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## ABOUT COVER

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## AIMS AND SCOPE

The primary aim of *World Journal of Hepatology* (*WJH*, *World J Hepatol*) is to provide scholars and readers from various fields of hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

*WJH* mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

## INDEXING/ABSTRACTING

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SCIENTOMETRICS

# Research hotspots and trends in gut microbiota and nonalcoholic fatty liver disease: A bibliometric study

Cai-Yun Huang, Zhong-Zhi Luo, Wei-Ping Huang, Li-Ping Lin, You-Ting Yao, Han-Xu Zhuang, Qiu-Yong Xu, Ya-Dong Lai

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## Abstract

### *BACKGROUND*

Recent research indicates that the intestinal microbial community, known as the gut microbiota, may play a crucial role in the pathogenesis of nonalcoholic fatty liver disease (NAFLD). To understand this relationship, this study used a comprehensive bibliometric analysis to explore and analyze the currently little-known connection between gut microbiota and NAFLD, as well as new findings and possible future pathways in this field.

### *AIM*

To provide an in-depth analysis of the current focus issues and research developments on the interaction between gut microbiota and NAFLD.

### *METHODS*

In this study, all data were collected from the Web of Science Core Collection, and the related searches were completed on one day (February 21, 2024). The data were stored in plain text format to facilitate subsequent analysis. VOSviewer 1.6.20 and CiteSpace 6.1R6 Basic were used for knowledge graph construction and bibliometric analysis.

### *RESULTS*

The study included a total of 1256 articles published from 2013 to 2023, and the number of published papers demonstrated an upward trend, reaching a peak in

the last two years. The University of California, San Diego held the highest citation count, while Shanghai University of Traditional Chinese Medicine in China led in the number of published works. The journal "*Nutrients*" had the highest publication count, while "*Hepatology*" was the most frequently cited. South Korean author Suk Ki Tae was the most prolific researcher. The co-cited keyword cluster labels revealed ten major clusters, namely cortisol, endothelial dysfunction, carbohydrate metabolism, myocardial infarction, non-alcoholic steatohepatitis, lipotoxicity, glucagon-like peptide-1, non-islet dependent, ethnicity, and microRNA. Keyword outbreak analysis highlighted metabolic syndrome, hepatic steatosis, insulin resistance, hepatocellular carcinoma, cardiovascular disease, intestinal permeability, and intestinal bacterial overgrowth as prominent areas of intense research.

*CONCLUSION*

Through the quantitative analysis of relevant literature, the current research focus and direction of gut microbiota and NAFLD can be more clearly understood, which helps us better understand the pathogenesis of NAFLD, and also opens up innovative solutions and strategies for the treatment of NAFLD.

**Key Words:** Gut microbiota; Nonalcoholic fatty liver disease; Bibliometric; Knowledge maps; VOSviewer; Citespace



**Core Tip:** Gut microbiota and nonalcoholic fatty liver disease (NAFLD) have been increasingly linked through mounting evidence, prompting a comprehensive bibliometric analysis in this study, which aimed to examine the emerging research trends and focuses in the relationship between the two fields. Over the past ten years, there has been a substantial rise in studies exploring the connection between gut microbiota and NAFLD. These investigations mainly concentrate on the function of gut microbiota in the development and potential therapy of NAFLD. By shedding light on the pathogenesis of NAFLD, these studies not only augment our comprehension of the disease's origin but also furnish novel therapeutic strategies and insights.

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## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a prevalent hepatic disorder characterized by the excessive accumulation of abnormal lipids in the liver, exceeding 5% of the organ's total weight, in the absence of significant alcohol consumption [1]. NAFLD is intricately associated with obesity, type 2 diabetes, and metabolic syndrome, impacting approximately 25% of the global population and swiftly emerging as the most prevalent chronic liver disease worldwide[2,3]. Concurrently, the term "gut microbiota" denotes the intricate ecosystem of microorganisms inhabiting the human gut, such as bacteria, fungi, viruses, and other microscopic life forms. This ecosystem supports various physiological functions, such as fortifying intestinal integrity, facilitating nutrient extraction, defending against pathogens and regulating host immune responses[4]. The interplay between gut microbiota and NAFLD has been a subject of extensive research, revealing a significant association between the two. Given the intricate anatomical and physiological link between the liver and the intestine, substances and immune elements from the gut can reach the liver through the portal vein, participating in intricate liver functions. This communication pathway is often referred to as the gut-liver axis (GLA)[5]. The gut microbiota potentially influences the development of NAFLD through the GLA, chiefly by affecting nutrient assimilation. Altered intestinal mucosal integrity permits toxic elements to infiltrate the liver, escalating hepatic stress and inducing metabolic dysregulation, as per this interaction[6].

However, current research on the relationship between the gut microbiota and NAFLD remains nascent, with many unresolved questions and controversies. Bibliometric analysis can objectively identify relevant literature, provide a clear overview of the field's development, determine the current status, and offer insights into future advancements[7]. This type of analysis is extensively utilized in the domains of oncology, ophthalmology, complementary medicine, and alternative medicine, among others[8,9]. Although there has been some literature available as of 2021, the field of bibliometric studies exploring the connection between gut microbiota and NAFLD remains underexplored[10]. Due to the impact of coronavirus disease 2019, further updates are needed for bibliometric studies on this topic.

This study conducts an extensive bibliometric analysis of research articles published from 2013 to 2023, shedding light on the prevailing landscape, evolving patterns, and priority themes within the domain of gut microbiota and its relationship with NAFLD. The resulting insights aim to enlighten and inform upcoming research by elucidating intricate dynamics between gut microbiota and NAFLD, thus guiding future investigative endeavors in this field.

## MATERIALS AND METHODS

### *Inclusion and exclusion criteria*

The screening of publications adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) methodology[11]. To ensure focus, the inclusion criteria were limited to English-language articles specifically examining the connection between gut microbiota and NAFLD. Publications that did not pertain to this specific topic, such as non-English texts, retracted articles, letters, conference abstracts, and editorial content, were excluded from the selection.

The source of data for this study was the Web of Science Core Collection (WoSCC). The search parameters were defined as follows: Searching for articles or reviews published between January 1, 2013 and December 31, 2023, written in English, and containing any of the following keywords in the title or subject fields: (TI = "NAFLD" or "nonalcoholic fatty liver disease" or "non-alcoholic fatty liver disease" or "MAFLD" or "metabolic dysfunction-associated fatty liver disease" or "metabolic associated fatty liver disease") and (TS = "gut flora" or "gut microbiota" or "gut microbiome" or "gut microflora" or "gut bacteria" or "intestinal flora" or "intestinal microbiota" or "intestinal microbiome" or "intestinal microflora" or "intestinal bacteria").

### *Data screening*

Two independent reviewers evaluated articles using pre-established inclusion and exclusion criteria. When disagreements arose, a third reviewer was consulted to resolve discrepancies and reach a consensus. The search outcomes were saved as a plain text file named "download_*.txt," comprising fully documented and cited references.

### *Data analysis and tools*

Using VOSviewer 1.6.20, a bibliometric mapping and cluster analysis were performed to create a visual representation of a bibliometric network. In this visualization, nodes on the map symbolize distinct parameters, such as countries, institutions, journals, authors, and keywords, with their sizes scaled according to their frequency in published works. Connections between these nodes, depicted as straight lines, denote collaborative relationships. Through clustering, nodes sharing the same color signify common membership, hence reflecting a strong association between them, as per reference[12].

The bibliometric tool, CiteSpace can identify publication trends and hotspots, thereby facilitating the exploration of expertise within the field as well as emerging research topics[13]. Keyword citation bursts, references, double graphs, and timeline views were analyzed using CiteSpace 6.1R6 Basic software. Data statistics and tabulation were performed using Origin 2023.

## RESULTS

The search performed on 21 February 2024 yielded a total of 1502 potentially relevant records. The PRISMA 2020 guidelines were adhered to in the study selection process, which is depicted in Figure 1. Following a thorough screening, a comprehensive bibliometric analysis was conducted on an initial pool of 1256 studies that met the established inclusion criteria.

### *Trends in global publishing*

The data presented in Figure 2 demonstrate a consistent upward trajectory in publications pertaining to the correlation between gut microbiota and NAFLD, with a notable surge observed within the past two years. This observation implies an escalating interest among researchers regarding the intricate association between the gut microbiota and NAFLD.

### *Distribution of countries/regions in terms of article publication*

Table 1 outlines the top 15 countries that have explored the connection between gut microbiota and NAFLD in 64 countries. China dominates this research area with 549 publications (33.85%), reflecting the highest number of annual publications in the field. The United States stands as the second leading contributor with 224 papers (13.81%), followed by Italy, which has published 147 studies (9.06%). In terms of total citation count, the United States leads with the highest number of citations (15,261), followed by China (12409), Italy (9552), the United Kingdom (6470), and France (4763). The substantial number of citations signifies the exceptional quality, influence, and significance of these research outputs. Figure 3A illustrates that there are a total of thirty-six countries/regions contributing more than five publications each, while Figure 3B shows that seventeen countries/regions exceed the threshold of twenty published articles.

### *Analysis of institutions*

Ranked first among the world's 15 most productive research institutions, as detailed in Table 2, is Shanghai University of Traditional Chinese Medicine, with 35 papers published. Trailing closely behind are Shanghai Jiao Tong University with 34 papers, and the University of California, San Diego (UCSD) ranks third with 29 papers. Notably, UCSD leads in citations with an impressive 2372, followed by the University of Sydney at 1471 citations. The third most cited institution is Shanghai Jiao Tong University (1013), indicating the strong influence of these research institutions in the field. Of these institutions, nine are from China, indicating that more institutions in China are focusing on the study of gut microbiota and NAFLD. Figure 4 shows a map illustrating the worldwide distribution of institutions engaged in research pertaining

**Table 1 Top 15 high-output countries/regions in the field of gut microbiota and nonalcoholic fatty liver disease, from 2013 to 2023**

| Ranking | Country | Documents | Citations |
|---|---|---|---|
| 1 | China | 549 | 12409 |
| 2 | United States | 224 | 15261 |
| 3 | Italy | 147 | 9552 |
| 4 | United Kingdom | 57 | 6470 |
| 5 | Spain | 56 | 1852 |
| 6 | South Korea | 56 | 1728 |
| 7 | Germany | 54 | 2624 |
| 8 | Japan | 54 | 2191 |
| 9 | Canada | 41 | 2775 |
| 10 | France | 37 | 4763 |
| 11 | Iran | 37 | 1486 |
| 12 | Australia | 29 | 3366 |
| 13 | Austria | 24 | 2777 |
| 14 | Netherlands | 24 | 2003 |
| 15 | Poland | 24 | 341 |

**Table 2 Top 15 high-output institutions in the field of gut microbiota and nonalcoholic fatty liver disease, from 2013 to 2023**

| Ranking | Organization | Documents | Citations |
|---|---|---|---|
| 1 | Shanghai Univ Tradit Chinese Medicine | 35 | 762 |
| 2 | Shanghai Jiao Tong Univ | 34 | 1013 |
| 3 | Univ Calif, San Diego | 29 | 2372 |
| 4 | Zhejiang Univ | 24 | 704 |
| 5 | Chinese Acad Sci | 22 | 857 |
| 6 | Hallam Univ | 18 | 360 |
| 7 | Jinan Univ | 17 | 591 |
| 8 | Inst Salud Carlos Iii | 16 | 861 |
| 9 | Tongji Univ | 15 | 555 |
| 10 | Univ Sydney | 15 | 1471 |
| 11 | Univ Tehran Med Sci | 15 | 919 |
| 12 | Hua Zhong University Sci & Technol | 14 | 532 |
| 13 | Sun Yat Sen Univ | 14 | 945 |
| 14 | Zhejiang Chinese Med Univ | 14 | 143 |
| 15 | Univ Naples Federico Ii | 13 | 572 |

to the gut microbiota and NAFLD. A total of 1755 institutions participated in the study, and 150 institutions published more than 5 papers. The size of the nodes in Figure 4 symbolizes the quantity of research papers published by each institution.

### *Analysis of journals*

Table 3 highlights the top 15 key publications focusing on gut microbiota and NAFLD. Notably, "*Nutrients*" stands out as the most productive journal, accounting for 76 articles, trailed closely by "*International Journal of Molecular Sciences*" with 60 contributions. "*Frontiers in Microbiology*" and "*World Journal of Gastroenterology*" tied for third place, each having published 28 articles. In terms of citation impact, "*Hepatology*" led with an impressive 3817 citations, albeit having only 13 papers. "*World Journal of Gastroenterology*" ranked second in citation rates (2119 times), followed by "*Nutrients*" with 1890

**Table 3 Top 15 high-output journals in the field of gut microbiota and nonalcoholic fatty liver disease, from 2013 to 2023**

| Ranking | Source | Documents | Citations |
|---|---|---|---|
| 1 | *Nutrients* | 76 | 1890 |
| 2 | *International Journal of Molecular Sciences* | 60 | 1787 |
| 3 | *Frontiers in Microbiology* | 28 | 530 |
| 4 | *World Journal of Gastroenterology* | 28 | 2119 |
| 5 | *Food & Function* | 23 | 478 |
| 6 | *Frontiers in Pharmacology* | 20 | 372 |
| 7 | *Scientific Reports* | 20 | 1269 |
| 8 | *Frontiers in Nutrition* | 19 | 143 |
| 9 | *Frontiers In Endocrinology* | 18 | 215 |
| 10 | *Journal of Agricultural and Food Chemistry* | 18 | 449 |
| 11 | *Frontiers in Cellular and Infection Microbiology* | 17 | 166 |
| 12 | *Biomedicines* | 15 | 252 |
| 13 | *Frontiers In Immunology* | 13 | 154 |
| 14 | *Hepatology* | 13 | 3817 |
| 15 | *Foods* | 12 | 66 |

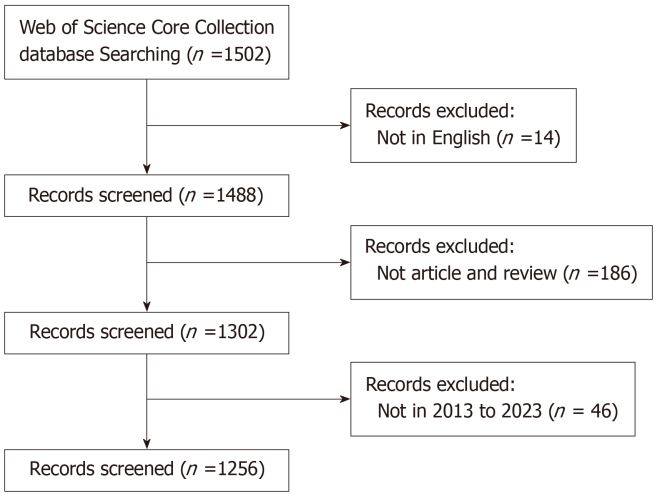



**Figure 1 Web of Science Core Collection retrieval strategies and inclusion criteria for articles on gut microbiota and nonalcoholic fatty liver disease.**

citations. This indicates the high scholarly standing and influence of these journals, as citation rates reflect the quality and significance of their research. As visualized in Figure 5, the journal network map, 409 journals have contributed to the field of gut microbiota and NAFLD studies, with 63 of them having over 5 publications. To explore the relationships between cited and co-cited journals, a double-graph overlay analysis was conducted (Figure 6), where lines connecting nodes on both sides demonstrate citation pathways and the interconnections among diverse research areas.

### *Analysis of authors*

It can be seen in Table 4 that, Suk Ki Tae from South Korea was the most prolific author in the field of gut microbiota and NAFLD with 14 publications (340 citations), followed by Abenavoli Ludovico from Italy (13 publications, 603 citations) and Nobili Valerio (13 publications, 1258 citations). The most cited authors were Targher Giovanni from Italy (2023 citations), followed by Tilg Herbert from Austria (1403 citations) and Schnabl Bernd from Germany (1308 citations), indicating that the studies of these authors are of interest to researchers. Figure 7 shows a network map of the authors. As of now, 7111 authors have contributed to research on the subject of gut microbiota in relation to NAFLD, with a notable group of 112 authors having published over five articles each on this topic.

**Table 4 Top 15 high-output authors in the field of gut microbiota and nonalcoholic fatty liver disease, from 2013 to 2023**

| Ranking | Authors | Documents | Citations |
|---|---|---|---|
| 1 | Suk Ki Tae | 14 | 340 |
| 2 | Abenavoli Ludovico | 13 | 603 |
| 3 | Nobili Valerio | 13 | 1258 |
| 4 | Byrne Christopher D. | 12 | 1245 |
| 5 | Gupta Hari Priya | 12 | 217 |
| 6 | Roomba Rohit | 12 | 1302 |
| 7 | Alisi Anna | 11 | 980 |
| 8 | Schnabl Bernd | 11 | 1308 |
| 9 | Targher Giovanni | 11 | 2023 |
| 10 | Bergheim Ina | 10 | 456 |
| 11 | Kim Dong Joon | 10 | 181 |
| 12 | Ganesan Raja | 9 | 54 |
| 13 | Hekmatdoost Azita | 9 | 552 |
| 14 | Nieuwdorp Max | 9 | 703 |
| 15 | Tilg Herbert | 9 | 1403 |

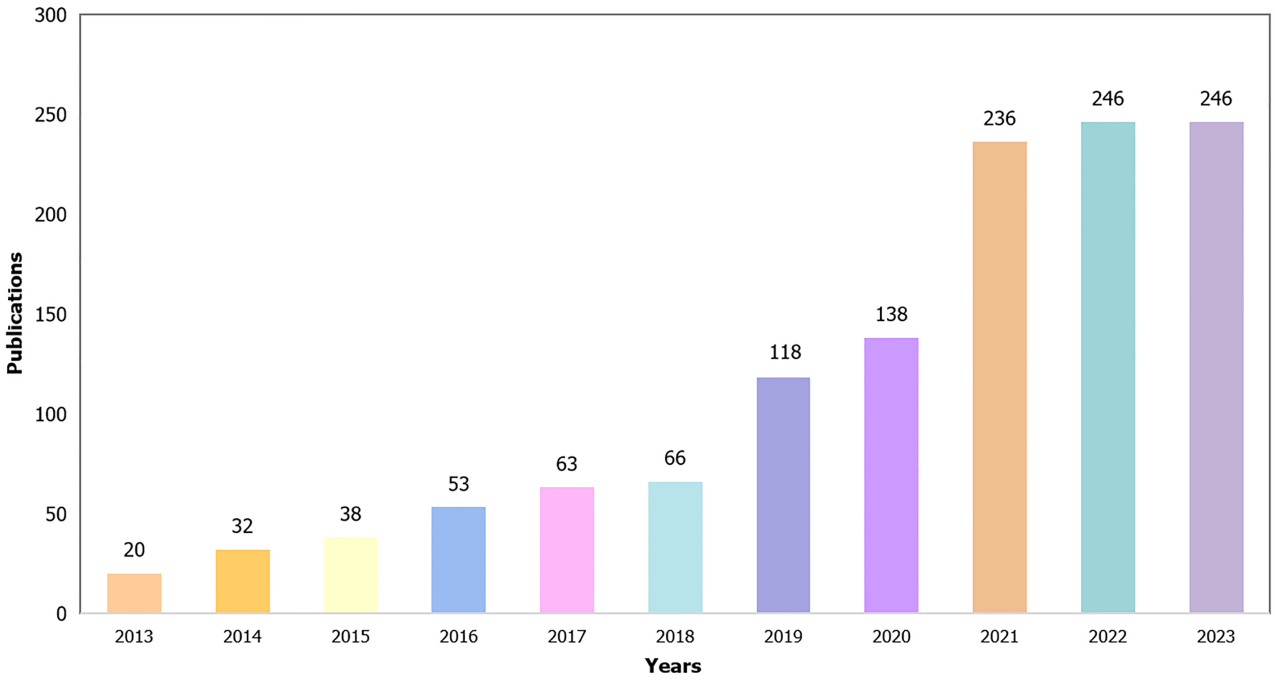



**Figure 2 Global trends in the publication of research on gut microbiota and nonalcoholic fatty liver disease, from 2013 to 2023.**

### *Analysis of references*

From 2013 to 2023, Table 5 documents the annual global citation counts (GCS) for the top 10 most cited articles, showcasing the cumulative number of times these articles have been referenced as recorded in the Web of Science database. The GCS represents the total citations garnered by a particular article over the years in question. It is used as a measure of the influence and scientific importance of the literature under consideration. Table 5 reveals that Buzzetti E's article published in *Metabolism-Clinical and Experimental* in 2016 obtained the highest GCS score. Ranking second on the GCS list was Boursier J's article published in *Hepatology* in 2016, followed by Canfora EE's article published in *Nature Reviews Endocrinology* in 2019. The network map depicting highly cited articles is illustrated in Figure 8.

Figure 9A depicts a co-citation analysis of the cited references. Co-citation refers to the relationship between two or more references when they are simultaneously cited by another reference (published later). This phenomenon of co-

**Table 5 Top 10 cited references related to research on gut microbiota and nonalcoholic fatty liver disease (from Web of Science Core Collection database)**

| Ranking | Title | First author | Journal | Year | Total citations |
|---|---|---|---|---|---|
| 1 | The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD) | Buzzetti E | *Metabolism-Clinical and Experimental* | 2016 | 1764 |
| 2 | The Severity of Nonalcoholic Fatty Liver Disease Is Associated with Gut; Dysbiosis and Shift in the Metabolic Function of the Gut Microbiota | Boursier J | *Hepatology* | 2016 | 869 |
| 3 | Gut microbial metabolites in obesity, NAFLD and T2DM | Canfora EE | *Nature Reviews Endocrinology* | 2019 | 724 |
| 4 | Non-alcoholic fatty liver disease and its relationship with cardiovascular; disease and other extrahepatic diseases | Adams LA | *Gut* | 2017 | 712 |
| 5 | Intestinal microbiota determines development of non-alcoholic fatty liver disease in mice | Le Roy T | *Gut* | 2013 | 660 |
| 6 | The role of the gut microbiota in NAFLD | Leung C | *Nature Reviews Gastroenterology & Hepatology* | 2016 | 624 |
| 7 | Gut Microbiome-Based Metagenomic Signature for Non-invasive; Detection of Advanced Fibrosis in Human Nonalcoholic Fatty Liver Disease | Loomba R | *Cell Metabolism* | 2017 | 613 |
| 8 | Bile Acid Control of Metabolism and Inflammation in Obesity, Type 2; Diabetes, Dyslipidemia, and Nonalcoholic Fatty Liver Disease | Chávez-Talavera O | *Gastroenterology* | 2017 | 580 |
| 9 | Intestinal Microbiota in Patients with Nonalcoholic Fatty Liver Disease | Mouzaki M | *Hepatology* | 2013 | 526 |
| 10 | Fructose and sugar: A major mediator of non-alcoholic fatty liver disease | Jensen T | *Journal of Hepatology* | 2018 | 521 |

citation serves as an indicator of the correlation and mutual influence between documents. A total of 49,633 articles were analyzed using VOSviewer, with nodes connected by lines denoting their citation in the same publication; shorter lines indicate a closer relationship.

Figure 9B shows the 10 major clusters of co-cited references, namely cortisol, endothelial dysfunction, carbohydrate metabolism, myocardial infarction, non-alcoholic steatohepatitis, lipotoxicity, glucagon-like peptide-1, non-islet dependent, ethnicity and microRNA.

Figure 9C displays the top 25 most frequently cited references. Among the burst strength results, Moran LJ exhibited the highest burst strength of 17.55. In addition, Legro RS had burst strength of 17.28, Diamanti-Kandarakis E had burst strength of 14.45, Wild RA had burst strength of 14.31, Fauser BCJM had burst strength of 13.3 and March WA had burst strength of 10.65. These references have received more attention.

### *Analysis of keywords*

Keywords serve as crucial indicators that reflect research hotspots and trends, while also refining the core content of literature. The analysis of keywords can shed light on the prominent research areas and evolving trends within an academic discipline. As depicted in Table 6, these are the 20 most recurrent keywords pertaining to gut microbiota and NAFLD from 2013 to 2023. The most common keyword was gut microbiota with 610 occurrences (5215 for connection strength), followed by NAFLD with 406 occurrences (3589 for connection strength). The third most frequent keyword was insulin resistance, which had a frequency of 336 times (with a connection strength of 3181 times). The keywords obesity, steatohepatitis, inflammatory, metabolic syndrome, fibrosis, oxidative stress, probiotics, and dysbiosis exhibited a higher frequency and stronger connections (keywords with similar meanings have been excluded). These keywords encapsulate the prevailing research hotspots and trends within the field of gut microbiota and NAFLD. The network visualization corresponding to these keywords is illustrated in Figure 10A. The dimensions of each node correspond to the frequency with which the pertinent keywords are represented in the literature. Node color is typically used to distinguish different categories or attributes of keywords, while lines represent associations between keywords, with line color often indicating the nature or intensity of these associations. Furthermore, as shown in Figure 10B, gut microbiota, oxidative stress, non-alcoholic fatty liver disease, liver metabolome, liver microbial intake, insulin resistance, brassica juncea var, and hepatocellular carcinoma have long been a focus of research on gut microbiota and NAFLD. The most popular topics of the last 10 years are illustrated in Figure 10C, encompassing metabolic syndrome (citation burst strength 14.23), hepatic steatosis (citation burst strength 9.09), insulin resistance (citation burst strength 8.26), hepatocellular carcinoma (citation burst strength 7.68) and cardiovascular disease (citation burst strength 6.33).

## DISCUSSION

Utilizing VOSviewer and CiteSpace, we analyzed the literature's temporal and spatial distribution, keyword frequency, citation data, and co-citation indicators. These tools enabled us to map out the current state of research, highlight key

**Table 6 Top 20 keywords with high frequency related to research on gut microbiota and nonalcoholic fatty liver disease**

| Ranking | Keywords | Frequencies | Total link strength |
|---|---|---|---|
| 1 | Gut microbiota | 610 | 5215 |
| 2 | NAFLD | 406 | 3589 |
| 3 | Insulin-resistance | 336 | 3181 |
| 4 | Obesity | 328 | 2869 |
| 5 | Steatohepatitis | 311 | 2899 |
| 6 | Inflammation | 256 | 2326 |
| 7 | Non-alcoholic fatty liver disease | 250 | 2204 |
| 8 | Hepatic Steatosis | 243 | 2286 |
| 9 | Nonalcoholic fatty liver disease | 216 | 1865 |
| 10 | Microbiota | 177 | 1571 |
| 11 | Intestinal microbiota | 169 | 1643 |
| 12 | Nonalcoholic steatohepatitis | 154 | 1514 |
| 13 | Metabolic syndrome | 149 | 1379 |
| 14 | Fatty liver disease | 148 | 1263 |
| 15 | Fibrosis | 146 | 1343 |
| 16 | Oxidative stress | 136 | 1197 |
| 17 | Probiotics | 134 | 1388 |
| 18 | Pathogenesis | 129 | 1184 |
| 19 | Diet | 127 | 1169 |
| 20 | Dysbiosis | 119 | 1053 |

NAFLD: Nonalcoholic fatty liver disease.

areas of focus, and identify evolving trends within the field of gut microbiota and NAFLD studies. By examining these insights, our study intends to offer valuable guidance for researchers exploring liver disease, thereby contributing to the advancement of knowledge in this domain.

A total of 1256 articles were included in our analysis. Between 2013 and 2023, we observed a consistent upward trend in the number of publications focusing on gut microbiota and NAFLD, which has attracted significant attention from researchers worldwide.

Among the 64 nations contributing to the field, China stands out as the leading producer of research papers, with the United States and Italy trailing closely behind. The surge in China's research output can be attributed to the rising incidence of NAFLD within the country. A growing focus of Chinese scientists has been the complex interactions between gut microbiota and NAFLD, as they diligently examine the disease's causality and potential therapies. These studies not only contribute to enhancing China's academic standing in this field but also serve as important references for related research worldwide. In terms of research into the association between gut microbiota and NAFLD, the United States exhibited the highest citation rate, signifying its predominant influence in this field. This notable advantage can be attributed to prominent scholars who possess advanced research facilities and cutting-edge technology.

The Shanghai University of Traditional Chinese Medicine leads in the number of published papers related to gut microbiota and NAFLD research, reflecting its substantial focus and support in these fields. Following closely are Shanghai Jiao Tong University and the UCSD in terms of publication volume. In terms of citation impact, the UCSD stands at the forefront, succeeded by the University of Sydney and Shanghai Jiao Tong University, demonstrating the significant influence of their research in this domain. It is noteworthy that nine out of the top 15 institutions engaged in this research are based in China, highlighting the growing interest and dedication of Chinese institutions to the study of gut microbiota and NAFLD.

High-impact factor journals are esteemed platforms for publishing top-tier research, thus articles appearing in these journals are considered to be of superior quality and significant contributions to the respective academic discipline. However, within gut microbiota and NAFLD research, there is a notable scarcity of publications in such prestigious journals (impact factor < 10 for most journals). *Nutrients*, a journal with an impact factor of 6.6, has significantly contributed to the field of gut microbiota and NAFLD research, boasting the highest volume of publications on this topic. Furthermore, it ranks third in citations, emphasizing its importance in the scientific community. *Hepatology*, despite its higher impact factor of 15.6, stands out as the most cited journal with 13 publications, indicating the premium quality of

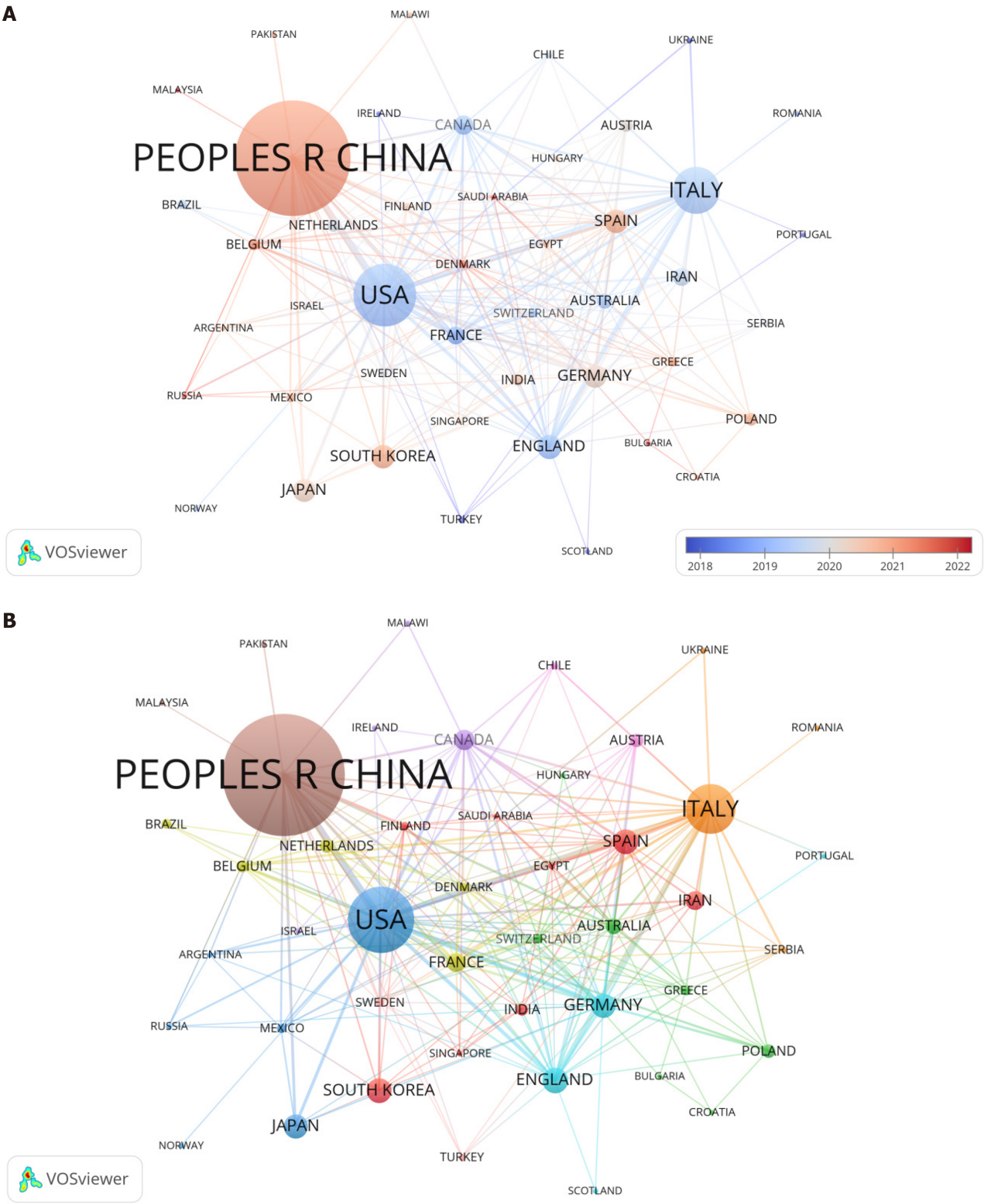



**Figure 3 Network map of the countries/regions in terms of article publication.** A: Network map of countries/regions with more than 5 publications; B: Network map of countries/regions with more than 20 publications.

its research. Thus, for scholars investigating gut microbiota and NAFLD, *Hepatology* merits particular attention due to its consistent production of high-caliber articles.

Suk Ki Tae, a researcher from the Institute of Liver Digestion at Hanlim University School of Medicine in South Korea, holds the distinction of being the most productive author in the field of gut microbiota and NAFLD research. He has authored 14 papers that have cumulatively been cited 340 times. Suk Ki Tae's primary area of interest lies in exploring the role of gut microbiota and its metabolites in the development and progression of NAFLD. Notably, his research prominently features studies on probiotics, investigating their potential as a promising therapeutic approach for treating NAFLD[14-16]. The article suggests that the consumption of probiotics like *Lactobacillus acidophilus, Lactobacillus*

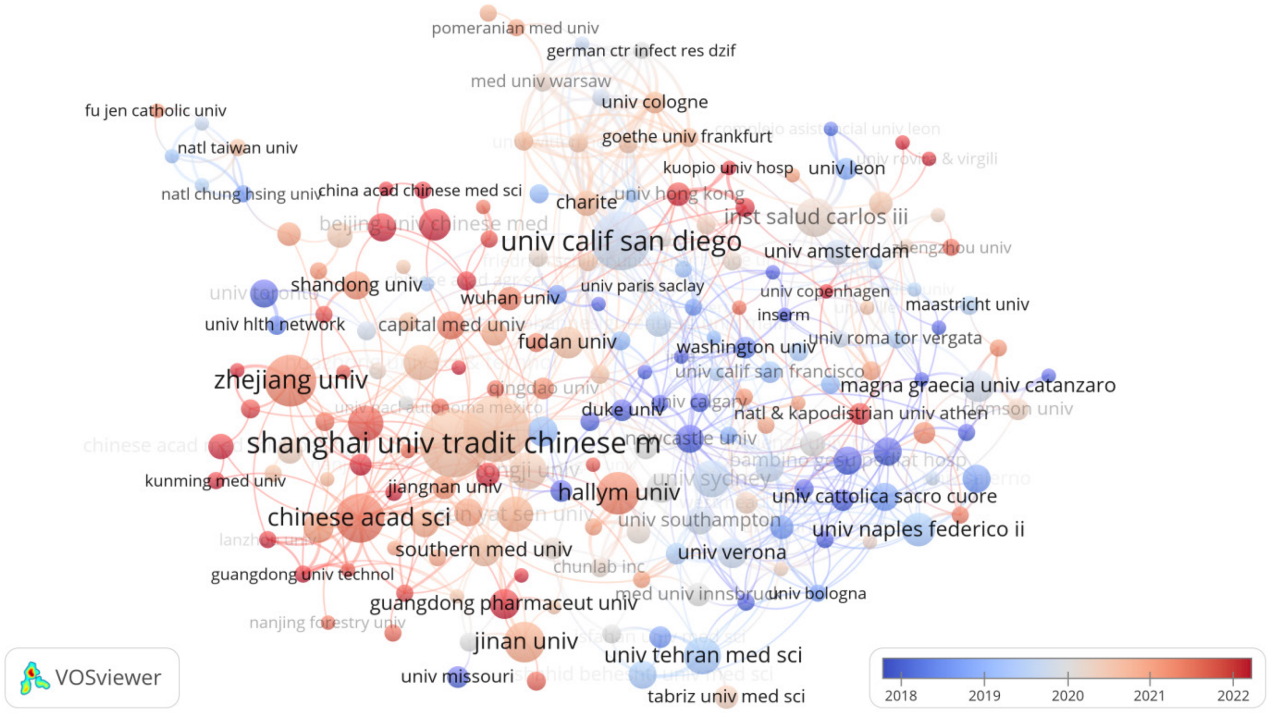



**Figure 4 Network map of the institutions.**

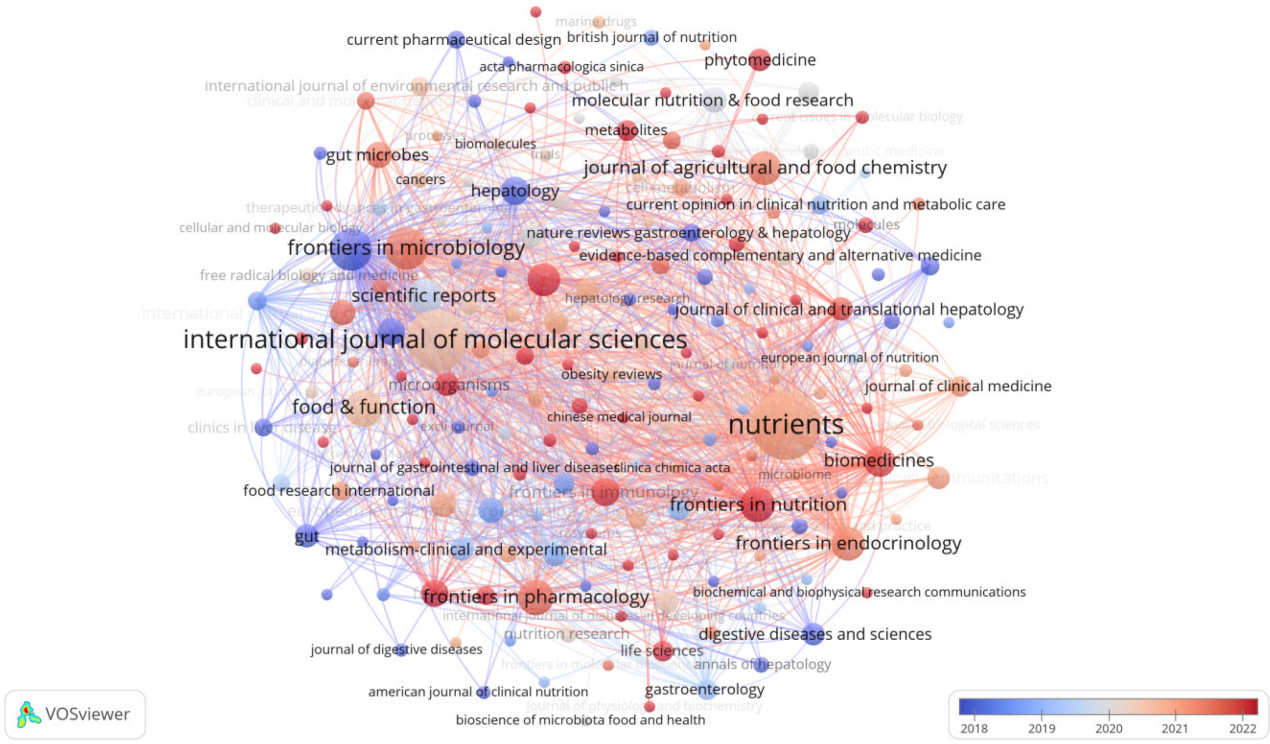



**Figure 5 Network map of the journals.**

*fermentans,* and *Lactobacillus plantarum* may potentially alleviate non-alcoholic steatosis by helping to reduce cholesterol levels and thus enhance the condition's positive progression[17]. Another study has demonstrated that short-chain fatty acids and indole compounds produced by Bifidobacteria can alleviate NAFLD through the modulation of the GLA pathway[18]. Abenavoli Ludovico and Nobili Valerio (both with 13 publications each) have secured the second position in the ranking and amassed 603 and 1258 citations respectively. Abenavoli Ludovico's research interests closely parallel Suk Ki Tae's work[19,20]. Nobili, Valerio's research centers on the investigation of the gut microbiota's influence in the development of pediatric NAFLD. The study reveals that children with NAFLD exhibit heightened intestinal permeability, a factor that positively correlates with the severity of the disease[21]. He dedicated significant attention to

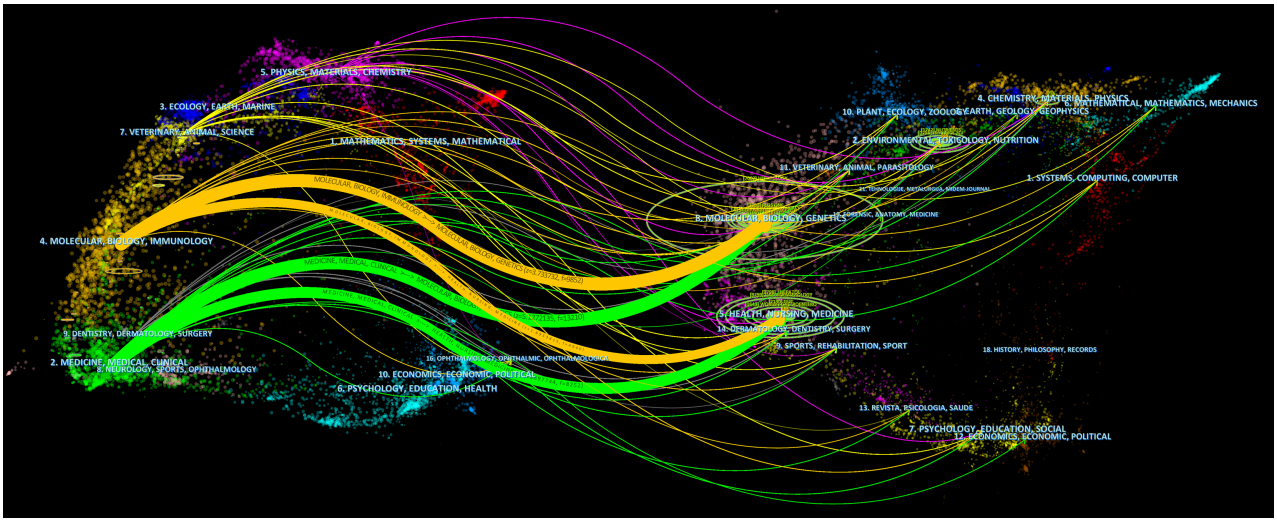



**Figure 6 Dual-map overlay of journals in the field of gut microbiota and nonalcoholic fatty liver disease.** Citing journals appear on the left, cited journals appear on the right, and citation relationships are represented by colored paths.

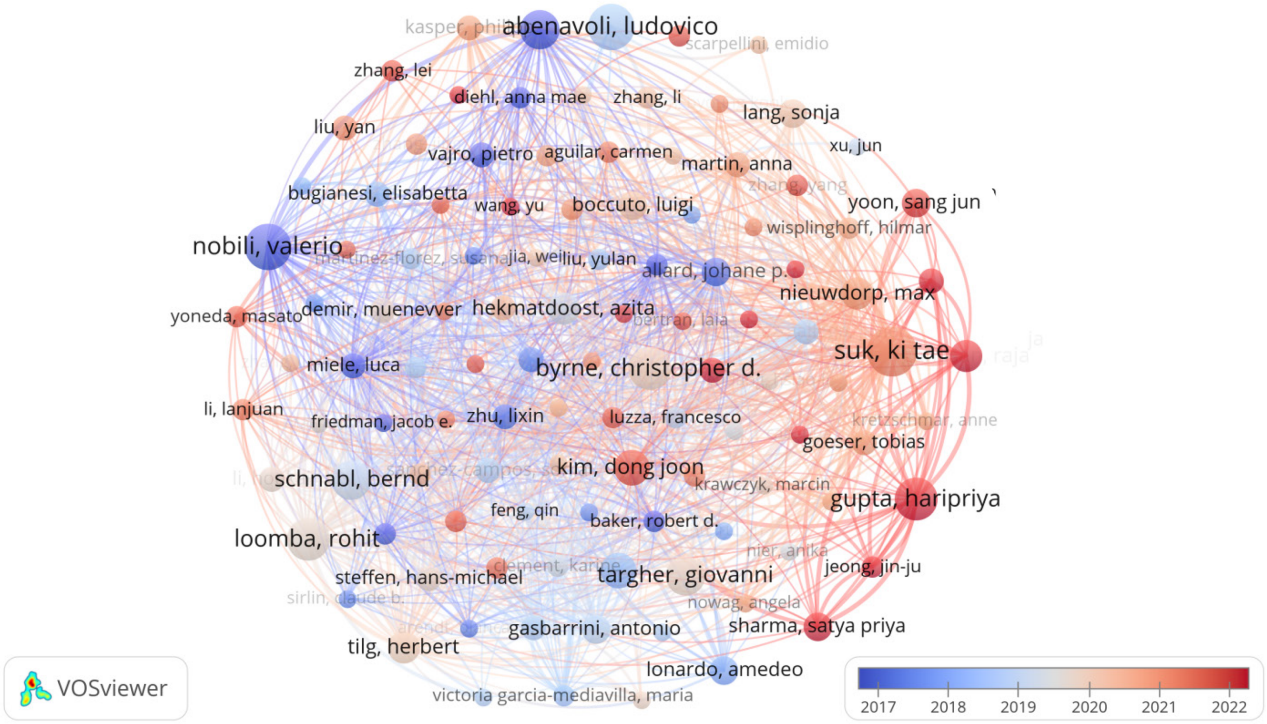



**Figure 7 Network map of the authors.**

exploring the therapeutic potential of probiotics in managing NAFLD. A review indeed confirmed the effectiveness of probiotics for treating NAFLD in pediatric patients[22]. A recent study suggests that Bifidobacterium could play a protective role in preventing the de-velopment of NAFLD and obesity, thereby emphasizing its significance in the creation of novel, targeted, and effective probiotics for potential therapeutic applications[23]. The most cited author was Targher Giovanni from Italy (2023 citations), followed by Tilg Herbert from Austria (1403 citations) and Schnabl Bernd from Germany (1308 citations), indicating that the research carried out by these authors is of greater interest to researchers.

Papers with high citation counts can serve as indicators of the prevailing issues of interest within a specific research domain. The papers written by Buzzetti E published in *Metabolism-Clinical and Experimental* in 2016 were ranked first in the GCS. This article primarily focuses on elucidating the pathogenesis of NAFLD. The "two-strike" hypothesis has been criticized for inadequately explaining some molecular and metabolic changes seen in NAFLD patients. A more comprehensive theory proposes that multiple factors, acting in synergy, contribute to the development of NAFLD in genetically prone individuals. These factors encompass insulin resistance, hormones from adipose tissue, dietary influences, gut microbiota composition, and genetic and epigenetic effects[24]. Boursier J's 2016 study in *Hepatology* explored the role of

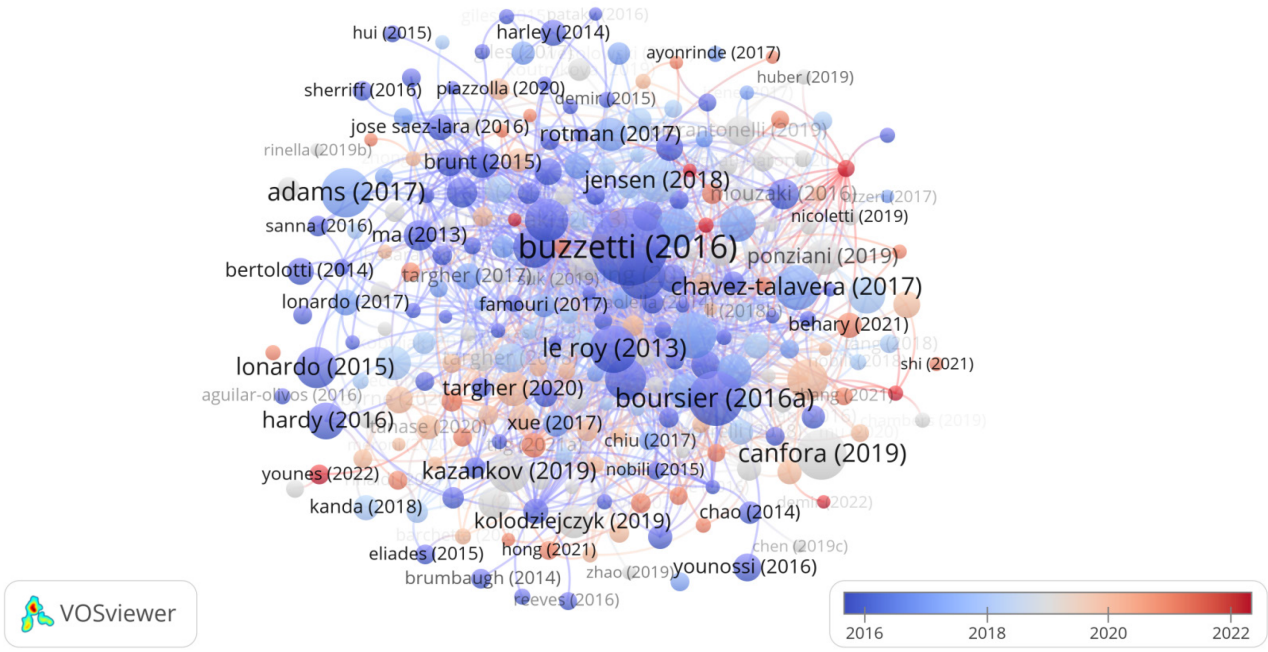


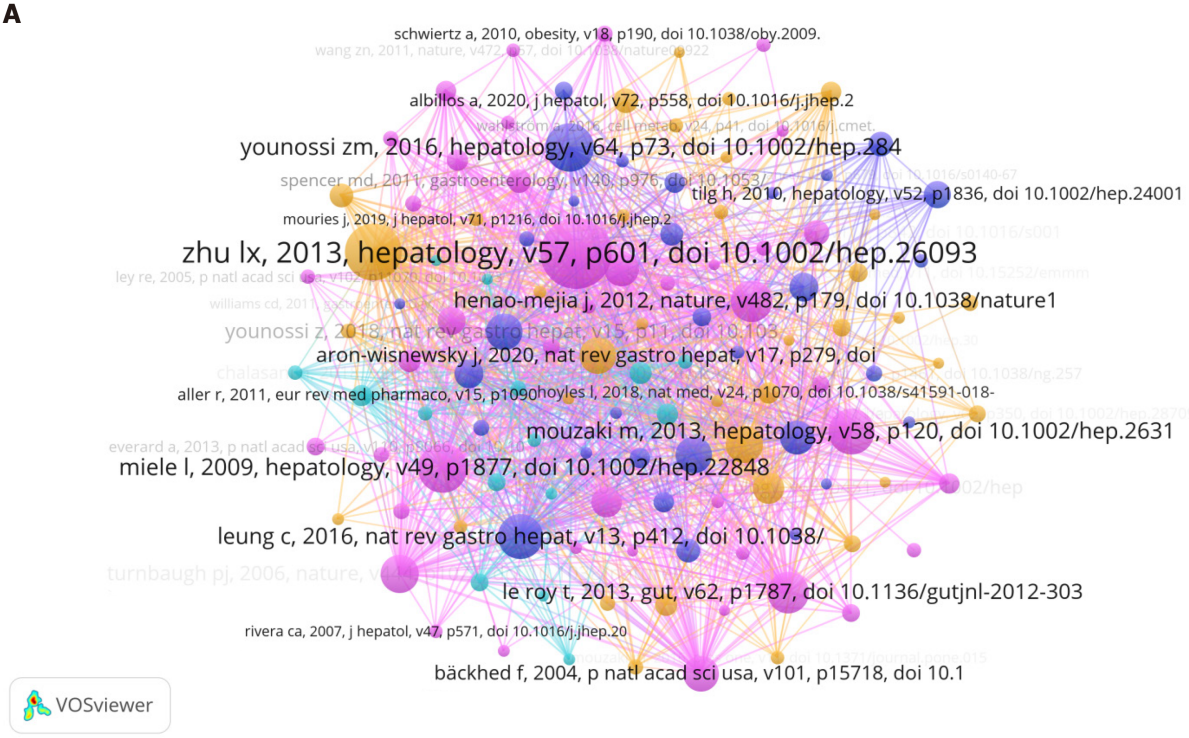

**Figure 8 Network map of document citation.**

gut microbiota dysregulation in determining the severity of NAFLD, ranking second in significance[25]. Canfora EE's article, published in *Nature Reviews Endocrinology* in 2019, secured the third spot on the GCS list by conducting a systematic review that illuminated the connection between microbial fermentation products from carbohydrates and proteins with obesity, obesity-related insulin resistance, type 2 diabetes mellitus, and NAFLD, further elucidating the mechanisms at play[26]. The involvement of gut microbiota in the pathogenesis of NAFLD is a persistent area of interest, as these studies demonstrate.

The visualization of keywords and their co-cited references through time can potentially uncover significant trends and focuses in the domain of gut microbiota and NAFLD research. According to the timeline of co-cited literature, cortisol, and endothelial dysfunction were the common focus, revealing their important roles in the pathophysiological mechanism of NAFLD. Chronic psychosocial stress and elevated cortisol levels have been identified by Demori and Grasselli [27] as contributing factors in the development of NAFLD, implying that targeting stress response may be a viable therapeutic approach. Yang and Song[28] investigated the GLA in NAFLD, revealing that imbalances in gut microbiota contribute to insulin resistance, endothelial dysfunction, and an increased risk of cardiovascular disease due to systemic inflammation. Wang *et al*[29] demonstrated the beneficial effects of green walnut hull polyphenol extract on high-fat diet-induced NAFLD in rats, as it helped avert endothelial issues and colon tissue damage. Caturano *et al*[30] in their review delved into the core pathophysiological mechanisms of NAFLD, emphasizing insulin resistance as a key factor and its links to endothelial dysfunction, concurrently discussing its implications for increased cardiovascular risks. Musso *et al* [31] reviewed emerging mechanistic links between NAFLD and chronic kidney disease, suggesting that excess dietary fructose may exacerbate liver and kidney damage by altering gut barrier function and microbiota composition. Shen *et al* [32] showed that *Escherichia coli (E. coli)*, through its flagellin-induced endothelial-mesenchymal transformation, exacerbates NAFLD progression, a finding that suggests *E. coli* and its flagellin may be novel targets for NAFLD treatment.

As research into gut microbiota and NAFLD advances, the research hotspot changes. The publications which exhibited the highest citation frequency, average annual keyword views, and emergence mapping effectively illustrate the prevailing research hotspots and trajectories. A literature review from the past five years underscored the primary research directions concerning gut microbiota and NAFLD, which are listed as follows: Aron-Wisnewsky *et al*[33] describe the challenges of distinguishing gut microbiota signatures specific to NAFLD from those associated with obesity and type 2 diabetes. They call for advanced metagenomics to better understand these signatures. Kolodziejczyk *et al*[34] investigated the impact of gut microbiota and their byproducts on hepatic metabolism and inflammation, thereby connecting these factors to the onset of NAFLD and its advancement to nonalcoholic steatohepatitis (NASH). Concurrently, Safari and Gérard[35] recognized the significance of gut microbiota in the development and progression of NAFLD, proposing that an imbalance in gut microbiota, or dysbiosis, and compromised gut barrier function can result in hepatic inflammation. They suggest that probiotics and prebiotics may improve liver health in NAFLD patients. Jiao *et al*[36] examined bile acid signaling in NAFLD, and found elevated primary and secondary bile acids and impaired FXR-mediated signaling. They suggest targeting FXR signaling and gut microbiota as potential therapeutic strategies. Pierantonelli and Svegliati-Baroni[37] reviewed the basic mechanisms of NAFLD progression from steatosis to NASH, emphasizing the role of lipotoxicity, mitochondrial dysfunction, and the GLA. This extensive review underscores the intricate interactions between diet, gut microbiota, immune response, and metabolic pathways in the etiology and progression of NAFLD. A thorough understanding of these mechanisms is essential in order to formulate effective

**A**




VOSviewer

**B**

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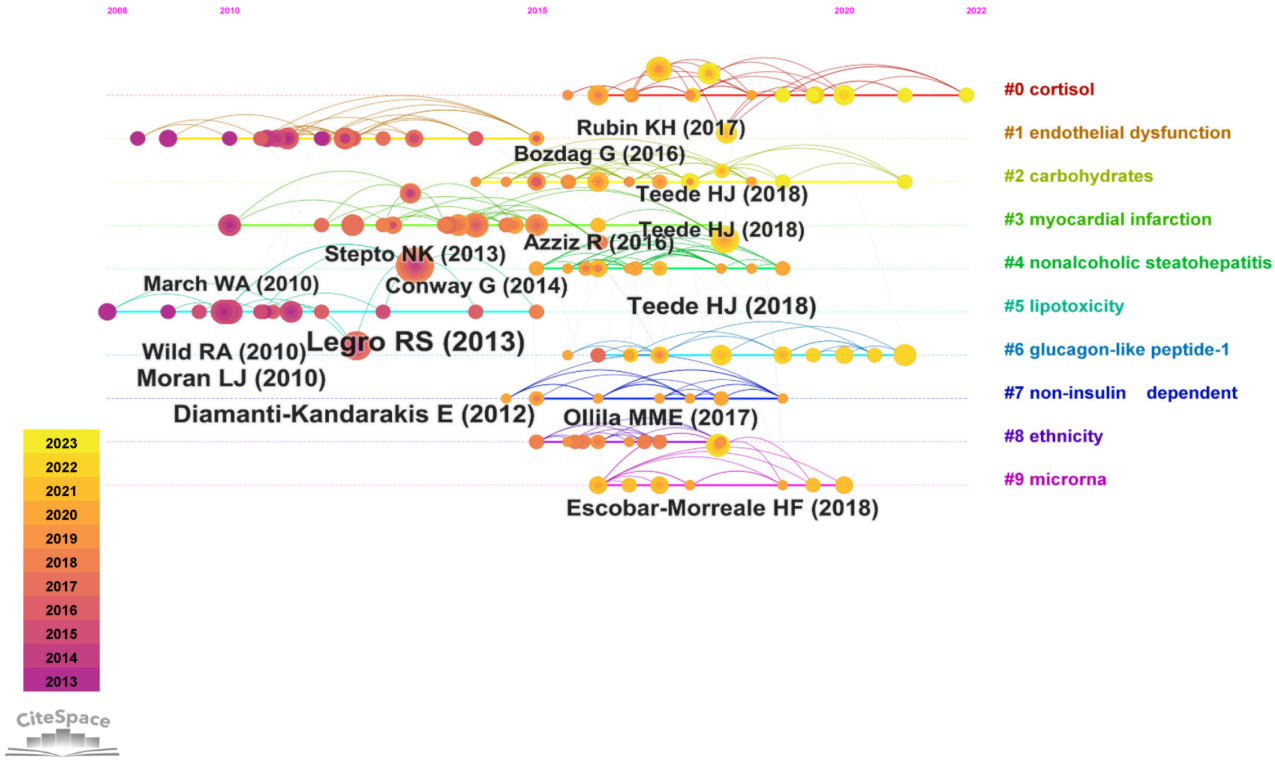
Timespan: 2013-2023 (Slice Length=1)
Selection Criteria: Top 15 per slice, LRF=3.0, L/N=10, LBY=5, e=1.0
Network: N=186, E=292 (Density=0.017)
Largest CC: 177 (95%)
Nodes Labeled: 1.0%
Pruning: Pathfinder
Modularity Q=0.7821
Weighted Mean Silhouette S=0.9245
Harmonic Mean(Q, S)=0.8474




CiteSpace

**C** **Top 25 references with the strongest citation bursts**

| References | Year | Strength | Begin | End | 2013-2023 |
|---|---|---|---|---|---|
| Moran LJ, 2010, HUM REPROD UPDATE, V16, P347, DOI 10.1093/humupd/dmq001, DOI | 2010 | 17.55 | 2013 | 2015 | |
| Wild RA, 2010, J CLIN ENDOCR METAB, V95, P2038, DOI 10.1210/jc.2009-2724, DOI | 2010 | 14.31 | 2013 | 2015 | |
| Fauser BCJM, 2012, FERTIL STERIL, V97, P28, DOI 10.1016/j.fertnstert.2011.09.024, DOI | 2012 | 13.3 | 2013 | 2017 | |
| March WA, 2010, HUM REPROD, V25, P544, DOI 10.1093/humrep/dep399, DOI | 2010 | 10.65 | 2013 | 2015 | |
| Azziz R, 2009, FERTIL STERIL, V91, P456, DOI 10.1016/j.fertnstert.2008.06.035, DOI | 2009 | 8.38 | 2013 | 2014 | |
| Goodarzi MO, 2011, NAT REV ENDOCRINOL, V7, P219, DOI 10.1038/nrendo.2010.217, DOI | 2011 | 6.86 | 2013 | 2016 | |
| de Groot PCM, 2011, HUM REPROD UPDATE, V17, P495, DOI 10.1093/humupd/dmr001, DOI | 2011 | 6.16 | 2013 | 2015 | |
| Diamanti-Kandarakis E, 2012, ENDOCR REV, V33, P981, DOI 10.1210/er.2011-1034, DOI | 2012 | 14.45 | 2014 | 2017 | |
| Yildiz BO, 2012, HUM REPROD, V27, P3067, DOI 10.1093/humrep/des232, DOI | 2012 | 6.43 | 2014 | 2017 | |
| Shi YY, 2012, NAT GENET, V44, P1020, DOI 10.1038/ng.2384, DOI | 2012 | 6.43 | 2014 | 2017 | |
| Wild RA, 2011, FERTIL STERIL, V95, P1073, DOI 10.1016/j.fertnstert.2010.12.027, DOI | 2011 | 6.07 | 2014 | 2015 | |
| Legro RS, 2013, J CLIN ENDOCR METAB, V98, P4565, DOI 10.1210/jc.2013-2350, DOI | 2013 | 17.28 | 2015 | 2018 | |
| Conway G, 2014, EUR J ENDOCRINOL, V171, PP1, DOI 10.1530/EJE-14-0253, DOI | 2014 | 8.38 | 2016 | 2019 | |
| Goodman NF, 2015, ENDOCR PRACT, V21, P1415, DOI 10.4158/EP15748.DSCPT2, DOI | 2015 | 8.85 | 2017 | 2019 | |
| Bozdag G, 2016, HUM REPROD, V31, P2841, DOI 10.1093/humrep/dew218, DOI | 2016 | 7.14 | 2018 | 2021 | |
| Teede HJ, 2018, CLIN ENDOCRINOL, V89, P251, DOI 10.1111/cen.13795, DOI | 2018 | 10.1 | 2019 | 2023 | |
| Rubin KH, 2017, J CLIN ENDOCR METAB, V102, P3848, DOI 10.1210/jc.2017-01354, DOI | 2017 | 7.7 | 2019 | 2023 | |
| Azziz R, 2016, NAT REV DIS PRIMERS, V2, P0, DOI 10.1038/nrdp.2016.57, DOI | 2016 | 7.69 | 2019 | 2021 | |
| Teede HJ, 2018, HUM REPROD, V33, P1602, DOI 10.1093/humrep/dey256, DOI | 2018 | 10.56 | 2021 | 2023 | |
| Day F, 2018, PLOS GENET, V14, P0, DOI 10.1371/journal.pgen.1007813, DOI | 2018 | 8.48 | 2021 | 2023 | |
| Escobar-Morreale HF, 2018, NAT REV ENDOCRINOL, V14, P270, DOI 10.1038/nrendo.2018.24, DOI | 2018 | 7.74 | 2021 | 2023 | |
| Kakoly NS, 2019, DIABETES CARE, V42, P560, DOI 10.2337/dc18-1738, DOI | 2019 | 7.45 | 2021 | 2023 | |
| Teede HJ, 2018, FERTIL STERIL, V110, P364, DOI 10.1016/j.fertnstert.2018.05.004, DOI | 2018 | 6.77 | 2021 | 2023 | |
| Wekker V, 2020, HUM REPROD UPDATE, V26, P942, DOI 10.1093/humupd/dmaa029, DOI | 2020 | 9.87 | 2022 | 2023 | |
| Kakoly NS, 2018, HUM REPROD UPDATE, V24, P455, DOI 10.1093/humupd/dmy007, DOI | 2018 | 8.16 | 2022 | 2023 | |

**Figure 9 The co-cited references map on gut microbiota and nonalcoholic fatty liver disease.** A: Network map of co-cited references; B: Timeline view of co-cited references. The term "citation bursts" refers to literature that is consistently cited over an extended period of time; C: Top 25 references with the strongest citation bursts.

prevention and treatment strategies.

The analysis of these keywords indicated that research on the gut microbiota and NAFLD predominantly centers on pathogenesis and therapeutic interventions. It is unequivocal that future investigations should explore the underlying mechanisms of NAFLD as well as the influence of gut microbiota on NAFLD treatment.

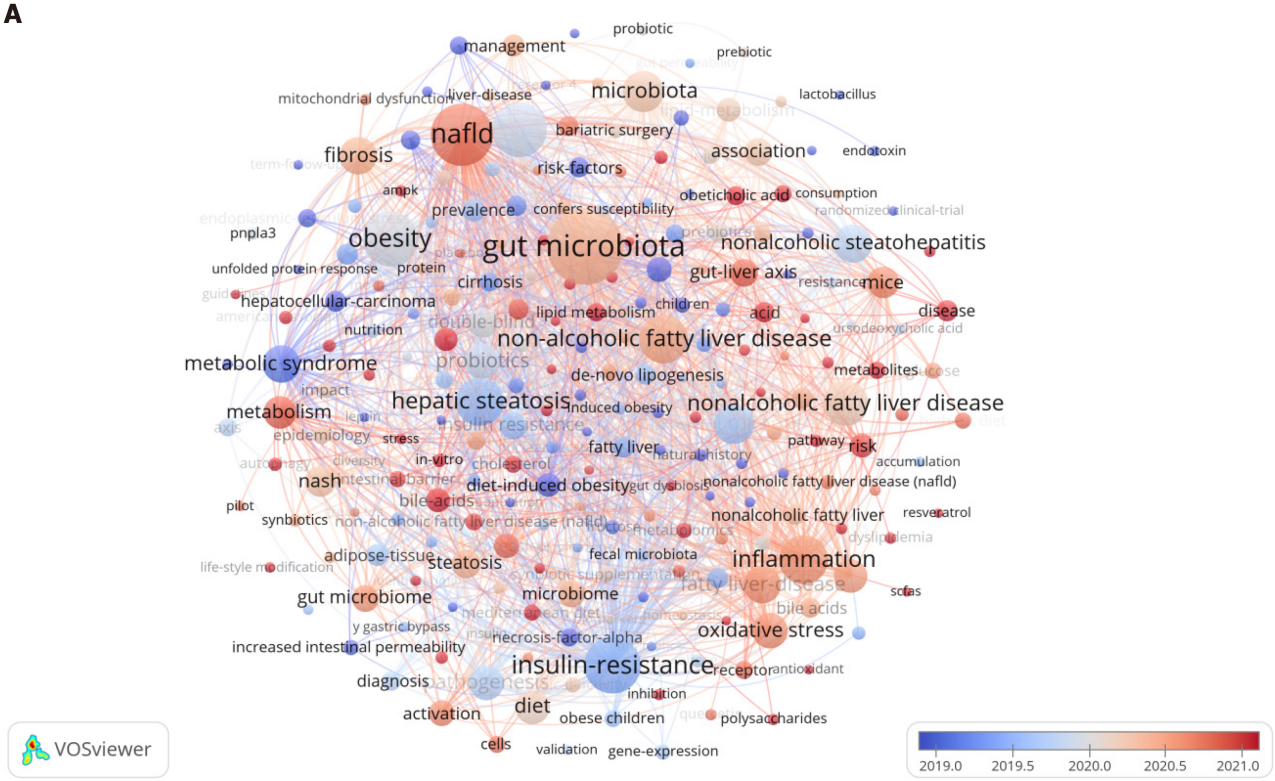
To objectively assess the connection between gut microbiota and NAFLD, an extensive citation analysis was conducted using CiteSpace and VOSviewer software. This investigation illuminated the current state, evolving patterns, and pivotal themes pertaining to gut microbiota and its association with NAFLD. Despite providing valuable insights, the study has limitations, chiefly the restriction to the WoSCC database and the exclusive inclusion of English-language publications, potentially leading to selection bias.

## CONCLUSION

Bibliometric research showed that publications on gut microbiota and NAFLD are increasing worldwide, and this disease is receiving significant attention. The results showed that China was the most prolific country in terms of the number of publications, the United States was the most influential country, Shanghai University of Traditional Chinese Medicine had a greater number of publications, and the UCSD was the most cited institution. The journal *Nutrients* was the most published journal, and *Hepatology* was the most cited journal. Suk Ki Tae from South Korea was the most prolific author.

The co-cited keyword cluster labels revealed the presence of ten major clusters, namely cortisol, endothelial dysfunction, carbohydrate metabolism, myocardial infarction, NASH, lipotoxicity, glucagon-like peptide-1, non-islet dependent, ethnicity and microRNA. Intense research efforts in the field have uncovered key areas of focus, including metabolic syndrome, hepatic steatosis, insulin resistance, hepatocellular carcinoma, cardiovascular disease, intestinal permeability, and intestinal bacterial overgrowth. These topics have emerged as critical subjects of investigation in the outbreak analysis.

**A**


probiotic
management
prebiotic
mitochondrial dysfunction
liver-disease
microbiota
lactobacillus
nafld
bariatric surgery
fibrosis
association
endotoxin
risk-factors
ampk
obeticholic acid
consumption
prevalence
confers susceptibility
randomized clinical-trial
pnpla3
obesity
gut microbiota
nonalcoholic steatohepatitis
unfolded protein response
protein
cirrhosis
gut-liver axis
resistance
mice
hepatocellular-carcinoma
lipid metabolism
children
acid
disease
double-blind
nutrition
non-alcoholic fatty liver disease
ursodeoxycholic acid
metabolic syndrome
probiotics
de-novo lipogenesis
metabolites
impact
hepatic steatosis
induced obesity
nonalcoholic fatty liver disease
metabolism
insulin resistance
epidemiology
stress
fatty liver
pathway
risk
in-vitro
natural-history
accumulation
cholesterol
nash
diet-induced obesity
gut dysbiosis
nonalcoholic fatty liver disease (nafld)
bile-acids
pilot
synbiotics
non-alcoholic fatty liver disease (nafld)
nonalcoholic fatty liver
resveratrol
metabolomics
dyslipidemia
adipose-tissue
steatosis
fecal microbiota
inflammation
life-style modification
fatty liver disease
scfas
gut microbiome
microbiome
bile acids
oxidative stress
y gastric bypass
necrosis-factor-alpha
increased intestinal permeability
insulin-resistance
receptor
antioxidant
diagnosis
pathogenesis
inhibition
activation
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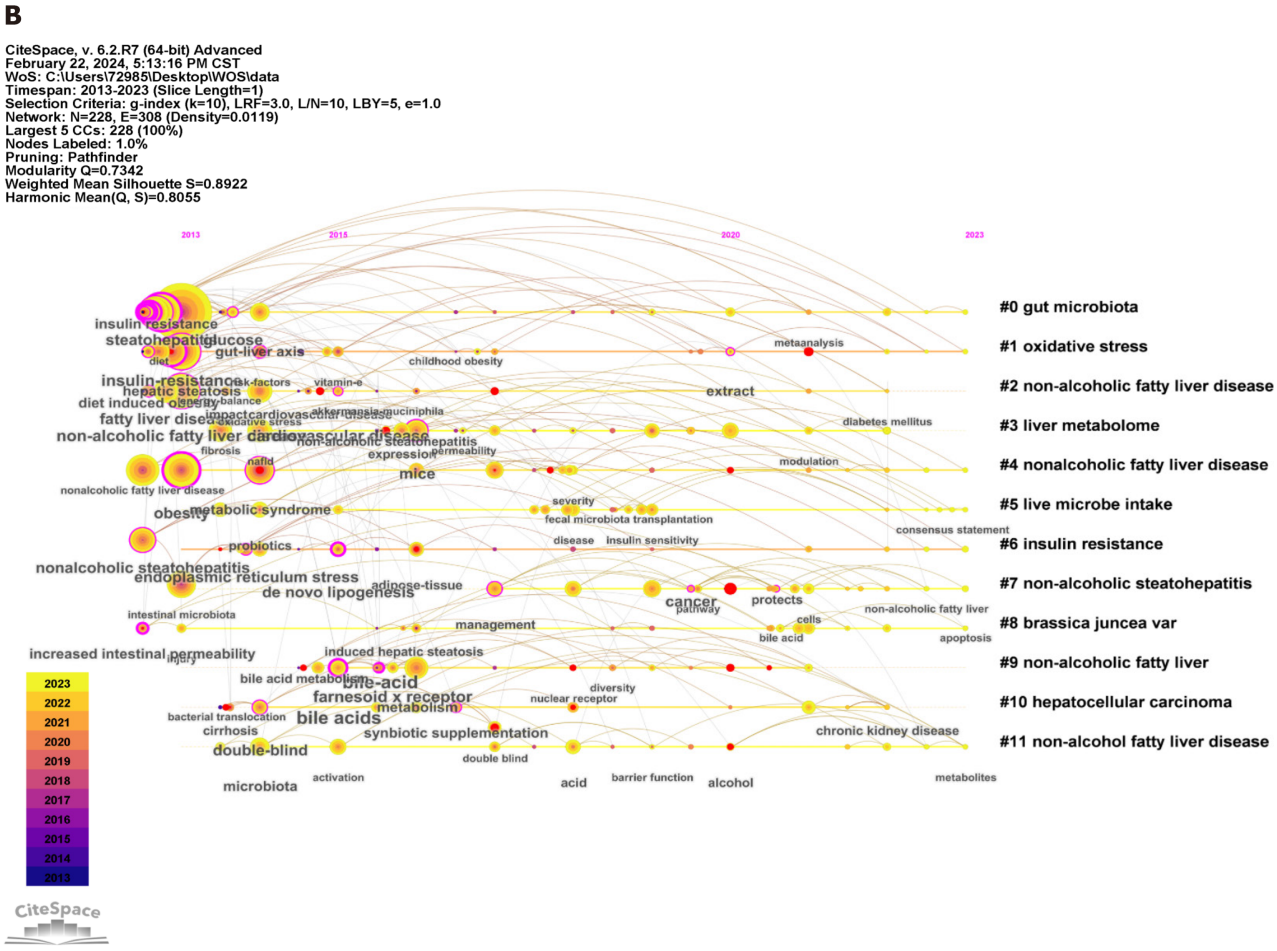
**B**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Timespan: 2013-2023 (Slice Length=1)
Selection Criteria: g-index (k=10), LRF=3.0, L/N=10, LBY=5, e=1.0
Network: N=228, E=308 (Density=0.0119)
Largest 5 CCs: 228 (100%)
Nodes Labeled: 1.0%
Pruning: Pathfinder
Modularity Q=0.7342
Weighted Mean Silhouette S=0.8922
Harmonic Mean(Q, S)=0.8055
2013
2015
2020
2023
insulin resistance
steatohepatitis
glucose
gut-liver axis
childhood obesity
metaanalysis
#0 gut microbiota
#1 oxidative stress
insulin-resistance
hepatic steatosis
diet induced obesity
fatty liver disease
non-alcoholic fatty liver disease
extract
#2 non-alcoholic fatty liver disease
diabetes mellitus
#3 liver metabolome
fibrosis
nafld
nonalcoholic fatty liver disease
mice
modulation
#4 nonalcoholic fatty liver disease
obesity
metabolic syndrome
severity
fecal microbiota transplantation
#5 live microbe intake
consensus statement
probiotics
disease
insulin sensitivity
#6 insulin resistance
nonalcoholic steatohepatitis
endoplasmic reticulum stress
de novo lipogenesis
adipose-tissue
cancer
protects
#7 non-alcoholic steatohepatitis
intestinal microbiota
management
cells
non-alcoholic fatty liver
#8 brassica juncea var
bile acid
apoptosis
increased intestinal permeability
induced hepatic steatosis
#9 non-alcoholic fatty liver
bile acid metabolism
bile-acid
farnesoid x receptor
diversity
nuclear receptor
#10 hepatocellular carcinoma
bacterial translocation
cirrhosis
bile acids
metabolism
synbiotic supplementation
chronic kidney disease
#11 non-alcohol fatty liver disease
double-blind
double blind
microbiota
activation
acid
barrier function
alcohol
metabolites
2023
2022
2021
2020
2019
2018
2017
2016
2015
2014
2013
CiteSpace

**C** **Top 25 keywords with the strongest citation bursts**

| Keywords | Year | Strength | Begin | End | 2013 - 2023 |
|---|---|---|---|---|---|
| hepatic steatosis | 2013 | 9.09 | 2013 | 2015 | |
| insulin-resistance | 2013 | 8.26 | 2013 | 2018 | |
| intestinal permeability | 2013 | 5.97 | 2013 | 2015 | |
| intestinal bacterial overgrowth | 2013 | 5.57 | 2013 | 2015 | |
| diet induced obesity | 2013 | 4.68 | 2013 | 2016 | |
| endotoxemia | 2013 | 4.13 | 2013 | 2016 | |
| increased intestinal permeability | 2013 | 4.05 | 2013 | 2016 | |
| nonalcoholic steatohepatitis | 2013 | 4.03 | 2013 | 2014 | |
| metabolic syndrome | 2014 | 14.23 | 2014 | 2018 | |
| hepatocellular-carcinoma | 2014 | 7.68 | 2014 | 2018 | |
| risk-factors | 2014 | 5.36 | 2014 | 2019 | |
| cardiovascular-disease | 2015 | 6.33 | 2015 | 2019 | |
| fatty liver | 2013 | 3.36 | 2015 | 2017 | |
| adipose-tissue | 2016 | 4.01 | 2016 | 2018 | |
| insulin resistance | 2013 | 3.75 | 2016 | 2017 | |
| double blind | 2017 | 6.59 | 2017 | 2019 | |
| obese children | 2018 | 4.95 | 2018 | 2019 | |
| nuclear receptor | 2018 | 4.86 | 2018 | 2019 | |
| dysbiosis | 2017 | 3.6 | 2018 | 2019 | |
| bacterial translocation | 2014 | 3.53 | 2019 | 2020 | |
| fecal microbiota | 2020 | 4.51 | 2020 | 2021 | |
| alcohol | 2020 | 4.2 | 2020 | 2021 | |
| obese | 2020 | 3.69 | 2020 | 2021 | |
| american association | 2021 | 3.23 | 2021 | 2023 | |
| nash | 2020 | 3.2 | 2021 | 2023 | |

**Figure 10 Keywords map for gut microbiota and nonalcoholic fatty liver disease.** A: Network map of the keywords; B: Keyword clustering timeline graph; C: Top 25 keywords with the strongest citation bursts.

The relationship between gut microbiota and its influence on the development and management of NAFLD has emerged as a key area of research. Studies in this domain aim to elucidate the function of gut microbiota in the initiation and progression of NAFLD, as well as its potential role in the therapeutic approach to NAFLD. These investigations not only advance our comprehension of NAFLD's etiology but also propose innovative strategies and techniques for its treatment.

## ACKNOWLEDGEMENTS

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## FOOTNOTES

**Author contributions:** Huang CY and Huang WP designed the study; Huang CY and Luo ZZ prepared the original manuscript; Luo ZZ conducted the CiteSpace and VOSviewer analysis; Huang CY, Huang WP, Lin LP and Yao YT searched and collected the data and participated in translation of the manuscript; Lai YD, Xu QY and Zhuang HX conducted a thorough review and revision of the manuscript. All authors contributed to this study and granted their final approval for the submitted version. Huang CY and Luo ZZ contributed equally to this work as co-first authors. During the preparation and revision of the manuscript, Lai YD and Xu QY shared the responsibility of comprehensively reviewing and revising the manuscript as well as communicating and coordinating with the reviewers, the editorial team, and other authors. Their close cooperation and efficient communication ensured the smooth progress and high quality of the manuscript. Setting them as co-corresponding authors can more fairly reflect the contribution of each author and help to improve the overall quality of the study.

**Conflict-of-interest statement:** The research was carried out on the assumption that there were no potential conflicts of interest regarding any business or financial relationships.

**PRISMA 2020 Checklist statement:** The authors have read the PRISMA 2020 Checklist, and the manuscript was prepared and revised according to the PRISMA 2020 Checklist.

**Country of origin:** China

**ORCID number:** Cai-Yun Huang 0009-0003-1488-672X; Ya-Dong Lai 0009-0006-8429-2734.

**S-Editor:** Qu XL
**L-Editor:** A
**P-Editor:** Zhao YQ

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