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A bibliometric analysis of the global trends and hotspots for the ketogenic diet based on CiteSpace

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Abstract

The ketogenic diet (KD) is a potential nutritional therapy that is frequently utilized in various conditions. More and more studies are being done on KD in recent years. However, as far as we know, few studies have made an effort to offer a thorough synthesis and assessment of this topic. This paper aims to do a rigorous and thorough evaluation of the knowledge structure, development trend, and research hotspot of scientific outputs connected to KD. The bibliographic records connected to KD from January 1, 2001 to April 22, 2022 were collected using the core collection database of Web of Science. The complex data input, that consisted of the amount of publications, journals, authors, institutions, countries, keywords and cited references, was generated and analyzed visually using CiteSpace. A total of 2676 literatures on the KD were published between 2001 and 2022. The most KD-related publications were found in Epilepsia and Epilepsia Research. The authors with the most KD-related papers are Kossoff EH and Rho J. The United States is the country with the most publications, and Johns Hopkins University, Johns Hopkins University Hospital, and Johns Hopkins Medical Institutions are the institutions with the most articles. The high frequency keywords are “KD,” “ketone body,” “children,” “efficacy,” “weight loss,” “low carbohydrate diet,” “metabolism,” “epilepsy,” “beta hydroxybutyrate,” and “modified atkins diet.” The 2018 study by Kossoff EH on epilepsia and the 2017 study by Puchalska P on ketone body metabolism earned 127 and 114 citations, respectively. The results of this bibliometric analysis provide information on the state and trends in KD and may be used by researchers to pinpoint hot issues and discover new areas of study.

Abbreviations: IL-1β = interleukin-1β, IL-6 = interleukin-6, KD = ketogenic diet.

Keywords: bibliometric analysis, CiteSpace, ketogenic diet, visualized analysis

1. Introduction

The ketogenic diet (KD) is characterized as a very low-carbohydrate, high-fat, and adequate-protein diet,[1] including four major types[2]: the classic KD, the modified Atkins diet, the medium chain triglyceride diet, and the low glycemic index treatment. The KD is a biochemical model of fasting,[3] which replaces glucose with ketone bodies (e.g., acetoacetate, β-hydroxybutyrate, and acetone) as the brain’s dominant fuel source.[4] This dietary buildup of ketones in the blood is also suggested as nutritional ketosis.[5] Since Dr Wilder first proposed the term “ketogenic diet” in 1921,[6] the KD has received attracted increasing attention due to its uses in various clinical conditions, such as epilepsy, Alzheimer’s disease, diabetes, obesity, autism and so on.[7] Currently, the underlying mechanisms of KD therapy have not yet been absolutely understood. Previous studies have shown that KD can modulate nicotinamide adenine dinucleotide levels,[8] decrease circular blood glucose levels,[9] reduce inflammatory and apoptotic mediators expression[10] and inhibit mammalian target of rapamycin signaling pathway.[11] According to a widely held belief, the effectiveness of KD therapy is dependent on a variety of advantageous mechanisms.[12] In spite of the fact that KD has been considered as a complementary or alternative therapy for several diseases, this diet, especially the classic KD, may cause different adverse effects. Gastrointestinal discomfort is the most frequently disclosed adverse effect that comprised of abdominal pain, diarrhea, constipation, vomiting, and gastroesophageal reflux.[13] KD may increase the risk of cardiovascular diseases, which could be due to an augmentation in apoB containing lipoproteins.[14] In addition, other adverse effects such as hyperuricemia, development disorders and kidney stones have also been depicted in related research.[15]

RY and YC contributed equally to this work.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Since our research has no direct connection to specific patients, there is no need for an ethical evaluation. Our study is a bibliographic analysis that primarily involves literature review and analysis.

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CiteSpace is a Java-based bibliometric analysis application used for timely detection and visualization of the status, hot spots and future research directions in scientific literature.[16,17] The visual network analysis of CiteSpace is based on three central concepts: heterogeneous networks, betweenness centrality, and burst detection.[18] Moreover, this software can produce two complementary visualization views: cluster views and time-zone views.[19] According to reports, this software has been downloaded more than 130,000 times in total for each of its versions.[20] Thus far, the CiteSpace platform has been applied to various areas, including medicine, eco-environmental management, agriculture, public health, and others.[21–24]

To our knowledge, bibliometric visualization tools have not been utilized in the domain of KD. Thus, the characteristics of the literature, the stage of the study, the research frontiers, and the research hotspots of KD have not been thoroughly investigated or summarized. In this study, we make an attempt to discuss the current status of KD research via Citespace, which can display the overall development trend of KD, provide meaningful information and give reference to future research.

2. Methods

2.1. Data acquisition

The core set of Web of Science, the most famous and trustworthy global research database, is where the study data was retrieved. All data were searched on April 22, 2022. The data retrieval strategy was as follows: Topic = KD. Document type = Article OR Review. Publication date (custom year range) = January 1, 2001 toApril 22, 2022. Language = English. A total of 3938 papers were obtained. We screened these publications by title, abstract, and even full text, after which 2676 papers were assessed for eligibility.

2.2. Visualization and analysis

In this study, version 6.1. R2 of CiteSpace was used for all visual analyses. After data acquisition, the data set was exported to CiteSpace for further analysis. We set the overall time span from January 2001 to April 2022, slice length: one-year, g-index (k = 25), choice Pathfinder and Pruning node, and ran CiteSpace to the generate networks. All of the other necessary parameters were set to the default values provided by CiteSpace. In the graph structure, diverse nodes represented different elements, including journals, authors, institutions, countries, and keywords. The size of the nodes reveals the frequency of occurrence, while the color of the nodes reveals the periods of occurrence. The co-occurrence relationship was considered to exist along the connection lines between nodes. Additionally, nodes with purple trims indicate strong betweenness centrality, which is frequently used to identify crucial or turning points in a field. The ethical approval was not necessary because the data do not contain any privacy information of patients.

3. Results

3.1. Research performance

We retrieved 2676 documents related to KD, as shown in Figure 1. The number of relevant articles published each year has been increasing from 2001 to 2022. Three phases can be seen in publishing trends. The first phase, runs from 2001 to 2012, saw a slight growth in the number of relevant studies. During this period, less than 100 articles were published annually, showing that relevant academics have not yet showed tremendous interest in the KD. The second phase, as well as stable growth stage, runs from 2013 to 2018. It is characterized by a steady development in the volume of related research. The third stage, rapid growth stage, which lasts from 2019 to 2022, saw a sharp rise in the number of articles produced. Increasing than 200 publications were published each year between 2019 and 2022, which shows that the research on the KD has gained more attention and produced concrete study results since 2019.

3.2. Publication performance by Journals

Articles about KD are distributed over hundreds of journals, with top 3 journals are Epilepsia (1587 articles), Epilepsia Research (1029 articles) and Neurology (920 articles). The top 10 publications were shown in Figure 2 and Table 1. One possible reason contributes to these 3 journals as top ones is that they focus on epilepsy, which is one of the research hotspots in the field of KD. As a result, they have a lot of influence on the topic of KD.

3.3. Co-authors analysis

The coauthors network is displayed in Figure 3. The larger the size of the circle, the more articles published by the scholar. The connection or cooperation amongst scholars is indicated by the line connecting the circles, and the thicker the line, the greater the degree of this cooperation. The purple rings reveal that these scholars are more central. Observing Figure 3, Kossoff EH was the most representative author in this area with 97 articles published, followed by Rho J and Kim H with 56 and 41 articles, respectively. It demonstrates the extraordinary contributions that these 3 authors have made to this field. In addition, the centrality of Kossoff EH, Rho J, Turner Z, and

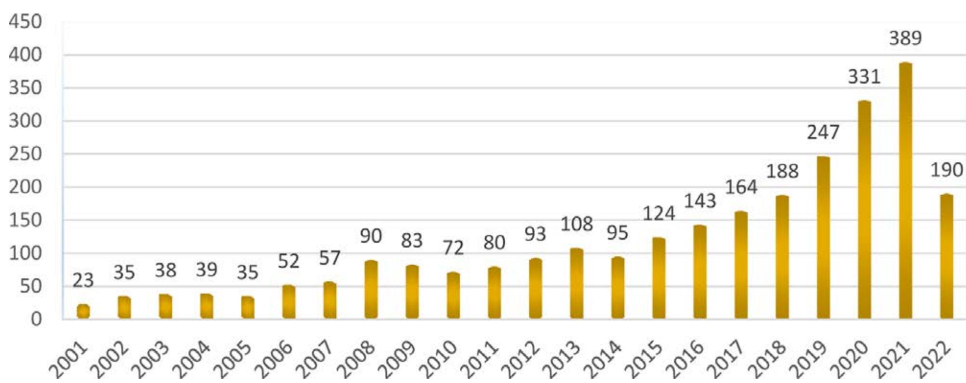

Figure 1. Time sequence of relevant papers on KD published from 2001 to 2022 in Web of Science. KD = ketogenic diet.

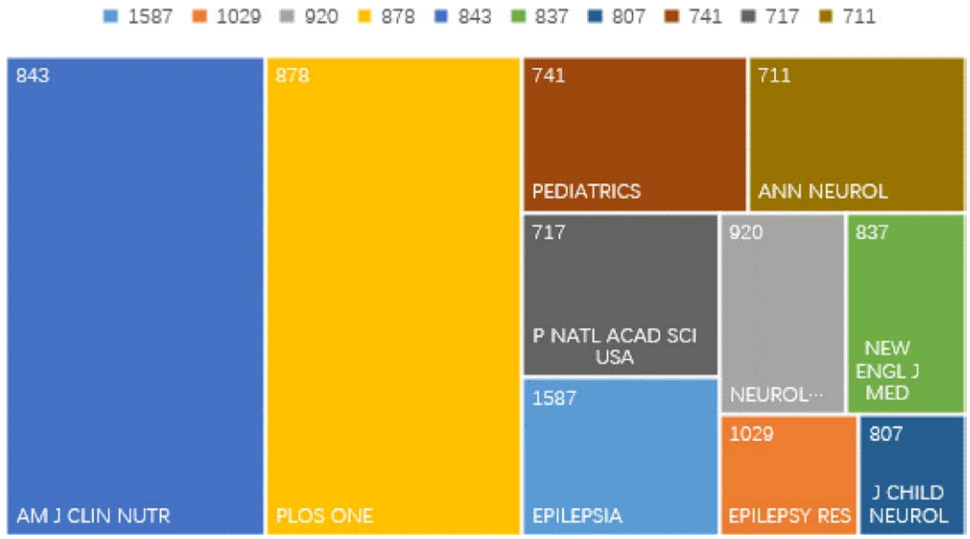

Figure 2. Top 10 Journals related to KD. KD = ketogenic diet.

Table 1

Top 10 most productive journals.

No.	Journals	Counts	IF
1	*Epilepsia*	1587	6.740
2	*Epilepsia Research*	1029	2.991
3	*Neurology*	920	11.800
4	*Plos One*	878	3.752
5	*American Journal of Clinical Nutrition*	843	8.472
6	*New England Journal of Medicine*	837	176.097
7	*Journal of Child Neurology*	807	2.363
8	*Pediatrics*	741	9.703
9	*Proceedings of the National Academy Of Sciences Of The United States Of America*	717	12.779
10	*Annals of Neurology*	711	11.274

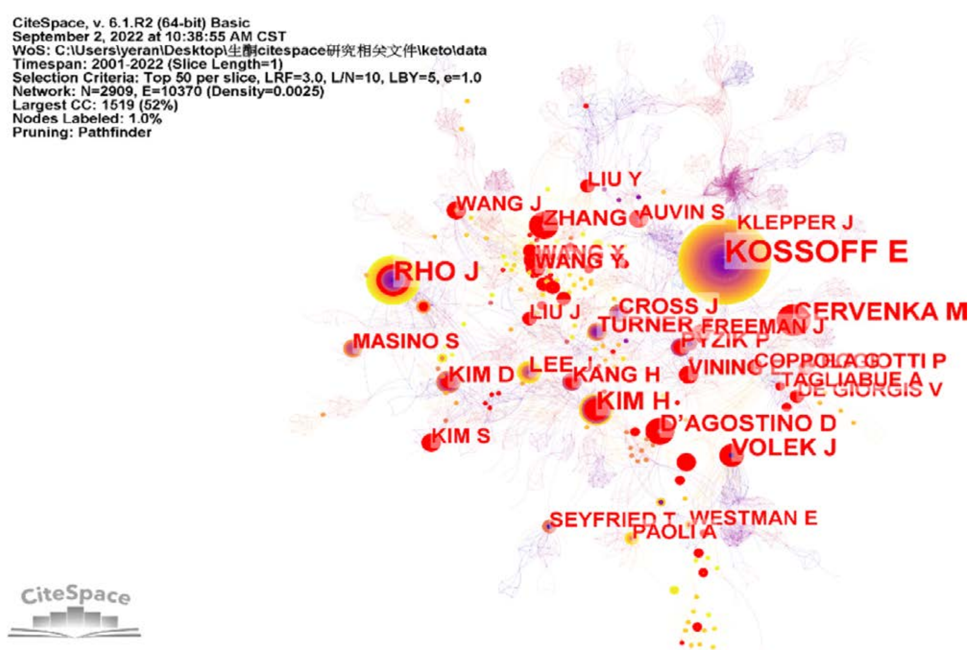

Figure 3. Map of authors' collaborations related to KD research. KD = ketogenic diet.

other scholars is remarkable and suggests that their scholarship is pivotal to this domain. The top 10 authors are displayed in Table 2.

3.4. Co-institutions analysis

Figure 4 exhibits co-institutes in the field of KD. A tight co-occurrence sub-network of institutions was established in this study, with Johns Hopkins Medical Institutions, Johns Hopkins University, etc serving as representative institutions, which implies that these institutes have carried out extensive research on the KD and have made a major contribution to the subject. The top 10 institutions in this study are shown in Table 3.

3.5. Co-countries analysis

Figure 5 displays co-country results in KD research. The United States is the country with the largest number of KD publications. The reasons are as follows. First of all, The United States was the first country that coined the term "ketogenic diet."[6] Secondly, many people could benefit from decreasing their carbohydrate intake since more than half of Americans have a chronic condition associated with their diet that involves some level of insulin resistance and carbohydrate intolerance.[25] Additionally, international collaborations are relatively close. The 10 most productive countries in this study are shown in Table 4.

3.6. Co-occurring keywords analysis

Co-occurring keywords depict the growth, direction, and emphasis of this field. The top 10 keywords for the KD are: "KD, ketone body, children, efficacy, weight loss, low carbohydrate diet, metabolism, epilepsy, beta hydroxybutyrate, modified atkins diet" (Fig. 6 and Table 5). We further divided keywords into clusters. The following six categories were determined: "obesity, epilepsy, ketone body, glucose, blood brain barrier and traumatic brain injury" (Fig. 7 and Table 6). A timeline diagram is created based on the clustering results to demonstrate the temporal evolution of these themes. In Figure 8, the paper's publication year is indicated by the horizontal line, while the various clusters are displayed by the vertical line. Each node corresponds to a keyword, and the bigger the node, the more frequently the keyword appears. It shows that cluster "obesity" has the longest research period, followed by "epilepsy," "glucose," "ketone body," "traumatic brain injury," and "blood brain barrier."

3.7. Document co-citation analysis

The co-citation literature demonstrates the authoritativeness of the research in this area as well as the significant contribution made by the authors. Statistics from CiteSpace found that Kossoff EH had the highest citations of 127 articles published in 2018 in the Optimal clinical management of children receiving dietary therapies for epilepsy: updated recommendations of the International KD Study Group at Epilepsia Open, the purpose of this study was to offer suggestions for standardized KD clinical implementation. The second most cited article, by Puchalska P, was published in 2017, in the Cell Metabolism, titled Multi-dimensional roles of ketone bodies in fuel metabolism, signaling, and therapeutics, with 114 citations. It implies

Table 2

Top 10 most productive authors.

No.	Authors	Counts	No.	Authors	Counts
1	Kossoff EH	97	6	D' Agostino D	30
2	Rho J	56	7	Kim D	26
3	Kim H	41	8	Zhang Y	26
4	Cervenka M	37	9	Turner Z	25
5	Volek J	32	10	Pyzik P	25

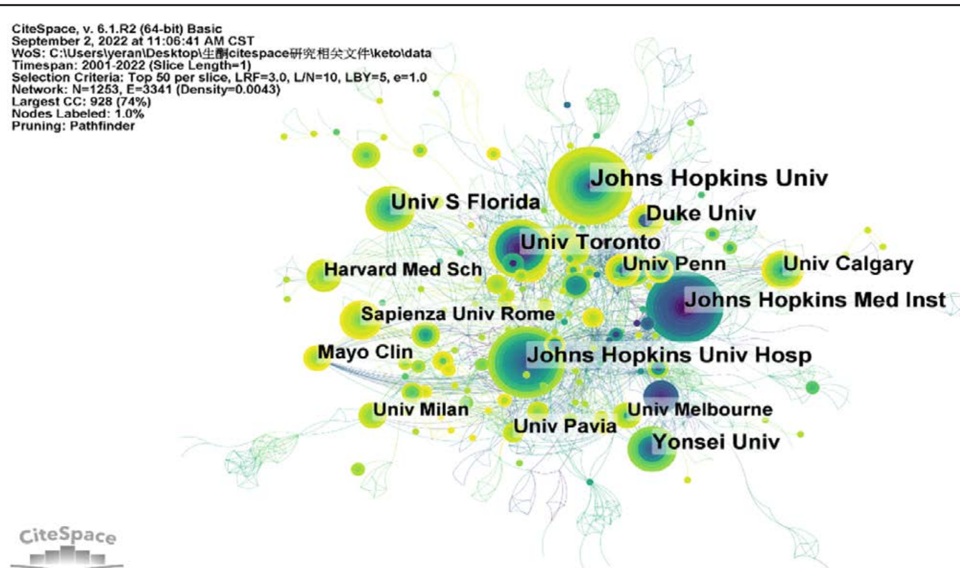

Figure 4. Map of institutions' collaborations related to KD research. KD = ketogenic diet.

Table 3

The 10 most productive and influential institutions sorted by total publication record.

No.	Institutions	Frequency	Yr
1	Johns Hopkins University	49	2001
2	Johns Hopkins University Hospital	46	2005
3	Johns Hopkins Medical Institutions	44	2001
4	University of Toronto	43	2001
5	Duke University	41	2002
6	Yonsei University	41	2004
7	University of South Florida	38	2006
8	University of Calgary	34	2002
9	University of Pennsylvania	31	2001
10	University of Pavia	49	2002

Figure 5. Map of country's collaborations related to KD research. KD = ketogenic diet.

Table 4

The 10 most productive countries.

No.	Frequency	Centrality	Yr	Country
1	1133	0.29	2001	USA
2	254	0.17	2002	Italy
3	202	0.05	2006	Peoples R China
4	174	0.21	2001	Canada
5	172	0.27	2005	England
6	149	0.11	2002	Germany
7	107	0.06	2005	Australia
8	100	0.03	2002	Japan
9	91	0.1	2005	France
10	89	0.03	2008	Spain

that ketone bodies are crucial metabolic products in the KD's treatment of various disorders (Fig. 9 and Table 7).

3.8. Keywords with citation bursts

Keywords that appear frequently over an extended period of time are thought to be indicative of frontier topics, active development, and the latest trends. This study illustrates the detection of emerging words at various time points from 2001 to 2022, as shown in Figure 10. In the burst map, the blue line depicts the time interval, while the red line depicts the time when a keyword bursts. The findings indicate that hotspots for study have evolved throughout time. Polyunsaturated fatty acid, randomized trial and body weight are among the keywords that have lasted longer than five years. The following keywords have large mutation values and have lasted until 2022: performance, mediterranean diet, high fat diet, fat and inflammation.

Figure 6. Map of co-occurring keywords related to KD research. KD = ketogenic diet.

Table 5

Top 10 keywords related to KD.

No.	Frequency	Keyword	No.	Frequency	Keyword
1	1847	Ketogenic diet	6	316	Low carbohydrate diet
2	402	Ketone body	7	307	Metabolism
3	375	Children	8	275	Epilepsy
4	342	Efficacy	9	243	Beta hydroxybutyrate
5	331	Weight loss	10	212	Modified atkins diet

KD = ketogenic diet.

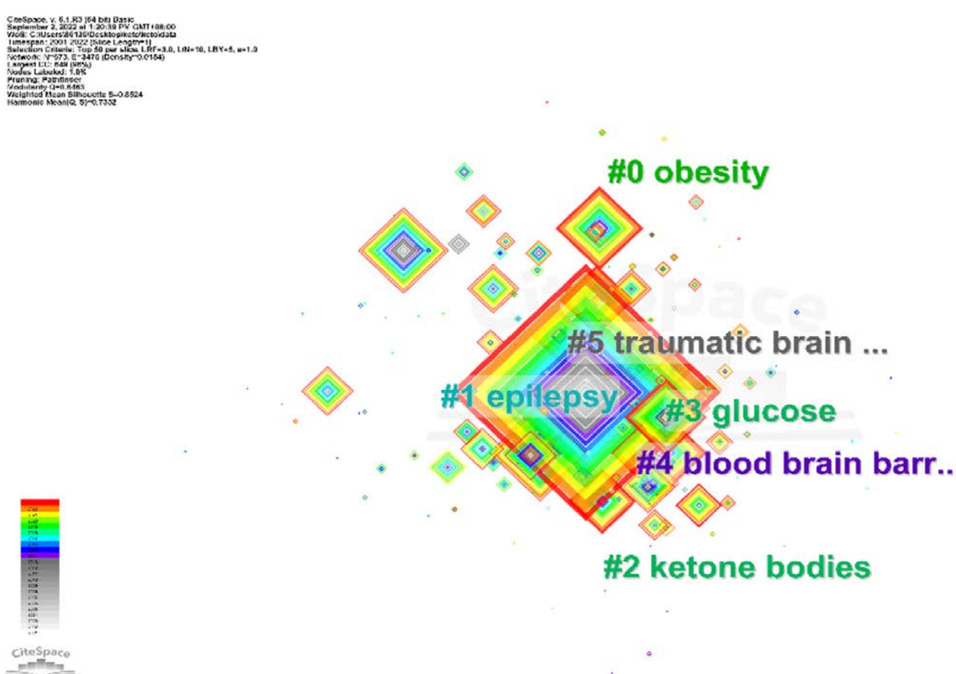

Figure 7. Clustering map of keywords related to KD research. KD = ketogenic diet.

Table 6

Subject of clusters analysis.

Cluster ID	Size	Silhouette	Yr	Cluster laber (LLR)
#0	99	0.778	2005	Ketogenic diet; animal models; acid-base safety; cardiac sarcoidosis; energy restriction | weight loss; mediterranean diet; glycemic index; caloric restriction; carbohydrate-restricted diet
#1	81	0.742	2005	Ketogenic diet; low glycaemic index treatment; alternative ketogenic diets; protein carbonylation; animal models | atkins diet; intractable epilepsy; low glycemic index diet; epileptic encephalopathies; protein carbonylation
#2	72	0.808	2003	Ketogenic diet; 3-butanediol monoester; carbohydrate ratio; animal models; hif-1 | ketone bodies; growth factors; expression profiling; 3-butanediol monoester; carbohydrate ratio
#3	68	0.82	2003	Ketogenic diet; caloric restriction; exercise; insulin; chronic ketosis | glucose; association; hemoglobin; endurance athletes; mice
#4	64	0.853	2003	Ketogenic diet; mutation; feature; phenotype; lamotrigine | glut1 deficiency syndrome; blood-brain barrier; drug-resistant epilepsy; clinical management; ampa receptors
#5	56	0.868	2003	Ketogenic diet; animal models; neuron; high fat diet; protein deficiency | kainic acid; intermittent fasting; animal models; neuron; high fat diet

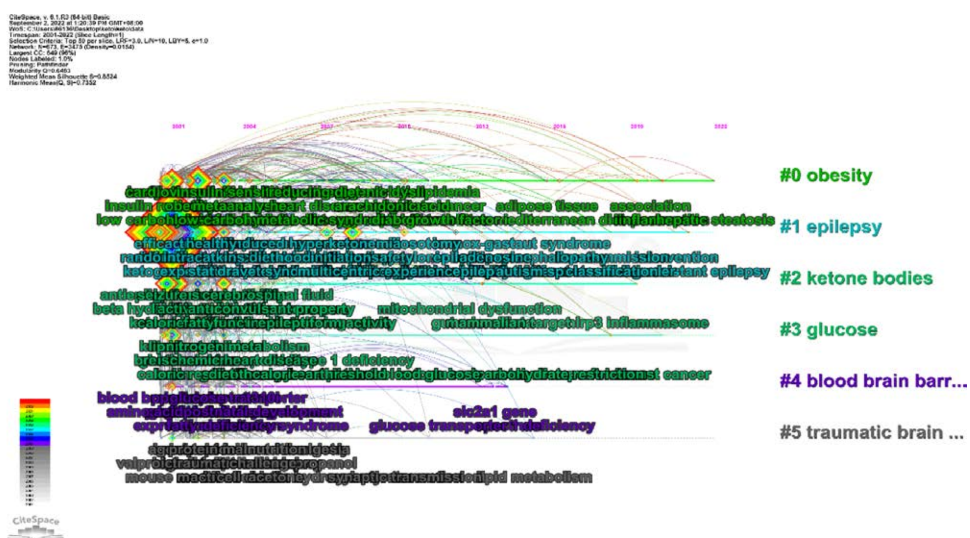

Figure 8. Recurring KD research after Figure 6. Date are sorted into chronological order. KD = ketogenic diet.

4. Discussion

4.1. The hotspots of the KD research

Figure 8 depicts the three stages of the evolution of research hotspots in the field of the KD. The first phase, which lasted from 2001 to 2004, concentrated on clinical investigations, fundamental research, and systematic reviews of the effectiveness of KD in treating obesity, diabetes, and epilepsy. Clinical studies concentrated on the efficacy of KD in the management of obesity and epilepsy; basic research was primarily concerned with ketone body metabolism and neuroprotective effect of the KD; systematic reviews concentrated on the improvement effect of KD on epileptic seizures. From 2004 through 2010, the second phase was in effect. The application of the KD to GLUT-1 deficient syndrome and cardiovascular disorders, as well as the advantages and mechanisms of the KD in the treatment of obesity, diabetes, and epilepsy, were among the subjects covered. From 2010 to the present, the third stage of study is focused mostly on the use of the KD to treat cancer, fatty liver disease, neurodegenerative illnesses, inflammation, and mitochondrial diseases. Additionally, cluster #0 obesity has been a focus of this field.

4.2. The emerging trends of the KD research

4.2.1. Development and application of exogenous ketone supplements. Exogenous ketone supplements, which manufacture ketone bodies while the patient maintains a regular diet, are mostly made up of ketone esters, ketone salts, and medium-chain triglycerides.[26] Exogenous ketones, as opposed to endogenous ketones, can elevate ketone body concentrations within minutes to hours and maintain a normal level of insulin in the body.[27] Exogenous ketone supplements are infused intravenously, inhaled orally, or given via nasogastric tubes.[28] Patients are more compliant with exogenous ketone supplements than with the KD. However, there are several drawbacks to using them. For instance, ketone salt induces a low blood ketone concentration, long-term use may raise the patients' mineral burden, high doses are not well tolerated by patients, and it must be taken several times per day.[28] Exogenous ketone supplements have been shown to be successful in a variety of animal studies, and they may offer patients with KD intolerance an alternative method for achieving therapeutic ketosis.[29] Although there is a lack of clinical evidence for exogenous ketone supplements, the results of the limited available research suggest that they may help with aging, neurodegenerative disorders, mental illnesses, and other conditions.[26,30] Medium-chain triglycerides oils, 1,3-butanediol, 3-butanediol-acetoacetate diester, K-β-hydroxybutyric acid, and others are examples of exogenous ketone supplements currently available.[26] Some preparations have a set composition, such as medium-chain triglycerides oil, which typically contains 60% octanoic acid and 40% decanoic acid.[26] Ketone salts are frequently combined

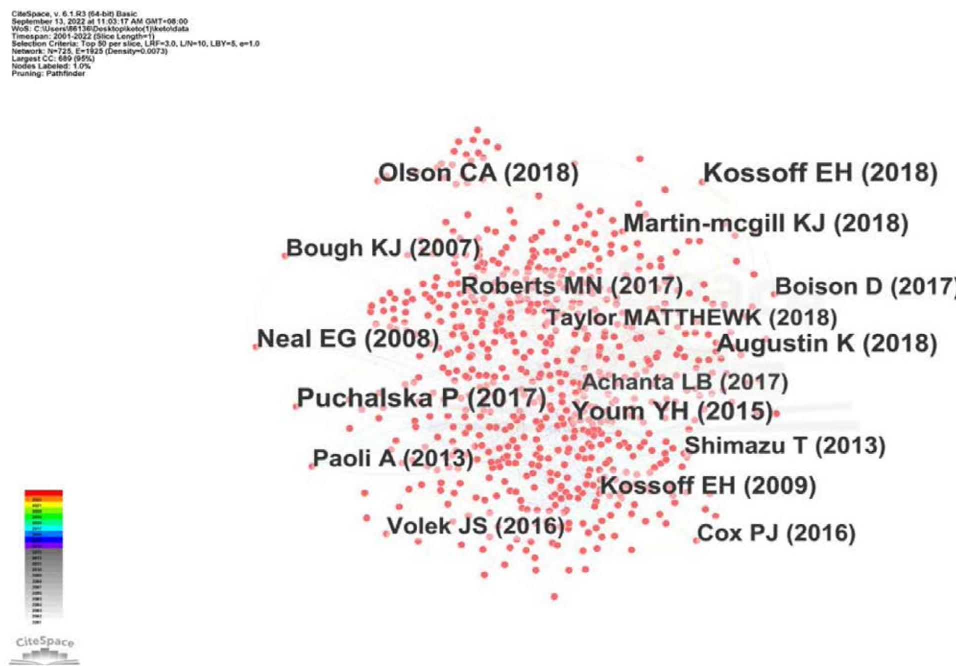

Figure 9. Document co-citation analysis in KD research. KD = ketogenic diet.

Table 7

Top 10 document co-citation related to KD.

No.	Frequency	Yr	Reference
1	127	2018	Kossoff EH, 2018, EPILEPSIA OPEN, V3, P175, DOI 10.1002/epi4.12225
2	114	2017	Puchalska P, 2017, CELL METAB, V25, P262, DOI 10.1016/j.cmet.2016.12.022
3	96	2015	Youm YH, 2015, NAT MED, V21, P263, DOI 10.1038/nm.3804
4	90	2018	Martin-mcgill KJ, 2018, COCHRANE DB SYST REV, V0, P0, DOI 10.1002/14651858.CD001903.pub4
5	89	2008	Neal e.g., 2008, LANCET NEUROL, V7, P500, DOI 10.1016/S1474-4422(08)70092-9
6	87	2018	Olson CA, 2018, CELL, V173, P1728, DOI 10.1016/j.cell.2018.04.027
7	84	2018	Augustin K, 2018, LANCET NEUROL, V17, P84, DOI 10.1016/S1474-4422(17)30408-8
8	73	2009	Kossoff EH, 2009, EPILEPSIA, V50, P304, DOI 10.1111/j.1528-1167.2008.01765.x
9	70	2017	Roberts MN, 2017, CELL METAB, V26, P539, DOI 10.1016/j.cmet.2017.08.005
10	68	2013	Paoli A, 2013, EUR J CLIN NUTR, V67, P789, DOI 10.1038/ejcn.2013.116

KD = ketogenic diet.

with medium-chain triglycerides in a ratio of 1:1 or 1:2.[31] Exogenous β-hydroxybutyric acid supplements have caught the interest of researchers lately. One significant ketone body is β-hydroxybutyrate, which can be used as a histone modification regulator, an energy substrate, and a signaling molecule to perform therapeutic functions. These therapeutic functions include inducing histone β-hydroxybutyrylation,[32] inducing and inhibiting the production of reactive oxygen species,[33] blocking the NLRP3 inflammasome,[34] inhibiting short-chain fatty acid signaling,[35] among others. D-β-hydroxybutyrate monoester has been suggested by several researchers as a possible exogenous ketone supplement for the treatment of numerous disorders.[27] According to studies, D-β-hydroxybutyrate monoester is salt-free compared to other exogenous ketone supplements, preventing a number of negative consequences brought on by excessive salt intake, such as hypertension.[36] D-β-hydroxybutyrate monoester is now primarily utilized by athletes, while a few studies have looked into its potential in diabetes and neurological illnesses.[27] Despite having several advantages, D-hydroxybutyrate monoester has a high economic cost.[27] In conclusion, exogenous ketone supplements are still in the early stages of development and use. Future research is required to determine the ideal dose, method of administration, length of therapy, and various formulations of exogenous ketone supplements in order to increase their tolerance and effectiveness.

4.2.2. Anti-inflammatory mechanisms of the KD. Inflammation is associated with illnesses of the immune system, metabolism, nervous system, etc. A meta-analysis demonstrated that patients with Alzheimer's disease had considerably higher expression of proinflammatory cytokines and chemokines, including interleukin-1β (IL-1β), interleukin-6 (IL-6), and interleukin-8.[37] Obese individuals have greater serum concentrations of tumor necrosis factor-α, IL-1β, and IL-6.[38] Patients with multiple sclerosis have high levels of interleukin-17 and have significant infiltration of macrophage and T cell into the central nervous system.[39] KD has a beneficial impact on reducing inflammation, and its anti-inflammatory activity across numerous systems has gradually been validated. KD can reduce inflammation by targeting adenosine, reactive oxygen species, and gut flora, among other things. Adenosine is a potent regulator of inflammation. KD reduces both cerebral and peripheral inflammation by activating adenosine receptors, raising extracellular adenosine levels, and blocking the production of proinflammatory mediators through ketone

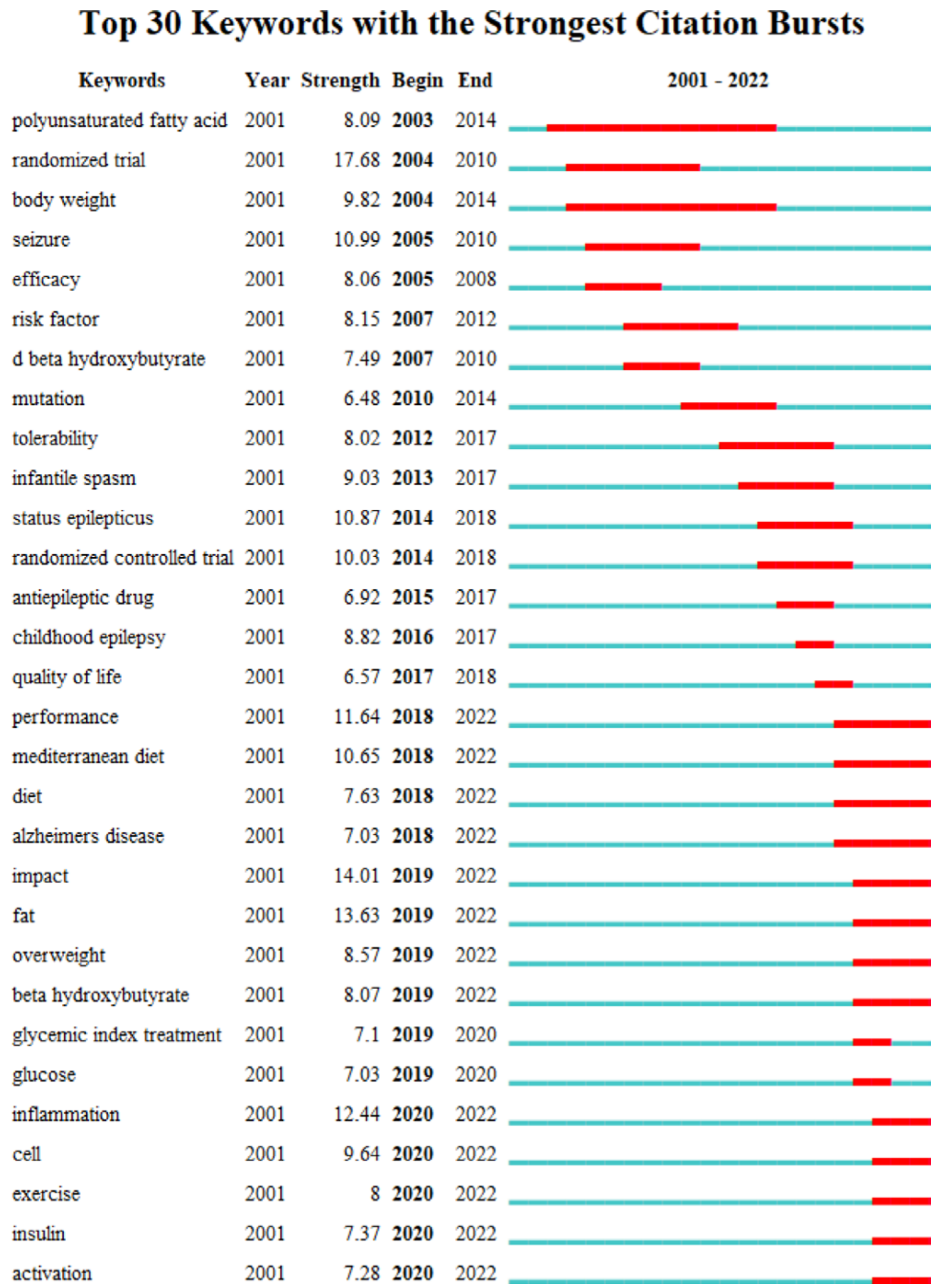

Figure 10. Top 30 keywords with the strongest citation bursts.

metabolism.[40] Previous investigation has also demonstrated that adenosine A2 receptors can change the shape and function of microglia.[41] Another way KD lowers inflammation is by reducing the production of reactive oxygen species. KD can decrease the production of reactive oxygen species by blocking the NLRP3 inflammasome, activating the nuclear factor erythroid 2-related factor 2 pathway, decreasing the activity of the NF-$_{\kappa}$B signaling pathway, increasing the ratio of nicotinamide adenine dinucleotide oxidation and reduction, up-regulating the expression of PPAPγ, reducing the expression of inflammatory mediators, increasing the expression of uncoupling protein, and inhibiting histone deacetylase.[42] The gut flora may play a role in the anti-inflammatory effects of KD. Studies have indicated that KD can exert its anti-inflammatory effects by raising the number of Akkermansia and decreasing the number of bifidobacterium, which in turn can limit the development of intestinal ILC3 cells and Th17 cells.[43,44] Gubert C et al discovered that KD alters particular microbes (such as Lactobacillus and Akkermansia mucosal bacteria), which in turn encourages the production of anti-inflammatory compounds and short-chain fatty acids.[45] Additionally, the n-3 polyunsaturated fatty acids in KD can lessen the synthesis of adhesion molecules, cytokines, reactive oxygen species, and inflammatory eicosanoids.[46] KD is an energy-restricted diet that boosts microRNAs like Mir-16-5p and noticeably lowers the mRNA expression of IL-1β, IL-6, and tumor necrosis factor-α.[46] In conclusion, a variety of advantageous pathways combine to produce anti-inflammatory effects.

4.2.3. Alzheimer's disease, obesity and diabetes. The most prevalent type of dementia, Alzheimer's disease, typically shows itself as a progressive loss of memory and cognitive abilities.[47] According to studies, the ameliorative effects of KD on Alzheimer's disease are associated with an increase in brain energy production, a restriction on the synthesis of reactive oxygen species, a decrease in the inflammatory response, and activation of potassium ion channels.[48] Recently, some scientists have suggested that the next area of fundamental study in this area should concentrate on neuroinflammatory processes and alterations in the gut microbiome.[49] Currently, clinical research has demonstrated that KD can delay cognitive decline in Alzheimer's disease patients, particularly in those without the apolipoprotein ε4 gene, and the extent of remission is correlated with the duration and the concentration of ketone bodies in the blood.[50,51] Most clinical research to date has been small-scale and has primarily examined the short-term effects of KD on cognitive function in Alzheimer's patients.[52] Therefore, in order to assess the effects of KD on patients' cognitive function, quality of life, EEG, and other aspects, as well as to monitor the negative effects of KD and patients' compliance with KD, it will be necessary to conduct sizable, lengthy randomized controlled studies.

A major public health issue on a global scale is obesity.[53] Statistics show that 41 million children and 2 billion adults globally are overweight or obese.[53] KD has gained popularity as a productive method of managing obesity in recent years. Weight is no longer the only metric utilized by researchers to assess the therapeutic efficacy of KD in current clinical studies. Researchers are now examining the impact of KD in obese individuals on their mood, body composition, quality of life, and metabolic markers unrelated to body weight. The findings demonstrated that the extremely low carbohydrate KD improved blood glucose, glycosylated hemoglobin, and lipid marker levels, reduced visceral fat mass, and had little to no impact on muscle mass, muscle strength, and resting metabolic rate in obese patients.[54,55] Additional studies have compared the effectiveness of the KD in comparison to other diets,[56] the effectiveness of the KD in terms of gender,[57,58] and the effectiveness of the KD in children who have obesity.[59] Moreover, obesity raises the risk of developing a number of ailments. As a result, in addition to concentrating on the use of KD in obesity, researchers have also looked into the use of KD in chronic conditions that are linked to obesity, such as type 2 diabetes mellitus, cardiovascular disease, polycystic ovary syndrome, nonalcoholic fatty liver disease, male hypogonadism, and cancer. Initial research suggests that KD may be beneficial for disorders linked to obesity, but the data is tenuous. Guidelines for the management of KD in obese patients have been established as a result of ongoing research.[60,61] According to basic research, hunger suppression, a decrease in the resting respiratory quotient, control of the energy heat effect, and the influence of hormones that control appetite secretion are all factors in the body weight loss of obese patients with KD. But the molecular mechanism of KD in combating obesity is still unknown.[62] Future research should focus on the mechanism and effectiveness of KD in treating disorders associated with obesity, as well as the molecular analysis of KD's mode of action against obesity.

There are currently just under 500 million diabetics in the world, and between 2030 and 2045, that number is expected to rise by 25% and 51%, respectively.[63] The beneficial effects of KD on diabetic individuals are primarily attributable to its metabolite decanoic acid. Decanoic acid can boost antioxidant capacity, mitochondrial function, and mitochondrial biogenesis.[64] More and more evidence has emerged in recent years demonstrating the positive effects of KD on body weight, metabolic parameters, consumption of oral antidiabetic medications, insulin resistance, and other factors in diabetic patients.[65,66] These trials do have significant limitations, though, including the absence of data on the long-term impacts of KD in diabetes patients, the efficacy of KD in children and adolescents with type 1 diabetes,[67] and the paucity of research on KD's impact on microvascular complications in diabetics.[68] When evaluating the causality of KD efficacy in diabetes, some clinical studies did not evaluate ketone levels in diabetic patients during KD administration.[69] To assess the security, effectiveness, and compliance of KD in diabetic patients of all ages, long-term, carefully planned randomized controlled trials are required.[70] Future research should investigate how KD affects glycemic variability (because glycemic variability has been identified as a determinant of vascular complications of diabetes mellitus[71]) as well.[69] Additionally, intermittent KD may be considered due to low KD compliance, although its effectiveness needs to be established.[69]

5. Conclusion

In conclusion, using CiteSpace software, this study visualized and evaluated pertinent literature on KD in the Web of Science Core Collection, reviewed its research status, hot spots, and frontiers, summarized and analyzed the advantages, shortcomings, and research directions of this field, and provided a reference for further investigation. Based on the study in this paper, it is necessary to further expand international collaboration between authors and institutions in order to increase the sharing of innovative scientific studies. The hotspots for study in this area include ketone metabolism, epilepsy, obesity, and more. Future study in related domains should emphasize on the creation and use of exogenous ketone supplements, the anti-inflammatory properties of KD, and the use of KD in the treatment of diabetes, obesity, and Alzheimer's disease.

Author contributions

Conceptualization: Ran Ye.
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