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\*CORRESPONDENCE Yuanyuan Yan ⊠ 13977124832@163.com Bo Zhang ⊠ zhang530021@163.com

<sup>†</sup>These authors have contributed equally to this work

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### Mapping the evolution and impact of ketogenic diet research on diabetes management: a comprehensive bibliometric analysis from 2005 to 2024

#### Zonghuai Li<sup>1†</sup>, Anxia Li<sup>2†</sup>, Pingping Liu<sup>2</sup>, Bo Zhang<sup>1\*</sup> and Yuanyuan Yan<sup>2\*</sup>

<sup>1</sup>Scientific Research Center, Guilin Medical University, Guilin, China, <sup>2</sup>Department of Pharmacy, Sanya Central Hospital (The Third People's Hospital of Hainan Province), Sanya, Hainan, China

**Objective:**The ketogenic diet (KD) has been explored for diabetes management; however, a quantitative synthesis of its specific effects on diabetes has not yet been conducted. This study aims to examine the current status and research hotspots of KD in diabetes management from 2005 to 2024, providing a reference for future research.

**Methods:** We retrieved articles published between 2005 and 2024 from the Web of Science database and analyzed them using R software, VOSviewer, and CiteSpace.

**Results:** This study includes 432 relevant publications. From 2005 to 2024, the volume of literature in this field has shown a steady upward trend, with a notable increase from 2017 to 2021, and a slight decline observed from 2021 to 2023. The United States is the leading country in terms of the number of publications, followed by China, Australia, and Canada. The United States not only leads in publication volume but also maintains a broader international collaboration network. *Nutrients* and the *American Journal of Clinical Nutrition* are the most frequently published and cited journals. Current research hotspots primarily focus on the impact of KD on blood glucose control, insulin resistance, and lipid metabolism in diabetic patients. Mechanistic studies on KD in diabetes management concentrate on aspects such as the "regulation of genes by  $\beta$ -hydroxybutyrate," "anti-inflammatory effects," and "oxidative stress." The role of the gut microbiome is also emerging as an important research area. Currently, exploring the application of KD in managing different age groups and types of diabetes has become a significant research trend.

**Conclusion:** As an emerging dietary intervention, KD is gradually attracting widespread attention from researchers around the world and is expected to become a major research focus in the future for diabetes management and control. This paper provides a systematic review and analysis of the current research status and hotspots of KD in diabetes management, offering important references and insights for future research in related fields.

#### KEYWORDS

ketogenic diet, diabetes, bibliometrics, insulin resistance, gut microbiome

#### 1 Introduction

Diabetes is a group of metabolic diseases caused by insulin secretion defects or insulin action disorders, primarily characterized by chronic hyperglycemia (1). The pathological mechanisms include impaired pancreatic β-cell function and insulin resistance (2). Hyperglycemia can trigger acute complications such as ketoacidosis and hyperosmolar coma and lead to long-term chronic complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy (3, 4). Additionally, diabetes is associated with an increased risk of various cancers (5). In recent years, the prevalence of diabetes has rapidly increased. According to the International Diabetes Federation, the global number of diabetes patients has surpassed 460 million and is projected to reach 700 million by 2045 (6). Both developed and developing countries are severely affected by diabetes, particularly due to lifestyle westernization, population aging, and obesity prevalence (7). The burden of diabetes is particularly heavy, significantly impacting patients' quality of life and imposing substantial social and economic costs. Current diabetes treatments include lifestyle interventions, oral hypoglycemic agents, and insulin therapy (8). Lifestyle interventions focus on diet control and increased physical activity (9). Common medications include metformin, sulfonylureas, GLP-1 receptor agonists, and SGLT2 inhibitors (10). Despite these treatments, many patients fail to achieve optimal glycemic control, and medications may have adverse effects. Thus, finding new treatment approaches has become a research focus.

The ketogenic diet (KD) induces ketosis by providing a high-fat, low-carbohydrate, and moderate-protein dietary pattern, replacing glucose with ketone bodies as the primary energy source (11). By significantly reducing carbohydrate intake, it lowers insulin levels, increases fat oxidation, and promotes ketone body production, physiologically mimicking fasting (12). Initially used to treat refractory epilepsy, KD has recently garnered attention for its potential in weight loss and metabolic disease management (13, 14). Several studies have found that the ketogenic diet can modulate the expression of specific microRNAs. For instance, under the ketogenic dietary condition, changes in the levels of miR-Let-7b-5p, miR-143-3p, and miR-504-5p have been observed. These microRNAs are associated with the regulation of mTOR and PPARs signaling pathways (15), which play a critical role in lipid metabolism and contribute significantly to weight reduction in patients (16). HOMA is an index used to quantitatively assess the effects of insulin resistance and  $\beta$ -cell dysfunction on fasting hyperglycemia (17). In one animal study, the ketogenic diet improved insulin sensitivity through the modulation of miRNAs such as miR-205 and miR-411, leading to weight loss and effectively regulating the HOMA index (18). Studies show that KD can significantly lower blood glucose and glycated hemoglobin levels in diabetic patients, improve insulin sensitivity, and aid in weight control (19, 20). Some studies have also shown indicates that KD can improve lipid profiles and reduce cardiovascular risk (21). Further studies indicate that the ketogenic diet markedly improves symptoms in migraine patients, significantly reducing pain (22). It also demonstrates beneficial effects in epilepsy control and has neuroprotective properties (23). For rare conditions like GLUT1 deficiency syndrome, KD has been widely recognized as the gold standard for treatment (24). By dramatically reducing carbohydrate intake and increasing fat consumption, KD enhances fat oxidation and reduces body weight, significantly alleviating symptoms of lipoedema (25). Simultaneously, this dietary pattern inhibits tumor cells from obtaining energy from the microenvironment, showing potential in cancer treatment. These findings collectively suggest that the ketogenic diet is a multifaceted dietary strategy with several health benefits. However, the long-term safety and feasibility of KD in diabetes management remain controversial, necessitating further research to validate its long-term effects and potential risks. For example, prolonged adherence to the ketogenic diet may increase levels of total cholesterol, low-density lipoprotein (LDL), and triglycerides in the body, consequently elevating the risk of cardiovascular diseases such as atherosclerosis (26, 27). Due to the unique nature of the ketogenic diet, individuals may also experience nutritional deficiencies, such as insufficient intake of vitamins A, D, or calcium, which could lead to conditions like night blindness or an increased risk of fractures. Additional side effects may include muscle weakness and arrhythmias (28). Another potential risk is the development of acute kidney injury. In one clinical case, a patient who strictly followed the ketogenic diet and took herbal supplements containing Uncaria tomentosa developed acute interstitial nephritis (AIN). The patient's kidney function improved significantly after discontinuing the supplement and receiving corticosteroid treatment (29). Regrettably, the lack of hotspot and frontier analyses in this research field hinders researchers from quickly and accurately identifying future research directions.

Bibliometrics, as a scientific quantitative analysis tool, reveals development trends, hot topics, and frontiers in specific research fields through the statistical analysis of scientific literature (30). For research on KD in diabetes management, bibliometric analysis not only helps systematically review the current research status but also identifies research gaps and future directions, providing reference and guidance for subsequent basic research and clinical applications. Therefore, this study will apply bibliometric methods to comprehensively analyze the research on KD in diabetes treatment, aiming to provide valuable references and insights for scholars and clinicians in the field and promote further development in this area.

#### 2 Materials and methods

#### 2.1 Data collection

The data we collected were sourced from Web of Science Core Collection (WoSCC; Guangxi Medical University Purchase Edition) on July 11, 2024. We employed the following search formula: ((((TS=("ketogenic diet")) AND TS=(diabetes)) AND PY=(2005-2024)) AND DT=(Article OR Review)) AND LA=(English). After eliminating irrelevant documents, a total of 432 papers (excluding duplicates) were identified. The retrieved papers were saved in plain text format and exported as complete records, including cited references.

#### 2.2 Data analysis

In this study, we utilized the previously established research methodology (31). For the analysis of annual publications, Origin 2018 was employed. Additionally, R software (version 3.6.3) with the bibliometrix package (version 4.0, http://www.bibliometrix.org) (32), VOSviewer (version 1.6.17) (33), and CiteSpace (version 6.1.4) (34) were utilized. To ensure data accuracy and reliability, two different authors independently performed data extraction and analysis management.

The Bibliometrix software enabled the visual analysis and mapping of scientific knowledge. VOSviewer was employed to visualize country and institutional co-authorship networks, source co-citation analysis, and keyword co-occurrence. In the coauthorship network analysis, parameters were set as follows: minimum number of documents for a country or institution  $\geq 4$ . For co-citation analysis, the parameter was set as a minimum number of citations for a source  $\geq 50$ . In keyword co-occurrence analysis, parameters included a minimum number of occurrences of a keyword  $\geq 10$ , with exclusions of keywords such as "ketogenic diet," "diabetes" and synonyms of above words. The journal impact factors (IFs) were retrieved from Journal Citation Reports (JCR) in 2023.

#### **3** Results

### 3.1 Overview of selected studies on KD in diabetes

A total of 432 unique records were obtained from WoSCC after removing duplicates. Between 2005 and 2024, the number of publications concerning KD and diabetes has shown a steady increase, as depicted in Figure 1A. This upward trajectory indicates

growing research interest in exploring the connection between KD and diabetes.

An analysis of the corresponding authors' countries indicated that USA (n = 142) was the leading publisher, followed by the Italy (n = 54), China (n = 49), Australia (n = 21), and Canada (n =21). Moreover, 17.6% of publications from USA and 24.1% from Italy involved multi-country collaborations (MCPs) as shown in Figure 1B and detailed in Table 1. Notably, the USA not only leads in the number of publications but also maintains a broader network of international partnerships, as shown in Figure 2. These data indicate that USA researchers place greater emphasis on studying the effects of KD on diabetes. This may be related to the unique context of the USA, such as dietary habits that are often high in sugar and carbohydrates, which are primary contributors to obesity and diabetes.

#### 3.2 Journal analysis and visualization

For examining the journals with the highest publication and citation contributions in the field of KD and diabetes, we utilized the Bibliometrix package in R software. Graphical representations were created using the ggplot2 package. Furthermore, co-cited journal analysis was conducted using VOSviewer.

Our investigation yielded a total of 432 documents dispersed across 230 scholarly journals (see Supplementary material 1 for detailed information). As illustrated in Table 2 and depicted in Figure 3A, the *Nutrients* (n = 40, IF = 4.8) emerged as the leading publisher, followed by *Frontiers in Nutrition* (n = 16, IF = 4), *Nutrition and Metabolism* (n = 9, IF = 3.9), *Nutrition* (n = 8, IF = 3.2), and *Diabetes Obesity and Metabolism* (n = 7, IF = 5.4). Table 3 and Figure 3B showcase the most frequently cited journals, including *American Journal of Clinical Nutrition* (n = 877, IF = 6.5), *Diabetes Care* (n = 797, IF = 14.8), *Nutrients* (n = 789, IF = 4.8), *Diabetes* (n = 512, IF = 6.2), and *New England Journal of* 

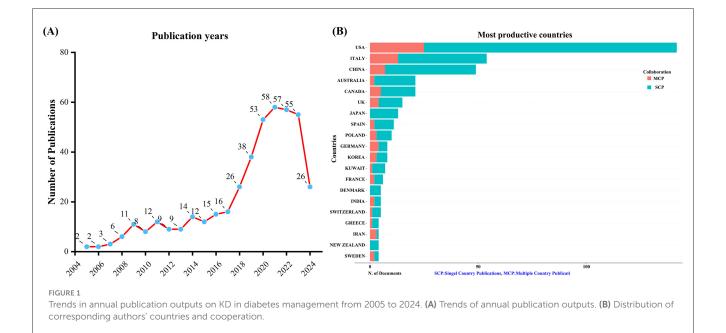


TABLE 1 Most relevant countries by corresponding authors.

Country	Articles	SCP	МСР	Freq	MCP_Ratio
USA	142	117	25	0.329	0.176
Italy	54	41	13	0.125	0.241
China	49	42	7	0.113	0.143
Australia	21	19	2	0.049	0.095
Canada	21	16	5	0.049	0.238
United Kingdom	15	11	4	0.035	0.267
Japan	13	13	0	0.03	0
Spain	11	9	2	0.025	0.182
Poland	10	7	3	0.023	0.3
Germany	8	4	4	0.019	0.5
Korea	8	5	3	0.019	0.375
Kuwait	7	6	1	0.016	0.143
France	6	4	2	0.014	0.333
Denmark	5	5	0	0.012	0
India	5	3	2	0.012	0.4
Switzerland	5	4	1	0.012	0.2
Greece	4	3	1	0.009	0.25
Iran	4	1	3	0.009	0.75
New Zealand	4	4	0	0.009	0
Sweden	4	2	2	0.009	0.5

MCP, Multiple country publication; SCP, Single country publication

*Medicine* (n = 483, IF = 94.3). Notably, the co-cited journals map in Figure 4 demonstrates that *Nutrients*, *Diabetes Care*, and *American Journal of Clinical Nutrition* act as central collaboration hubs. These findings collectively underscore the influential role of the *Nutrients* in the field of KD in diabetes.

#### 3.3 Citation bursts

To delve deeper into the exploration of the forefront and focal areas of KD in diabetes, we utilized CiteSpace to identify the top 25 most significant citation bursts related to KD in diabetes (refer to Figure 5). The titles of these citations, along with their respective DOIs, are listed in Supplementary material 2. Remarkably, the three citations exhibiting the most pronounced citation bursts were: (1) "Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base (strength: 12.31);" (2) "Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets (strength: 8.73);" (3) "The ketone metabolite  $\beta$ -hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease (strength: 7.74)." Furthermore, the titles of the three most cutting-edge citation bursts were: (1) "Effects of a ketogenic diet in overweight women with polycystic ovary syndrome;" (2) "European guidelines for obesity management in adults with a very low-calorie ketogenic diet: a systematic review and meta-analysis;" (3) "Low-carb and ketogenic diets in type 1 and type 2 diabetes."

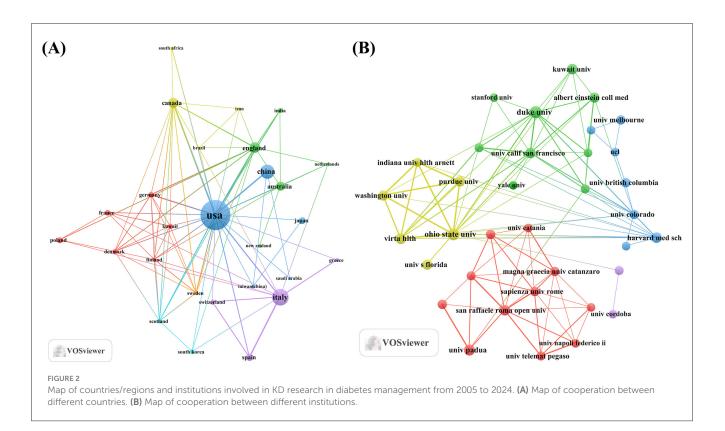
Overall, through the most cited references and reference burst analysis, we have identified two key areas of focus within the field of KD in diabetes: 1. Metabolic effects of KD on diabetes patients, including glycemic control, insulin resistance, and lipid metabolism; 2. Mechanistic studies of KD, including the multidimensional roles of ketone bodies (such as  $\beta$ -hydroxybutyrate) in metabolism, signaling, and therapeutics.

## 3.4 Keyword clusters and evolution of themes

Keyword clusters are essential for rapidly grasping the main research themes and directions in a particular area. In our study, VOSviewer was used to identify 2,145 keywords. Table 4 displays the top 20 keywords, each occurring more than 27 times, highlighting the prominent research focuses. The most frequently appearing keyword was "weight loss" (n = 131), followed by "obesity" (n = 127), "insulin-resistance" (n = 108), "ketone-bodies" (n = 62), "beta-hydroxybutyrate" (n = 56), and "metabolism" (n = 56).

Through cluster analysis, we observe four different colored clusters in Figure 6. (1) Effects of the ketogenic diet on diabetes and related metabolic syndrome (red dots), there are 20 keywords, including energy-expenditure, glycemic control, insulin-resistance, metabolic syndrome, weight loss, and so on. (2) Metabolic and physiological mechanisms of the ketogenic diet in diabetes management (green dots), there are 19 keywords, including ketonebodies, mechanisms, metabolism, mitochondria, oxidative stress, and so on. (3) Efficacy and applications of the ketogenic diet in different populations (blue dots), there are 18 keywords, including adults, children, hyperglycemia, intervention, therapy, and so on. (4) Long-term effects of the ketogenic diet on diabetes-related lipid metabolism and inflammation (yellow dot), there are 12 keywords, including inflammation, lipid-metabolism, gut microbiota, longterm, obesity, and so on. All keywords contained in the four clusters can be found in Supplementary material 3.

Additionally, in order to project forthcoming trends within this domain, we utilized the bibliometrix toolkit within the R programming environment to construct a dynamic thematic progression chart (Figure 7). The period from 2005 to 2013 was characterized by a predominant focus on the pathophysiological mechanisms of diabetes, encompassing insulin resistance and metabolic disorders, alongside the exploration of diagnostic approaches and disease classification. Transitioning into the years 2013 to 2015, there was a discernible shift toward the examination of the ketogenic diet's potential impact on diabetes management, with a particular emphasis on weight loss and body composition modulation, as well as the influence of lowcarbohydrate diets on metabolic pathways. From 2015 to 2021, the research community expanded its scope to include the effects of ketogenic diets on inflammation and cardiovascular risk factors, while also investigating the implications of glycemic control and the role of high-protein, weight-loss diets. In the most recent phase, spanning 2021 to 2023, the adoption of rigorous scientific



Sources	Documents	IF (2023)	Cites
Nutrients	40	4.8	789
Frontiers In Nutrition	16	4	99
Nutrition and Metabolism	9	3.9	335
Nutrition	8	3.2	275
Diabetes Obesity and Metabolism	7	5.4	151
Frontiers In Endocrinology	7	3.9	108
Metabolites	7	3.4	19
PLoS One	7	2.9	469
Current Diabetes Reports	6	5.2	72
Current Opinion In Endocrinology Diabetes	6	2.6	35

TABLE 2 Top 10 journals with the most published.

methodologies, such as randomized trials and double-blind studies, became prominent, enhancing the validity of research findings. Additionally, the impact of low-fat diets and calorie restriction on diabetes and weight management garnered increased attention. Our thematic evolution map suggests that future research is poised to delve deeper into the risk factors associated with diabetes, especially in pediatric populations and the prevalence of the disease. Furthermore, obtaining more comprehensive and reliable clinical data will be crucial for advancing research on the ketogenic diet's impact on diabetes.

#### 3.5 Comprehensive analysis of hotspots

In conclusion, our extensive analysis, which includes citation bursts, keyword frequency analysis, keyword clustering, and thematic evolution, has identified emerging research hotspots in the intersection of KD and diabetes. Our findings reveal that the research hotspots in this field are primarily focused on three key directions. (1) Metabolic effects of KD in diabetic patients: impacts on blood glucose control, insulin resistance, and lipid metabolism. (2) Mechanisms of KD in diabetes improvement: roles of ketone bodies in metabolic and signaling pathways. (3) Application of KD in various populations: efficacy across different age groups and types of diabetes, supported by clinical evidence.

#### 4 Discussion

#### 4.1 General information

In this study, we collected a comprehensive corpus of 432 publications covering the period from 2004 to 2024. The results indicate a steady increase in the number of publications on the KD and diabetes from 2004 to 2024. This upward trend suggests a growing interest among researchers in exploring the relationship between KD and diabetes. However, it is noteworthy that there has been a decline in the number of publications in 2022 and 2023 compared to 2021. This decline may be attributed to the following four reasons: (1) Conceptual Ambiguity: The definition of the KD is not uniform across different studies, particularly regarding standards and methods for calculating carbohydrate intake. Variations in carbohydrate intake standards

And Obesity

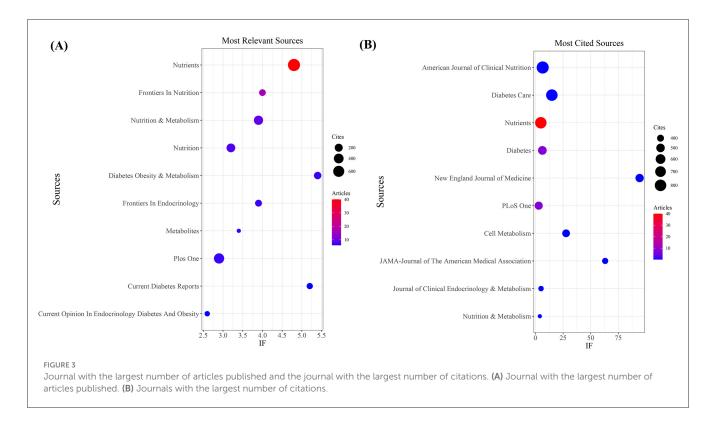


TABLE 3	Top 10	journals	with	the	most	cited.
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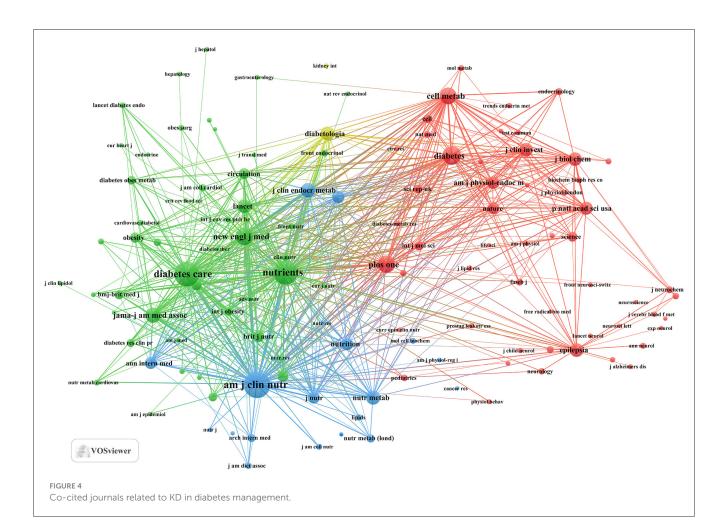
Sources	Cites	IF (2023)	Documents
American Journal of Clinical Nutrition	877	6.5	0
Diabetes Care	797	14.8	0
Nutrients	789	4.8	40
Diabetes	512	6.2	7
New England Journal of Medicine	483	94.3	0
PLoS One	469	2.9	7
Cell Metabolism	446	27.7	0
JAMA-Journal of The American Medical Association	370	63.1	0
Journal of Clinical Endocrinology and Metabolism	348	5	0
Nutrition and Metabolism	335	3.9	0

(e.g., net carbohydrates vs. total carbohydrates) and whether other factors (such as protein intake) are considered can affect the comparability and consistency of study results. The lack of a clear definition of KD poses significant challenges for researchers (11). (2) Participant Adherence and Long-Term Sustainability: KD is a highly restrictive dietary pattern requiring participants to strictly control carbohydrate intake. Many studies have found that participants struggle to adhere to this diet over the long term, which affects the reliability of study results and increases the difficulty of follow-up and data collection (35, 36). (3) High Restrictiveness of KD: KD imposes strict limitations on daily food intake, and long-term adherence may lead to side effects such as visceral damage, which can reduce patient adherence (37, 38). Consequently, researchers face increased challenges in exploring this area. (4) Shift in Research Interest: Over time, researchers and clinicians have shown increased interest in other dietary interventions, such as the Mediterranean diet and low-calorie diets. These methods have demonstrated better outcomes in some studies for diabetes management (39). As a result, research interest has gradually shifted from KD to these alternative dietary approaches.

In the field of research on the relationship between KD and diabetes, the United States is the country with the highest number of published articles. This trend may be related to the unique dietary environment in the U.S., where diets typically include high levels of carbohydrates and sugary foods, potentially leading to a higher prevalence of diabetes and thus a greater need to explore new dietary habits. The 432 publications are distributed across 230 journals, with prominent journals such as *Nutrients, Frontiers in Nutrition*, and *Nutrition and Metabolism* contributing a substantial number of articles. Notably, *Nutrients* has emerged as a major research focus, publishing a significant volume of articles and receiving a considerable number of citations. Its prominent position highlights *Nutrients* as a key publication in the field of KD and diabetes research, confirming its role as a primary channel for disseminating research findings in this area.

#### 4.2 Hotspots and development trends

As mentioned above, through a comprehensive analysis of literature clustering, keyword frequency analysis, keyword



clustering, and topic evolution, we identified potential research hotspots regarding the impact of KD on diabetes. The results show that the research frontiers and hotspots in this field mainly focus on three aspects. First, the metabolic effects of KD on diabetic patients, including its impact on blood glucose control, insulin resistance, and lipid metabolism. Second, the mechanisms by which KD improves diabetes, particularly the role of ketone bodies in metabolic and signaling pathways. Finally, the application of KD in different populations, including its efficacy in various age groups and types of diabetes, with existing clinical evidence supporting these applications.

## 4.2.1 The metabolic effects of KD on diabetic patients, including its impact on blood glucose control, insulin resistance, and lipid metabolism

Based on our analysis of the existing literature, the ketogenic diet exerts a substantial regulatory impact on blood glucose control, insulin resistance, and lipid metabolism. One significant characteristic of KD is its low carbohydrate intake, which reduces the availability of glucose as an energy source (40, 41). HbA1c, a commonly used marker for blood glucose control, reflects the average blood glucose levels over the past 3 months (42). Research indicates that KD can effectively improve blood glucose fluctuations in individuals with Type 1 diabetes and lower HbA1c levels (43, 44). Additionally, low carbohydrate intake further shifts the body's energy supply from glucose metabolism to lipid metabolism, inducing a new metabolic pathway (45). This metabolic pathway can enhance the efficiency of fat metabolism, particularly visceral fat. However, increased visceral fat may also lead to further insulin resistance (46, 47). Importantly, KD also affects the composition of lipids in the body. It can modestly lower low-density lipoprotein cholesterol (LDL-C), known as "bad" cholesterol (48), while modestly increasing high-density lipoprotein cholesterol (HDL-C), known as "good" cholesterol (49, 50).

## 4.2.2 Mechanisms by which KD improves diabetes, particularly the role of ketone bodies in metabolic and signaling pathways

Through the analysis of keywords and related information, we identified that the primary mechanisms by which the ketogenic diet affects diabetic patients include the regulation of  $\beta$ -hydroxybutyrate-related genes, anti-inflammatory effects, and oxidative stress. During the ketogenic diet, oxaloacetate rapidly participates in gluconeogenesis; however, as the concentration of ketone bodies in the body increases, the production of hepatic glycogen gradually declines. Therefore, the ketogenic diet can modulate the level of gluconeogenesis to a certain

Top 25	References	with the	Strongest	Citation Bursts
1			0	

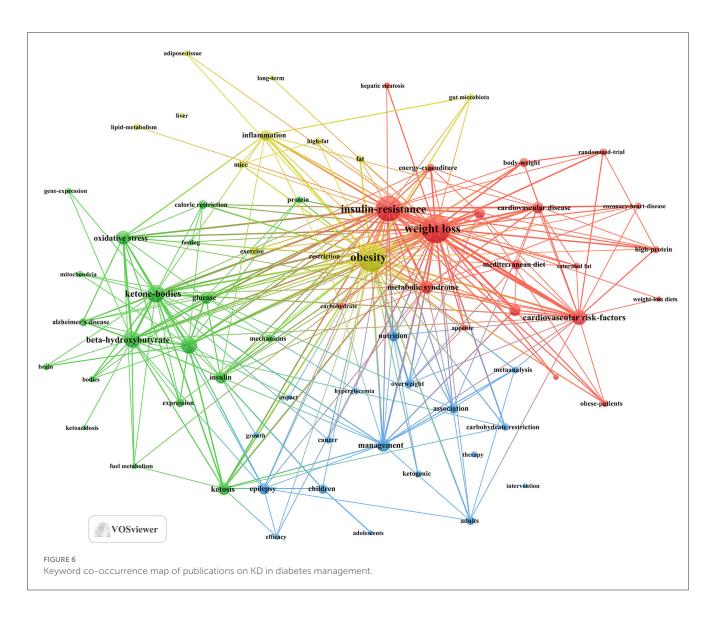
References	Year	Strength Begin	
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Accur so A, 2008, NUTR ME TAB, V5, P0, DOI 10.1186/1743-7075-5-9, DOI	2008	6.07 2008	2013
Amer Diabet Associat, 2008, DIABE TES CARE, V31, PS61, DOI 10.2337/dc08-S061, DOI	2008	4.96 2008	2013
Dashti HM, 2007, MOL CELL BIOCHEM, V302, P249, DOI 10.1007/s11010-007-9448-z, DOI	2007	6.52 2009	2012
Westman EC, 2008, NUTR ME TAB, V5, P0, DOI 10.1186/1743-7075-5-36, DOI	2008	5.93 2009	2012
Shai I, 2008, NE W ENGL J MED, V359, P229, DOI 10.1056/NE JMo a0708681, DOI	2008	6.08 2010	2013
Hussain T A, 2012, NUTRITION, V28, P1016, DOI 10.1016/j.nut.2012.01.016, DOI	2012	7.42 2013	2017
Paoli A , 2013, EUR J CLIN NUTR, V67, P789, DOI 10.1038/ejcn.2013.116, DOI	2013	8.73 2014	2018
Shimazu T , 2013, SCIENCE, V339, P211, DOI 10.1126/science.1227166, DOI	2013	5.44 2014	2018
Feinman RD , 2015, NUTRITION, V31, P1, DOI 10.1016/j.nut.2014.06.011, DOI	2015	12.31 2016	2020
Gibson AA , 2015, OBES REV , V16, P64, DOI 10.1111/obr .12230, DOI	2015	4.72 2016	2020
Hall KD, 2016, AM J CLIN NUTR, V104, P324, DOI 10.3945/ajen.116.133561, DOI	2016	5.39 2017	2021
Tay J, 2015, AM J CLIN NUTR, V102, P780, DOI 10.3945/ajcn.115.112581, <u>DOI</u>	2015	4.7 2017	2018
Cox PJ, 2016, CELL ME TAB, V24, P256, DOI 10.1016/j.cmet.2016.07.010, DOI	2016	4.61 2017	2020
Youm YH, 2015, NA T MED, V21, P263, DOI 10.1038/nm.3804, DOI	2015	7.74 2018	2020
Rober ts MN, 2017, CELL ME TAB, V26, P539, DOI 10.1016/j.cmet.2017.08.005, DOI	2017	4.73 2018	2020
Goday A , 2016, NUTR DIABE TES, V6, P0, DOI 10.1038/nut d.2016.36, DOI	2016	6.01 2019	2021
Puchalska P , 2017, CELL ME TAB, V25, P262, DOI 10.1016/j.cmet.2016.12.022, DOI	2017	6 2020	2022
Kosinski C, 2017, NUTRIENTS, V9, P0, DOI 10.3390/nu9050517, DOI	2017	4.82 2020	2022
Kirkp atrick CF , 2019, J CLIN LIPIDOL, V13, P689, DOI 10.1016/j.jacl.2019.08.003, DOI	2019	5.43 2021	2024
Yuan X J, 2020, NUTR DIABE TES, V10, P0, DOI 10.1038/s41387-020-00142-z, DOI	2020	7.12 2022	2024
Choi Y J, 2020, NUTRIENTS, V12, P0, DOI 10.3390/nu12072005,DOI	2020	6.31 2022	2024
Bolla AM, 2019, NUTRIENTS, V11, P0, DOI 10.3390/nu11050962, DOI	2019	4.85 2022	2024
Muscogiuri G, 2021, OBESIT Y FACTS, V14, P222, DOI 10.1159/000515381, DOI	2021	4.78 2022	2024
Paoli A , 2020, J TRANSL MED , V18, P0, DOI 10.1186/s12967-020-02277-0, DOI	2020	4.78 2022	2024
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FIGURE 5			

Top 25 references with the strongest citation bursts in KD for diabetes management.

Rank	Keywords	Count
1	Weight loss	131
2	Obesity	127
3	Insulin-resistance	108
4	Ketone-bodies	62
5	Beta-hydroxybutyrate	56
6	Metabolism	56
7	Cardiovascular risk-factors	48
8	Oxidative stress	42
9	Metabolic syndrome	41
10	Management	40
11	Ketosis	37
12	Glucose	34
13	Insulin	34
14	Glycemic control	33
15	Epilepsy	32
16	Cardiovascular disease	31
17	Inflammation	30
18	Nutrition	30
19	Body-composition	29
20	Mediterranean diet	27

#### TABLE 4 The top 20 keywords.

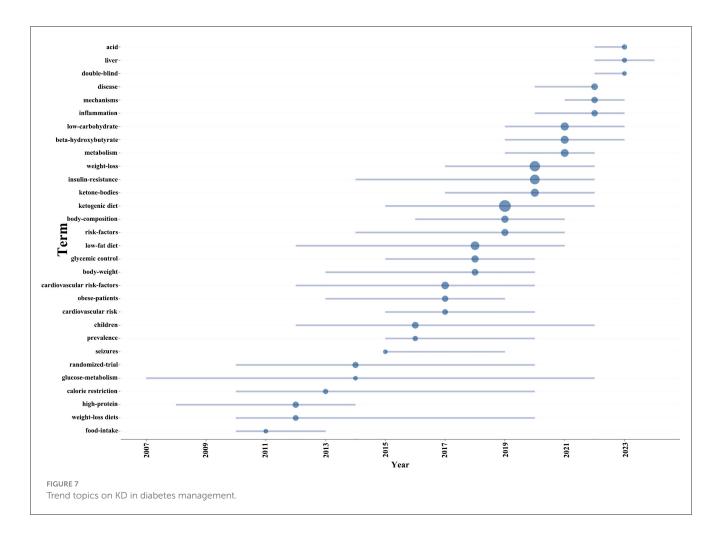
extent, effectively preventing excessive blood glucose levels and achieving good glycemic control (51). In the pathway of insulin resistance, the effector protein GLUT4 is closely related to the fatty acid metabolism-associated protein HADH1 (52). GLUT4 translocates from storage vesicles to the cell membrane under insulin stimulation, subsequently acting as a glucose transporter to facilitate glucose entry into the cells, thereby lowering blood glucose levels. The enhanced expression of HADH1 regulates GLUT4 activity, thereby improving insulin sensitivity (53, 54). β-Hydroxybutyrate ( $\beta$ OHB) is one of the primary ketone bodies in KD (55). Research indicates that  $\beta$ OHB can inhibit the activity of certain histone deacetylases (HDACs) (56). HDACs regulate gene expression by removing acetyl groups from histones (57). When HDACs are inhibited, the expression of brain-derived neurotrophic factor (BDNF) is enhanced, and BDNF expression can reduce oxidative stress and inflammatory responses in the body (56). In addition, HDAC inhibition can reduce the activity of nuclear factor  $\kappa B$  (NF- $\kappa B$ ) (58). These factors play a key role in the expression of pro-inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$  (59), which are crucial contributors to the inflammatory response (58). Oxidative stress and inflammation induced by diabetes can impair  $\beta$ -cell function, leading to insulin resistance and disrupted blood glucose regulation (60), which in turn causes a range of diabetes-related complications (61, 62). Additionally, a low-carbohydrate diet can improve the gut microbiota through various mechanisms (63). For example, it can increase the abundance of Lactobacillus murinus ASF361, which encodes bile



salt hydrolase (BSH). This change leads to elevated levels of tauroursodeoxycholic acid (TDCA) and tauroursodeoxycholic acid (TUDCA) in the serum. These bile acids reduce intestinal energy absorption by inhibiting the expression of intestinal carbonic anhydrase 1 (Car1). This process not only helps with weight loss but may also lower fasting blood glucose levels, thereby positively impacting metabolic diseases like diabetes (60). Through these mechanisms, KD may offer new perspectives for improving metabolic health, particularly in the management and treatment of diabetes.

# 4.2.3 Application of KD in different populations, including its efficacy for various age groups and types of diabetes, with existing clinical evidence supporting it

Certainly, after analysis, investigating diabetes across various age groups and types is currently a focal point of research in this field. (1) Type 1 Diabetes (T1D) in Adults: Before the discovery of insulin, strict daily control of carbohydrate intake was the only effective treatment for T1D (64). Despite advances in modern medicine with various treatment options for T1D, KD remains an effective method for blood glucose control (65). Numerous studies have shown that KD not only helps reduce blood glucose fluctuations but also lowers HbA1c levels (66, 67). However, maintaining a KD long-term presents a significant challenge for many patients, as most find it difficult to adhere to this diet over time (68). (2) T1D in Children: Many studies indicate that the KD can provide significant benefits for children with T1D in the short term (69). However, regular monitoring of growth and nutritional markers is necessary to ensure these remain within normal ranges (70). This is because the KD may increase the risk of cardiovascular diseases and other health issues in children (71, 72). (3) Type 2 Diabetes (T2D) in Adults: As demonstrated by Goldenberg et al., shortterm KD can significantly improve blood glucose control and aid in weight management for T2D patients (36). However, further research is needed to clarify the long-term effects and potential risks of sustained KD. (4) T2D in Children: Research on adolescent T2D patients is still limited. A retrospective study showed that adolescents following a KD experienced shortterm diabetes remission and reduced BMI. However, due to



participant attrition in the study, the long-term effects may be underestimated (73).

#### 4.3 Strengths and limitations

This study provides a comprehensive overview of the general landscape, hotspots, and research trends in a specific field using the WoSCC database as the data source, aiding in a deeper understanding of the field and exploring future research directions. However, this study also has some notable limitations. First, reliance solely on the WoSCC database may result in the omission of some relevant literature, despite its reputation for high quality and broad recognition as an ideal tool for bibliometric analysis (74). Second, this study includes only English-language publications, which may introduce language bias and limit the generalizability of the findings. Additionally, due to the large number of authors with similar names in China, this study did not conduct an indepth analysis of authors to avoid potential misleading results. Furthermore, analyses conducted using CiteSpace and VOSviewer cannot fully replace systematic searches, and bibliometrics cannot assess the quality of individual studies, as citation metrics are time-dependent, with recent articles possibly having fewer citations primarily due to their publication date (75). Despite these limitations, the conclusions of this study remain highly reliable and provide valuable insights and references for academic research in the field, laying the groundwork for understanding (76). However, the long-term effects of the ketogenic diet on diabetic patients, as well as the potential for other adverse effects, still require further investigation and analysis by additional researchers.

#### 5 Conclusion

This study provides an in-depth exploration of the primary research hotspots and cutting-edge trends related to the application of the ketogenic diet in diabetes management. The key findings are summarized as follows:

- a. The application of the ketogenic diet in diabetes management has garnered substantial global attention, particularly from researchers in the United States, China, Australia, and Canada. These countries are among the most active in this field, and there is significant international collaboration.
- b. Within this research domain, Nutrients and Frontiers in Nutrition are the most active journals. The American Journal of Clinical Nutrition and Diabetes Care are also frequently cited, with Nutrients standing out for both its publication volume and citation frequency, indicating its prominence as a representative journal in this field.

- c. Current research hotspots include the impact of the ketogenic diet on glucose control, insulin resistance, and lipid metabolism in diabetic patients.
- d. Mechanistic studies on the ketogenic diet for diabetes management are focusing on trends such as " $\beta$ -hydroxybutyrate-regulated genes," "anti-inflammatory effects," and "oxidative stress." Additionally, the role of the "gut microbiome" is emerging as an important area of interest.
- e. Research on the management of various types of diabetes across different age groups with the ketogenic diet is a prominent current trend.

In summary, this study offers valuable insights into the research trends and hotspots related to the ketogenic diet in diabetes management by outlining current research prospects and potential focal areas. The findings not only enhance the understanding of the existing state of research but also establish a robust foundation for future research directions. The impact of the ketogenic diet on microRNA is likely to become a primary focus in upcoming studies, as it may promote effective weight reduction and significant improvements in the HOMA index, thereby providing substantial benefits for diabetic patients. However, the potential adverse effects associated with long-term adherence to the ketogenic diet, such as cardiovascular diseases and nutritional deficiencies, must also be addressed as critical areas of investigation. Furthermore, given that the ketogenic diet may influence insulin sensitivity and fat metabolism differently among individuals, personalized ketogenic dietary approaches could emerge as a significant research direction in diabetes management.

#### Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

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#### Author contributions

ZL: Visualization, Writing – original draft. AL: Software, Writing – original draft. PL: Data curation, Writing – original draft. BZ: Writing – original draft, Writing – review & editing. YY: Writing – original draft, Writing – review & editing.

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#### Supplementary material

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