o principal jornal científico. Esses artigos foram elaborados por 2467 autores, de 81 instituições, com destaque para a *Udice - French Research Universities*. Entre os 81 países identificados, a China figurou proeminente. Os artigos acumularam o total de 8.964 citações. As KeyWords Plus™ evidenciaram o enfoque na infecção e suas vias de transmissão, notadamente a vertical/perinatal, na imunização contra a infecção e no tratamento utilizando antirretrovirais. **Implicações:** Foi identificada a necessidade de novos estudos voltados para intervenções educativas relacionadas à prevenção da hepatite B, incluindo a criação, aplicação e avaliação de tecnologias educativas.

DESCRITORES

Hepatite B; Transmissão Vertical de Doenças Infecciosas; Infecções Sexualmente Transmissíveis; Controle de Doenças Transmissíveis.

RESUMEN

Introducción: La Organización Mundial de la Salud estima que la infección crónica por el Virus de la Hepatitis B afecta globalmente a alrededor de 296 millones de individuos, con 1,5 millones de nuevas infecciones por año. Los afectados suelen permanecer asintomáticos durante largos períodos, pero pueden transmitir inadvertidamente el Virus de la hepatitis B a otras personas. **Objetivo:** analizar las publicaciones científicas relacionadas con la prevención de la hepatitis B en el período de 2013-2023. **Delineación:** Estudio bibliométrico con enfoque cuantitativo de 333 artículos utilizando el paquete *Bibliometrix R* y su interfaz web *Biblioshiny*. **Resultados:** Los artículos fueron publicados principalmente en 2018 y 2019, siendo el *Journal of Viral Hepatitis* la principal revista científica. Estos artículos fueron elaborados por 2467 autores, de 81 instituciones, con destacada participación de la *Udice - French Research Universities*. Entre los 81 países identificados, China figuró de manera prominente. Los artículos acumularon un total de 8,964 citas. Las KeyWords Plus™ evidenciaron un enfoque en la infección y sus vías de transmisión, especialmente la vertical/perinatal, así como en la inmunización contra la infección y en el tratamiento con antirretrovirales. **Implicaciones:** Se identificó la necesidad de nuevos estudios centrados en intervenciones educativas relacionadas con la prevención de la hepatitis B, incluyendo la creación, aplicación y evaluación de tecnologías educativas.

DESCRIPTORES

Hepatitis B; Transmisión Vertical de Enfermedad Infecciosa; Enfermedades de Transmisión Sexual; Control de Enfermedades Transmisibles.

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