Paradigm Academic Press
Journal of Innovations in Medical Research
ISSN 2788-7022
JUN. 2023 VOL.2, NO.6

Bibliometric Analysis of Vitamin D and Non-Alcoholic Fatty Liver Disease

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doi:10.56397/JIMR/2023.06.07

Abstract

Background: The relationship between vitamin D and non-alcoholic fatty liver disease (NAFLD) has been a subject of significant interest. This study aimed to assess the current research status of vitamin D and NAFLD through a systematic analysis using bibliometric methods. ***Methods:*** A search of the Web of Science Core Collection database was conducted to identify relevant literature meeting the study criteria. Key information such as the number of publications, authors, countries, and keywords was extracted. ***Results:*** A total of 416 articles were included for analysis. The findings revealed an increasing trend in research on vitamin D and NAFLD in recent years. The dominant forces in the field were concentrated in China and the United States. A few institutions contributed to the majority of the research output, and the research topics primarily covered the association between vitamin D and NAFLD in terms of disease risk, severity, and treatment efficacy. ***Conclusion:*** The bibliometric analysis of the literature in this study provided insights into the current status and trends of research on vitamin D and NAFLD. These findings are of significant importance in guiding future research directions and collaborations, offering new perspectives and strategies for the prevention and treatment of NAFLD. Further research should delve into the mechanisms underlying the association between vitamin D and NAFLD, and more clinical trials should be conducted to evaluate the potential role of vitamin D in the treatment of NAFLD.

Keywords: NAFLD, vitamin D, bibliometric, VOSviewer

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a rapidly increasing metabolic disorder worldwide, characterized by excessive accumulation of fat in the liver without a significant history of alcohol consumption, affecting approximately 24% of the global population (Jiang X, Hu R, Huang Y, et al, 2023). With the rising prevalence of obesity, type 2 diabetes, and metabolic syndrome, NAFLD has emerged as a significant concern in clinical and public health domains (Ciccarelli G, Di Giuseppe G, Cinti F, Moffa S, Mezza T & Giaccari A, 2023). Although NAFLD is generally considered a benign condition, it can progress to non-alcoholic steatohepatitis (NASH), liver fibrosis, cirrhosis, and hepatocellular carcinoma, among other serious consequences. Therefore, gaining a comprehensive understanding of the pathophysiological mechanisms underlying NAFLD and identifying novel preventive and therapeutic strategies is of paramount importance.

In recent years, vitamin D, as a fat-soluble vitamin, has gained significant attention. Apart from its crucial role in maintaining bone health, vitamin D is involved in regulating various physiological processes such as immunity, inflammatory response, cell proliferation, and apoptosis (Sohouli MH, Wang S, Almuqayyid F, et al, 2023;

Karras SN, Wagner CL & Castracane VD, 2018; Kwok RM, Torres DM & Harrison SA, 2013). Consequently, researchers have started to focus on the relationship between vitamin D and metabolic disorders, including the association between vitamin D and NAFLD (Zhang Z, Moon R, Thorne JL & Moore JB, 2023). The exact nature of the relationship between vitamin D and NAFLD is not fully understood. Some studies have found that vitamin D levels are generally lower in NAFLD patients, and vitamin D deficiency is negatively correlated with the occurrence and severity of NAFLD (Kwok RM, Torres DM & Harrison SA, 2013). This association may involve the regulatory effects of vitamin D on aspects such as fat metabolism, inflammatory response, and fibrosis.

Bibliometrics is a quantitative analysis method used to evaluate scientific literature. By collecting, organizing, and analyzing a large volume of literature data, it allows for the assessment of research trends, key contributors, publishing journals, and countries/regions within a specific field. In this study, we will employ bibliometric methods to assess the development of research on the relationship between vitamin D and NAFLD. By analyzing indicators such as the quantity of literature, citation frequency, and collaboration networks, we aim to gain a comprehensive understanding of the research dynamics in this field.

2. Methods

The literature search was conducted using the Web of Science Core Collection database. The search query was formulated as TS=("vitamin D") and TS= (NAFLD OR "Nonalcoholic Fatty Liver*"). To ensure the database's currency, the search was completed as of June 16, 2023. A total of 467 articles were retrieved from the search results, excluding three non-English articles. Only articles and reviews were included, resulting in a final selection of 416 articles relevant to the association between vitamin D and NAFLD. Literature retrieval is shown in Figure 1. The retrieved articles were exported in plain text format and imported into Excel 2019 and VOSviewer software. Excel 2019 was used to generate a graph depicting the annual publication output, while VOSviewer was employed to visualize the collaboration network.

Figure 1. Documents retrieval flow chart

3. Results

A total of 416 articles related to the research on vitamin D and NAFLD were identified. Figure 2 presents the

overall publication trend, showing an increasing trend in research on vitamin D and NAFLD from 2005 to 2023. During the period from 2005 to 2011, the research output was relatively slow, with an annual publication volume of fewer than five articles. However, since 2011, the publication output has experienced rapid growth, reaching a peak of 57 articles in 2021. Similarly, the citation count for the research from 2005 to 2011 remained low, but it started to rise after 2011. These results indicate that research on the association between vitamin D and NAFLD has garnered substantial attention and interest within the academic community from 2005 to 2023.

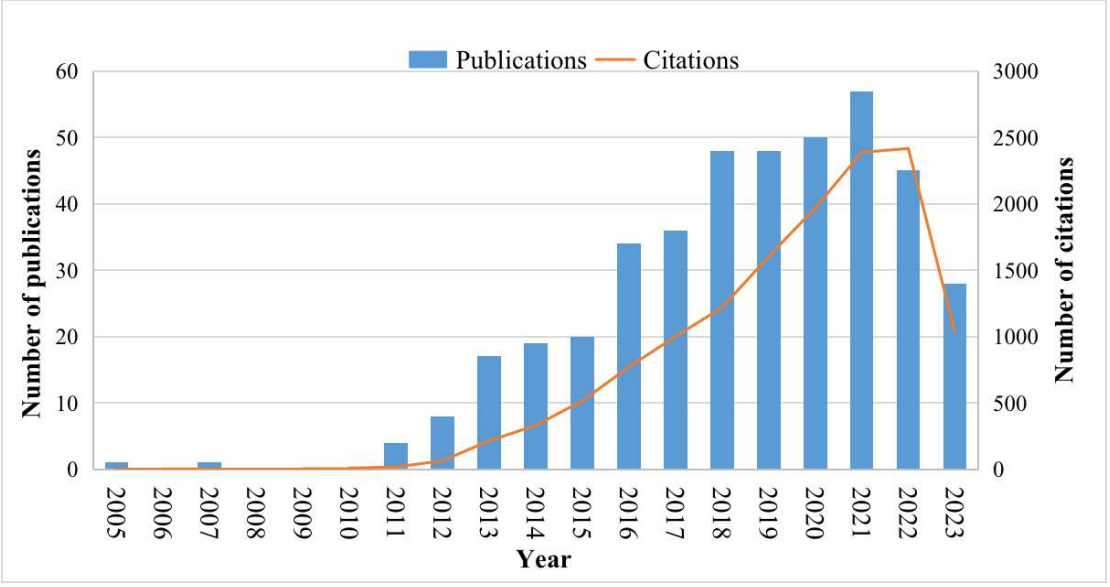
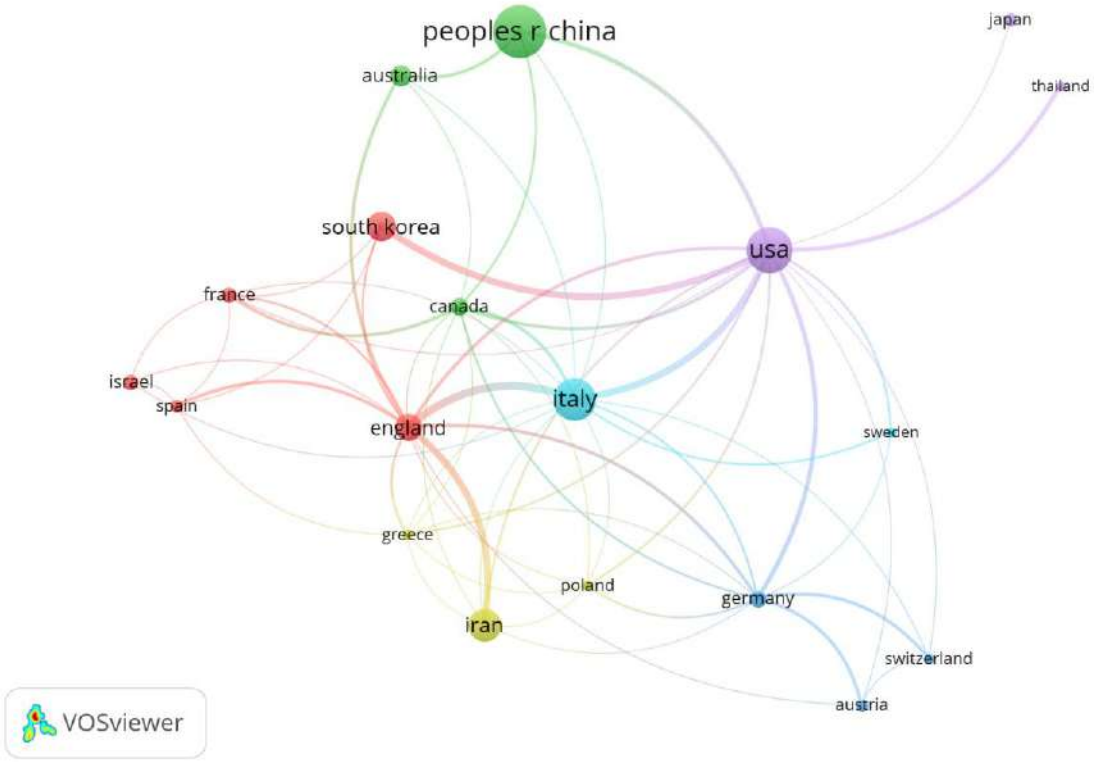


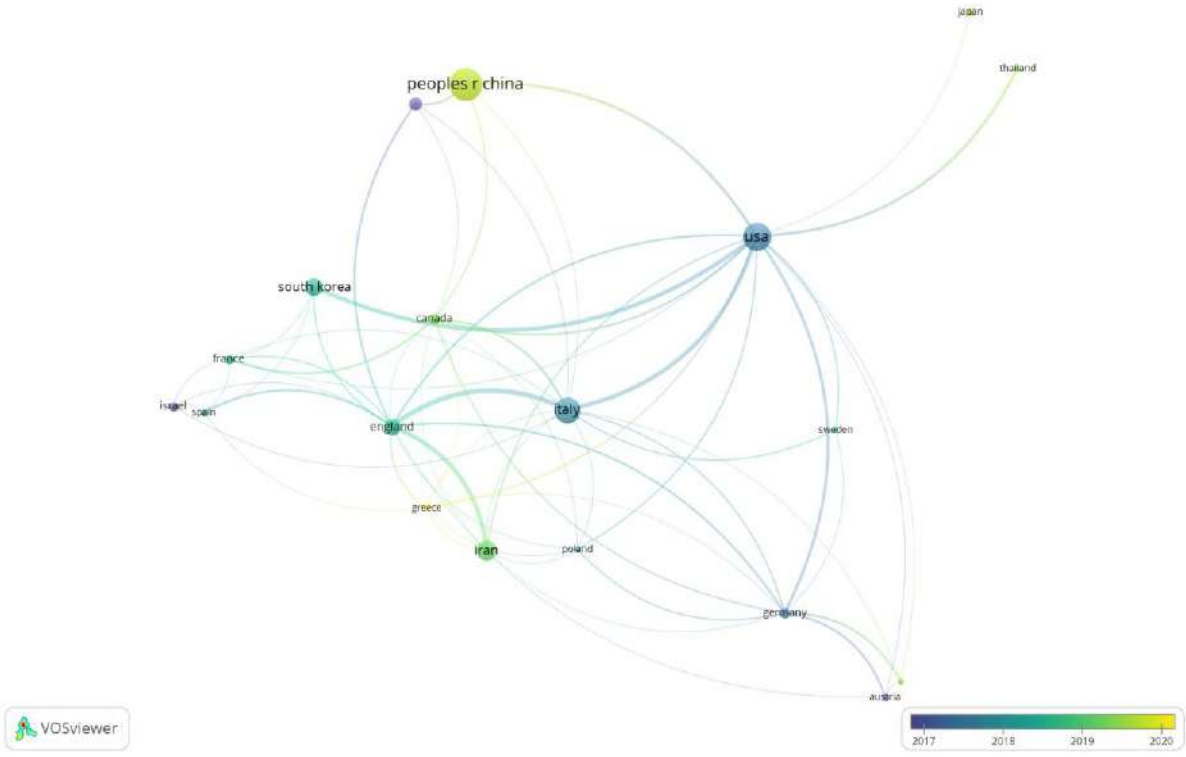
Figure 2. The annual number of publications and citations related to vitamin D and NAFLD

3.1 Country/Region Analysis

A total of 51 countries/regions were involved in research related to vitamin D and NAFLD. The top three countries in terms of publication output were China (86), the United States (67), and Italy (60). In terms of citations, the top three countries were the United States (4042), Italy (3587), and England (1787). China, the country with the highest publication output, ranked fourth in terms of citations with 1437. Figure 3A displays the collaborative relationships among countries, with China having close collaborations with the United States, Australia, Canada, and Italy, while the United States has close collaborations with Korea, England, and Italy. As shown in Figure 3B, Australia and Israel have an earlier average publication time, while China and Greece have a later average publication time. This suggests that although China ranks first in terms of publication output in vitamin D and NAFLD research, its citation count may be a factor that prevents it from entering the top three. Therefore, China can be considered a core country in vitamin D and NAFLD research.



(**A**) Cooperation networks across countries

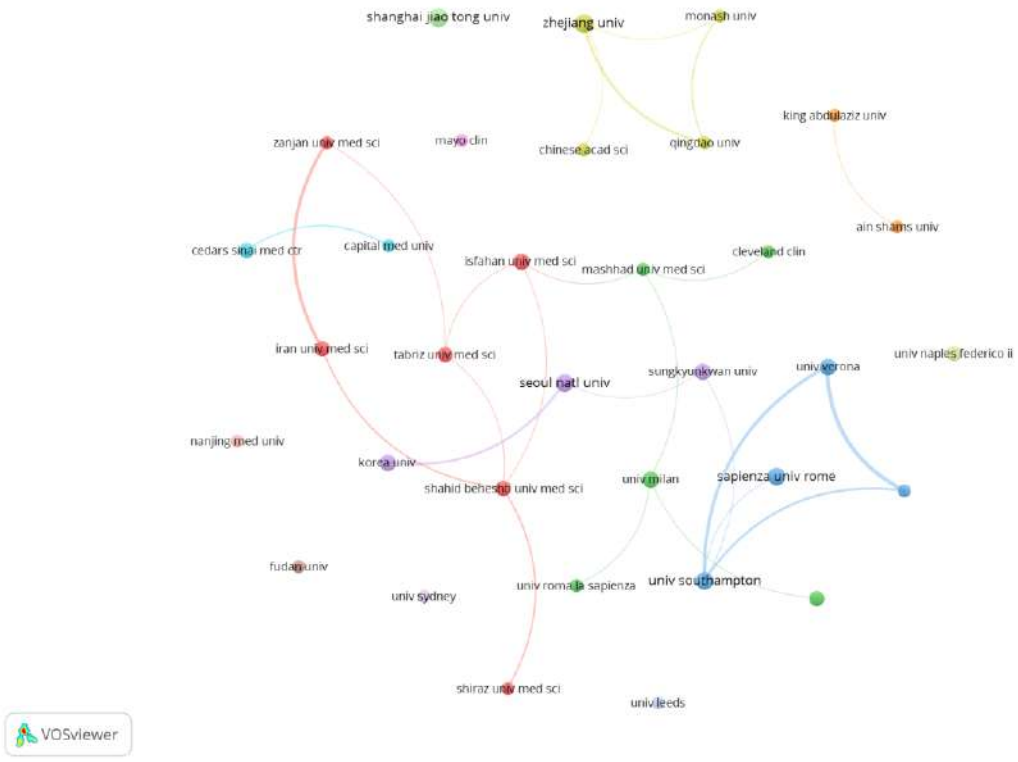


(**B**) Overlay Visualization of countries

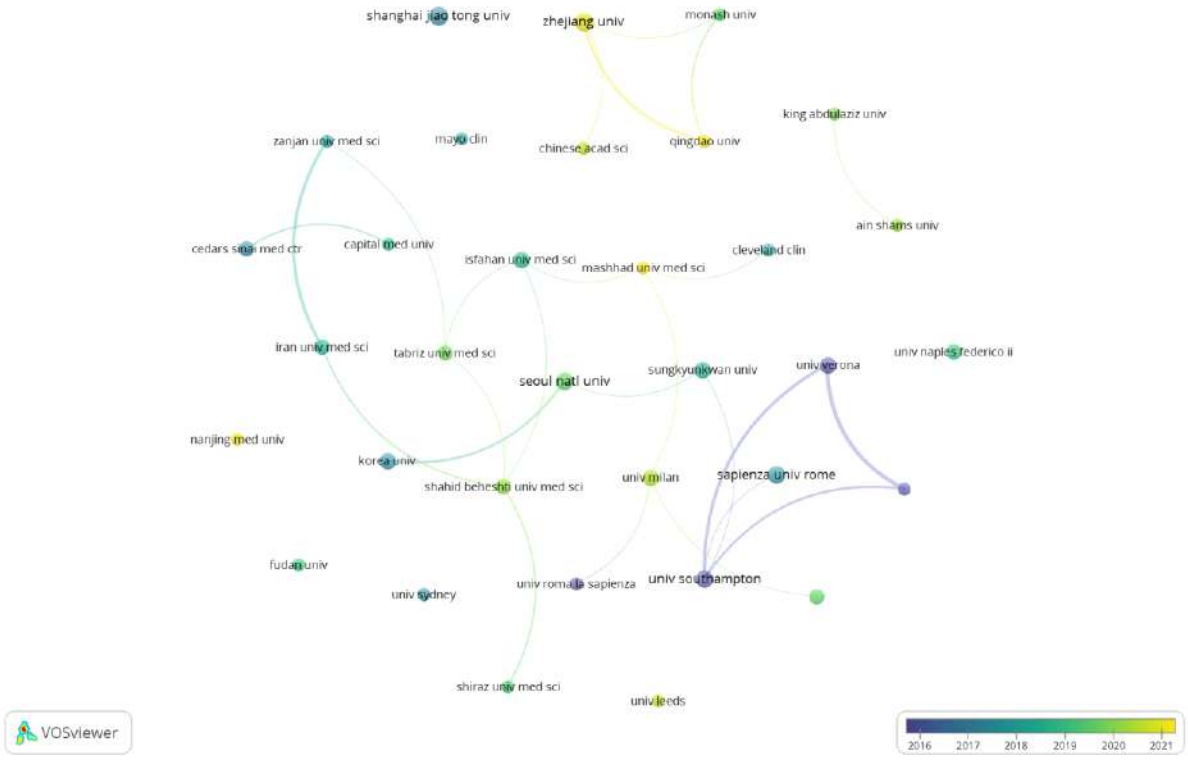
Figure 3. Co-authorship analysis of countries

3.2 Institution Analysis

A total of 743 institutions participated in research related to vitamin D and NAFLD. The top three institutions in terms of publication output were Shanghai Jiao Tong University (9), Zhejiang University (9), and University of Southampton (8). In terms of citations, the top three institutions were University of Verona (722), University of Modena & Reggio Emilia (648), and University of Southampton (8). Figure 4A illustrates the collaboration relationships among institutions, indicating that collaborations between institutions are generally loose and predominantly occur within their own countries. The overlay map of institutions in Figure 4B reveals that Zhejiang University and Qingdao University have a later average publication time compared to University of Southampton and University of Verona, which have an earlier average publication time. Publication time may influence the citation count of institutions. Therefore, Shanghai Jiao Tong University can be considered a core institution in vitamin D and NAFLD research.



(**A**) Cooperation networks across institutions

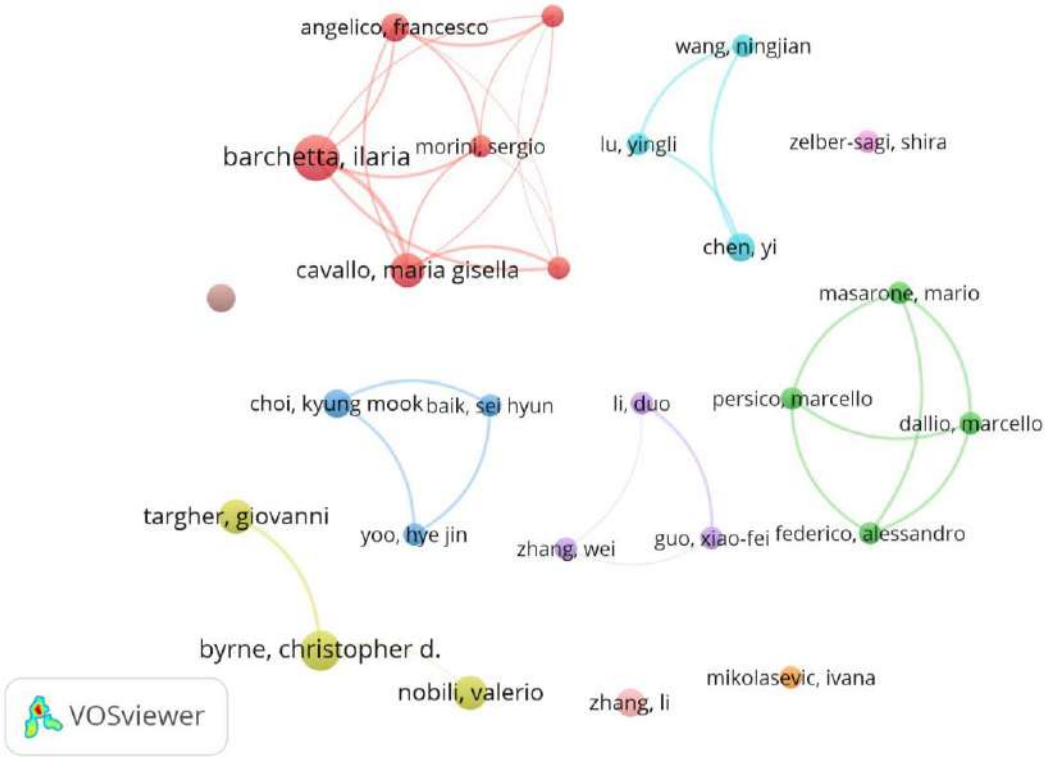


(**B**) Overlay Visualization of institutions

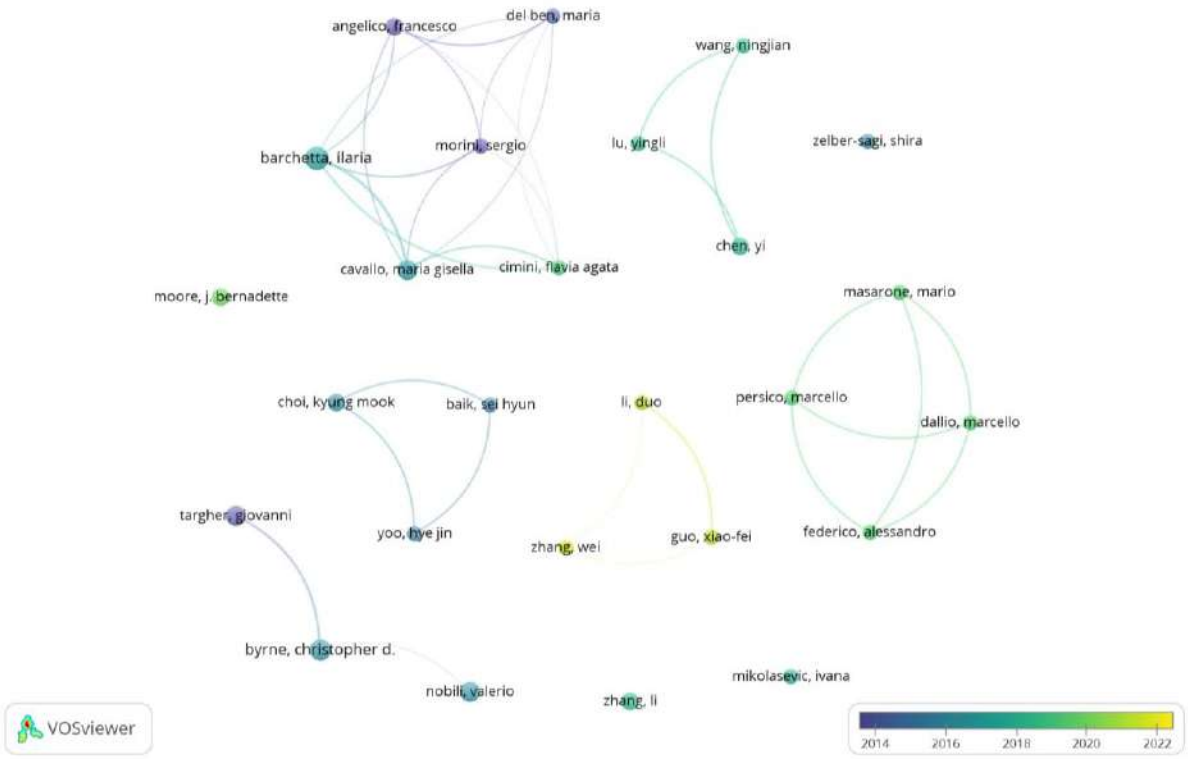
Figure 4. Co-authorship analysis of institutions

3.3 Author Analysis

A total of 2397 authors participated in research related to vitamin D and NAFLD. The top three authors in terms of publication output were Barchetta, Ilaria (8), Byrne, Christopher D (7), and Cavallo, Maria Gisella (6), Targher, Giovanni (6). In terms of citations, the top three authors were Targher, Giovanni (937), Byrne, Christopher (685), and Barchetta, Ilaria (676). Figure 5A illustrates the collaboration relationships among authors, showing that collaborations between authors from the same country are relatively close, while collaborations across regions are less common. The overlay map of authors in Figure 5B reveals that Targher, Giovanni and Byrne, Christopher have an earlier average publication time, while Duo, Li and Wei, Zhang have a later collaboration time. Therefore, Barchetta, Ilaria can be considered a core author in vitamin D and NAFLD research.



(**A**) Cooperation networks across authors



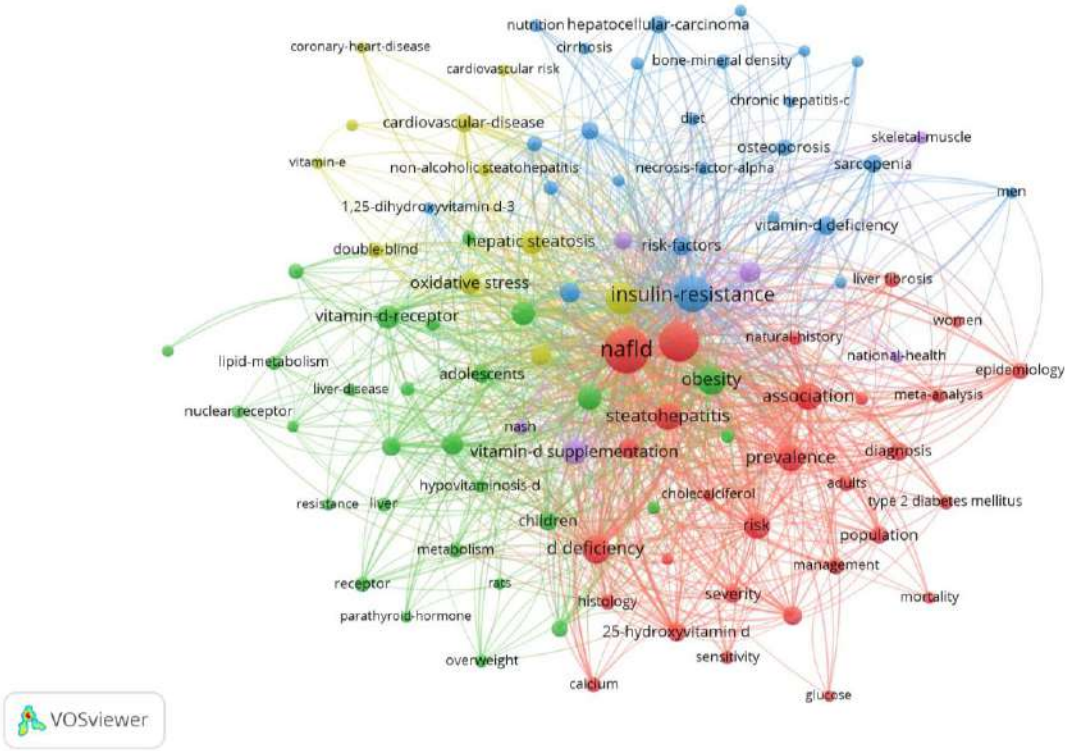
(**B**) Overlay Visualization of authors

Figure 5. Co-authorship analysis of authors

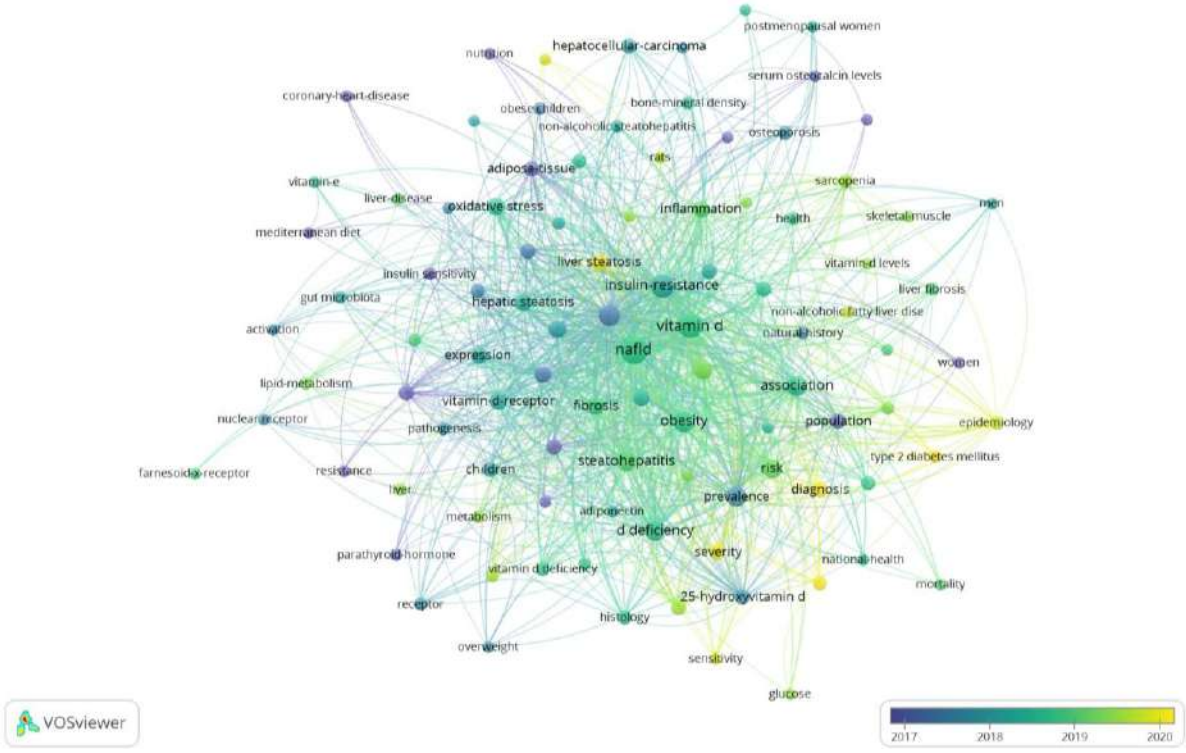
3.4 Keyword Analysis

A total of 1703 keywords were generated from research related to vitamin D and NAFLD. The top 10 keywords were NAFLD, Vitamin D, Insulin-resistance, metabolic-syndrome, obesity, D-deficiency, Association,

steatohepatitis, Prevalence, Risk. Figure 6A displays a keyword clustering map, categorizing the keywords into five clusters: green, purple, red, blue, and yellow. The research topics primarily covered the association between vitamin D and non-alcoholic fatty liver disease (NAFLD) in terms of disease risk, severity, and treatment efficacy. Figure 6B is an overlay map of keywords, where the yellow nodes represent more recent occurrences. Therefore, liver steatosis is the latest research hotspot in vitamin D and NAFLD-related studies.



(**A**) Cooperation networks across keywords



(**B**) Overlay Visualization of keywords

Figure 6. Co-authorship analysis of keywords

4. Discussion

This study conducted a bibliometric analysis of research on the relationship between vitamin D and NAFLD to understand the development trends and research hotspots in this field. The findings reveal a significant and vigorous growth in research on vitamin D and NAFLD over the past two decades, particularly with a noticeable increase in research interest since 2011. It is evident that China and institutions from China have a relatively high publication output, although their advantage is not particularly prominent. Countries like the United States have traditionally held influence in this area due to their earlier contributions. However, considering China's growing focus on and investment in research related to vitamin D and NAFLD, it is reasonable to expect that China will also establish a competitive position in this field in the future. Additionally, Byrne, Christopher has an earlier average publication time, and both the publication output and citations of Byrne, Christopher D rank highly. Therefore, taking all factors into consideration, Barchetta, Ilaria appears to be a top author in research related to vitamin D and NAFLD. In terms of keyword analysis, previous studies have primarily focused on exploring the relationship between vitamin D and NAFLD, including epidemiological investigations and mechanistic research.

4.1 Hotspot and Frontier Analysis

4.1.1 The Link Between Vitamin D and Liver Steatosis

The relationship between vitamin D and liver steatosis is a current hot topic in research and represents a frontier area of investigation. Liver steatosis, also known as fatty liver, is a common liver disease characterized by abnormal accumulation of fat in liver tissue. While the exact nature of the relationship between vitamin D and liver steatosis is not yet fully understood, there is evidence suggesting an association between the two. Population-based studies have found a positive correlation between low vitamin D levels and non-alcoholic fatty liver disease (NAFLD) (Liu SY, Liu YX, Wan B, et al, 2019), indicating that individuals with lower vitamin D levels are more prone to developing NAFLD. Additionally, studies as early as 2011 have demonstrated that mice lacking the vitamin D receptor develop liver steatosis (Zuniga S, Firriencieli D, Wendum D, et al, 2011), suggesting a potential role of vitamin D in liver fat metabolism. Furthermore, liver vitamin D receptor (VDR) expression is increased in alcoholic fatty liver disease (AFLD) patients, which is essential for the development of liver steatosis in NAFLD mouse models (Garcia-Monzon C, Petrov PD, Rey E, et al, 2018), highlighting the importance of VDR in liver fat metabolism. The gut serves as a major regulator of vitamin D and VDR activity, exerting significant influence on systemic lipid balance. Consequently, vitamin D deficiency is often observed in patients with fatty liver disease (Jahn D, Dorbath D, Schilling A-K, et al, 2019). In a clinical context, some studies have indicated that vitamin D supplementation can improve the severity of fat accumulation and fibrosis in patients with non-alcoholic fatty liver disease, contributing to the prevention of fibrosis progression (Taghvaei T, Akha O, Mouodi M, et al, 2018). These findings suggest a potential positive role of vitamin D in the treatment and prevention of NAFLD. In summary, while the exact mechanisms underlying the relationship between vitamin D and liver steatosis remain unclear, existing research supports an association between low vitamin D levels and liver fat accumulation, with vitamin D supplementation potentially improving the condition of NAFLD patients. Therefore, the relationship between vitamin D and liver steatosis is poised to be a key focus of future research. With further in-depth investigation into the association between vitamin D and liver steatosis, the following areas of exploration can be expected: mechanistic studies, where researchers will delve into the detailed mechanisms underlying the interplay between vitamin D and liver fat metabolism, investigating how vitamin D regulates processes such as fatty acid synthesis, oxidation, and transport in the liver through the vitamin D receptor (VDR); population-based studies, encompassing large-scale research to further validate the association between vitamin D and liver steatosis, as well as determine the correlation between vitamin D levels and different subtypes of fatty liver; clinical trials, aiming to assess the therapeutic effects of vitamin D supplementation on fatty liver patients, investigating the impact of vitamin D supplementation on the degree of liver steatosis, liver function indicators, liver fibrosis severity, and inflammation levels; and molecular targeted therapies, such as the development of molecular targeted treatment approaches focusing on vitamin D metabolism and signaling pathways. These may involve modulating VDR activity or intervening in vitamin D metabolism through alternative means to prevent or reverse liver steatosis. In conclusion, the relationship between vitamin D and liver steatosis will continue to be a hot topic of research. Further investigations will contribute to revealing the underlying mechanisms of this association, providing new insights and strategies for the treatment and prevention of fatty liver disease.

5. Conclusion

This study provides valuable insights into the trends and current state of research on the relationship between vitamin D and non-alcoholic fatty liver disease (NAFLD). The findings reveal key authors, countries, and research topics within this field, contributing to a comprehensive understanding of the subject and guiding future research directions and collaborations. Future studies will continue to explore the relationship between vitamin D and NAFLD from mechanistic, epidemiological, and therapeutic perspectives.

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