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Research hotspots in urticaria: A bibliometric study of the top 100 most cited articles

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Abstract

Background and Purpose: Urticaria is a prevalent recurrent skin allergic condition. Severe itching significantly impacts patients' quality of life. This paper aims to investigate the development status of urticaria through bibliometric analysis to predict future research hotspots and trends.

Methods: On October 29, 2023, a literature search was conducted in the Web of Science (WOS) database to collect urticaria-related publications. The top 100 most cited articles were charted, and VOSviewer software was utilized for the literature data analysis. A visual analysis was performed on the number of articles, journals, main researchers, keywords, and so on.

Results: The research involved 415 authors from 28 countries, published across 25 journals, ranging from 1963 to 2023. Marcus Maurer was the leading author, with the United States being the foremost country in urticaria research. CEH Grattan received the most citations, and The Medical University of South Carolina had the highest number of publications. Key research focuses include epidemiology, pathogenesis, drug therapy, and quality of life assessments. "Anti-high affinity IgE receptor α chain (FcεRIα)," "chronic idiopathic urticaria," "autoantibodies," "histamine-release" emerged as the keywords with the highest prominence.

Conclusion: The field of urticaria research has attracted substantial attention over the past few decades, witnessing rapid development. This study highlighted the top 100 articles by citation frequency within the urticaria field. Bibliometric analysis revealed a shift in treatment methods from traditional antihistamines to biological agents, with significant emphasis on improving the quality of life in chronic urticaria management. These areas represent the current research focal points and indicate future trends in urticaria research.

KEYWORDS
bibliometry, pathogenesis, therapy, urticaria

1 | INTRODUCTION

Urticaria is a prevalent clinical skin condition. According to the presence or absence of specific predisposing factors, chronic urticaria (CU) is divided into chronic spontaneous urticaria (CSU) and chronic induced urticaria (CIndU).[1] CSU accounts for 2/3 of the incidence, and different types of CU can be combined.[2] This point of view has also been verified through literature retrieval. This study on urticaria is mainly focused on CU, with CSU being the primary focus of the research. According to international urticaria guidelines, the lifetime prevalence of acute urticaria is approximately 20%.[1] The lifetime prevalence of CU stands at 1.8%.[3] Women exhibit a higher incidence of CU than men, with 8.7% of patients experiencing the condition for 1–5 years and 11.3% for more than 5 years. The average age at onset is 40 years.[4] Its clinical manifestations include wheals, severe itching, and erythema that persist for more than 6 weeks, making it a common immune-related skin condition. Without timely and appropriate treatment, or in cases of treatment resistance, CU can develop, leading to prolonged duration, recurrence, delayed healing, and negative impacts on patients' lives and psychological well-being.[5] It is necessary to call for re-emphasis on the pathogenesis of CSU as an internal trigger rather than external interference. The pathogenesis of CSU is characterized by immune and allergic reactions. Mast cell degranulation, histamine and cytokine release are the core links in the pathogenesis of urticaria.[6] T cells, B cells, monocytes, and eosinophils may also be involved in the pathophysiological process of CU.[7,8] In recent years, with the deepening of research, the research on the pathogenesis and treatment of urticaria has attracted more and more attention from the society. More immune and non-immune mechanisms have been gradually revealed in the pathogenesis of CU. Potential molecular biomarkers such as high-affinity IgE receptor (FcεRI),[9] anti-thyroid peroxidase (anti-TPO),[10,11] complement 5a (C5a),[12–14] and thymic stromal lymphopoietin (TSLP)[15] have been discovered one after another, which provides ideas for us to develop new treatment strategies. Conventional antihistamine drug therapy has been unable to meet people's needs, and by increasing the dose one can obtain certain benefits, but cannot be cured.[16,17] Dupilumab is a monoclonal antibody[18] that inhibits signal transduction through IL-4 and IL-13. Clinical reports in the treatment of CSU have shown that dupilumab can effectively improve patient annoyance and is generally well tolerated, but the cure rate is limited.[19] Biotherapy using anti-IgE antibody Omalizumab can bind IgE against autoantigens, and then inhibit the activity of IgE receptors IgE receptor,[20–25] which can significantly improve most symptoms,[26–29] but there are still some people who do not respond to CSU treatment. Therefore, it is necessary to create a more effective anti-IgE drug, which led to the development of ligelizumab. The results showed that ligelizumab was superior to omalizumab in terms of efficacy.[30] As research data grow and new findings emerge, the challenge lies in efficiently navigating the vast literature to grasp the field's overview, frontiers, and hotspots.

The concept of bibliometrics was first introduced by Alan Pritchard in 1969, becoming a standard approach in literature analysis. This methodology employs mathematical and statistical techniques with scientific rigor to quantify the social dimensions of science. Bibliometric analysis offers a quantitative strategy for reviewing and investigating the existing literature within specific domains.[31] Bibliometrics has been applied in dermatology, including bibliometric analysis of the impact of dermatology on the characteristics of citations,[32] and literature dosimetry that analyzes the global publishing productivity of dermatology.[33] Moreover, in terms of specific skin diseases, it has been well explored through bibliometric analysis, such as psoriasis,[34] melanoma,[35] psoriatic arthritis,[36] rosacea,[37] hidradenitis suppurativa,[38] Pityriasis rubra pilaris,[39] psoriasis,[40] and dissecting cellulitis of the scalp.[41] Through literature analysis, we can understand the future development direction of discipline development and research in the field of dermatology. VOSviewer, a software designed for visualizing network data maps, serves as a potent tool for comprehending the comprehensive landscape and trends of research areas. Utilizing a data normalization technique grounded in probability theory, VOSviewer emphasizes the level of aggregation analysis. It supports various visual presentations in publication volume, keywords, co-authors, co-institutions, and co-literature domains, featuring clustering views, temporal views, and density views. Renowned for its ease of use and visually appealing outputs, VOSviewer enables the display of research overviews, focal points, and emerging trends in specific fields.[42,43]

Yet, the detailed development status, key authors, institutions, and research hotspots pertaining to urticaria have not been thoroughly examined through bibliometric analysis. In this study, VOSviewer software was employed to visualize literature related to urticaria research, reflecting the field's current state and identifying future research priorities, thereby offering insightful directions for subsequent studies (Supporting information).

2 | MATERIALS AND METHODS

2.1 | Literature search

Web of Science (WOS), recognized for its high-quality digital literature resources, is widely used by researchers for obtaining accurate and comprehensive data on highly cited papers and prominent research. It is deemed the most suitable database for bibliometric analysis.[44,45] A keyword search was conducted in the WOS core collection database on October 29, 2023, performed independently by two research institutions with the following strategy: TS = (urticaria OR "spontaneous urticaria" OR "chronic urticaria" OR "acute urticaria"). The search scope encompassed all English literature types in the database, restricting the language to English and the article type to articles, comments, or online publications. Initially, 12 619 documents were screened, sorted by descending citation frequency in WOS. Following independent abstract screenings by senior dermatologists (Yuhong Wu and Ruoxin Wang), the top 100 articles most relevant to urticaria and with the highest citation frequency were selected. The search strategy is illustrated in Figure 1.

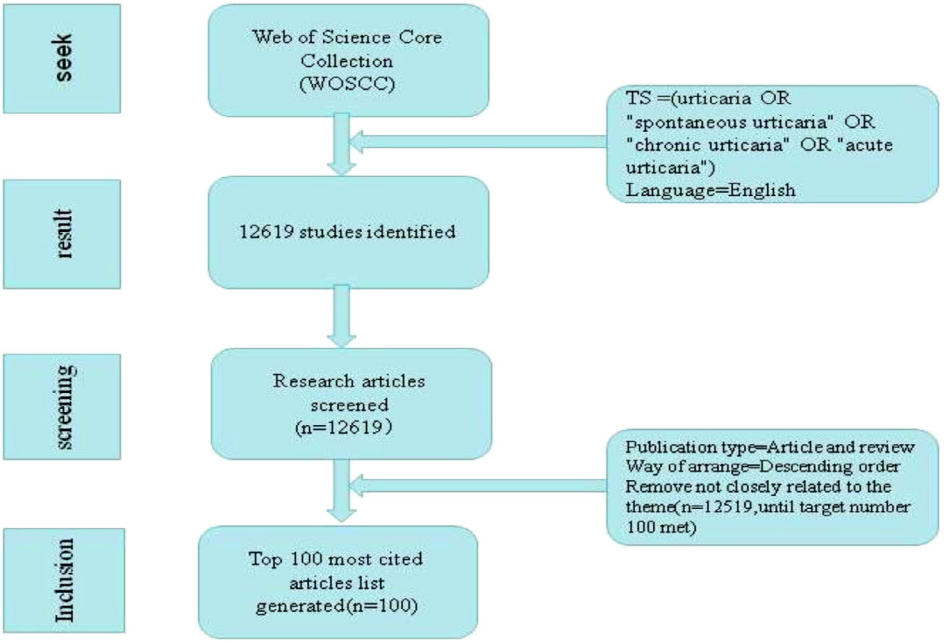

FIGURE 1 Literature retrieval strategy.

2.2 | Analysis method

The literature from the WOS core collection database was downloaded as "full record and cited references" in "plain text" format. VOSviewer (V.1.6.19) software visualized the collaboration networks among countries, institutions, authors, journals, and keywords, creating relevant visual maps. Additionally, Pajek software was employed to further visualize and analyze the focal points of urticaria research.

3 | RESULTS

3.1 | Year of publication and number of publications

The Web of Science database yielded a total of 12 619 publications. The schedule highlights the 100 most frequently cited articles, ranging from 1963 to 2023. Figure 2 depicts the distribution of publications in 5-year intervals. Before 1997, the publication frequency every five years was below 10, whereas from 1998 to 2017, it exceeded 10. The period from 1963 to 1967 saw a minimum of two papers published, while the maximum of 19 papers occurred from 1998 to 2002.

3.2 | Citation analysis

The total citation count was 21 310, with a median of 188 and an average of 213.1. These 100 articles were categorized based on their research focus: pathology (6%), etiology and pathogenesis (38%), treatment (26%), quality of life (6%), related diseases (12%), epidemiology (2%), and others (10%). Specifically, 38 articles delved into the pathogenesis of urticaria, and 26 articles examined the efficacy and mechanisms of antihistamine therapy and biological agents in treating urticaria. Among the top 100, the article "Autoantibodies against the High-Affinity IgE Receptor as a Cause of Histamine Release in Chronic Urticaria" by M Hide et al. received the highest number of citations, totaling 718. The study by CEH Grattan et al., "Blood basophil numbers in chronic ordinary urticaria and healthy controls: diurnal variation, influence of loratadine and prednisolone, and relationship to disease activity," had the lowest citation count of 126. The earliest published article was "The natural course of urticaria pigmentosa: analysis and follow-up of 112 cases," with a citation frequency of 196, while the most recent was "Prevalence of chronic urticaria in children and adults across the globe: Systematic review with meta-analysis," cited 150 times. The articles were divided into seven clusters based on citation analysis and topic relevance (Figure 3). Cluster 1 is clustered by Altrichter, Asero, and so on, which is represented by red groups. The clustering focuses on the physiological pathology and pathogenesis in the mind. Cluster 2 is grouped by Baiardini, Fricke, and so on. The graph is composed by green color groups. Clustering focuses on the management of the quality of life of urticaria. Cluster 3 is clustered by Boyce, Chang, and so on. It is represented by dark green population in the figure. Cluster 3 focuses on the assessment and management of quality of life in urticaria. Cluster 4 consists of Fujisawa, Grattan, and so on which is represented by yellow groups in the figure. The cluster focuses on the etiology of urticaria. Cluster 5 is clustered into one class by Champion and Doeglas, and so on, and is represented by the purple colored group in the figure. The cluster focuses on the clinical characteristics of all kinds of urticaria. Cluster 6 was clustered by Grandel, Hermes, etc., which is represented by blue groups. The focus of clustering is on the study of cold urticaria. Cluster 7 is clustered by Greaves, Kaplan, and so on, which is represented by orange groups. The cluster

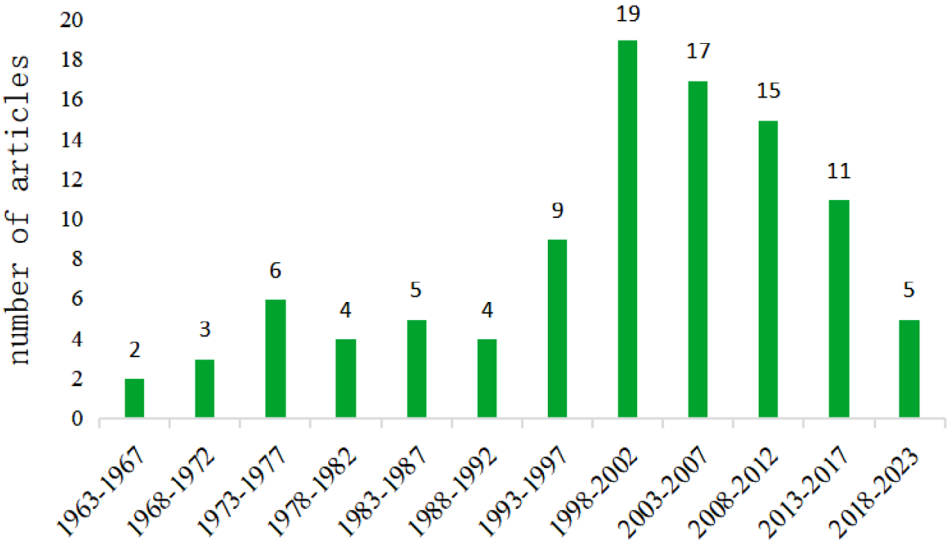

FIGURE 2 Statistics on the number of publications every 5 years.

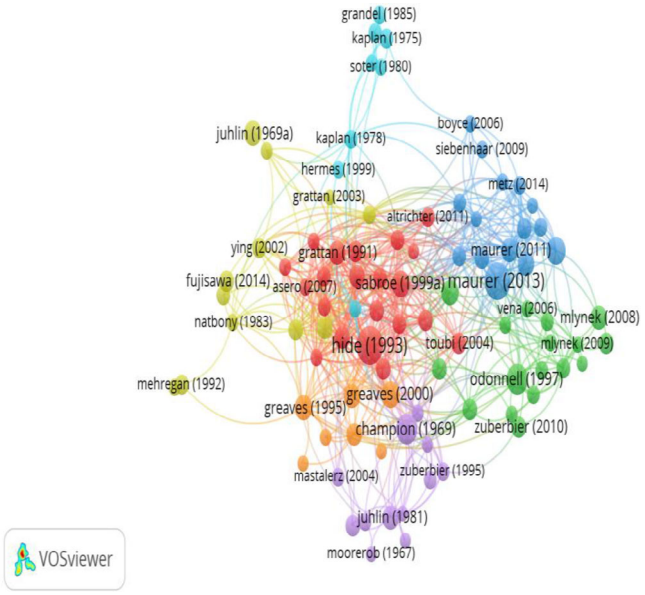

FIGURE 3 The bibliometric map of the selected articles based on citation patterns. (Cluster colors are as follows: Cluster 1 - Red, Cluster 2 - Green, Cluster 3 - Dark blue, Cluster 4 - Yellow, Cluster 5 - Purple, Cluster 6 - Blue, Cluster 7 - Orange).

focuses on diseases related to urticaria, such as angioneurotic edema. Each cluster is represented by a color, with each node denoting an author. Nodes are interconnected on a map, and the size of each node correlates with the citation count. In the time view of citation analysis, the node color gradually changes from blue-black to yellow, reflecting the chronological order of citations. Nodes representing earlier citations tend to be blue-black, while those representing later citations are yellow (Figure 4). From Figure 4, it can be seen that articles published after 2020 have become new research hotspots.

3.3 | Statistics of countries and institutions

The United States exhibited the greatest interest in urticaria research, leading with 39 articles, followed by Germany with 26 articles, and England with 25 articles. In terms of citation frequency, publications from the United States were cited 8787 times, ranking first. England's publications followed with a total of 6660 citations, and Germany's with 5666 citations (Table 1). The top nine institutions in terms of publication volume were analyzed (Table 2), with Charité leading with 13 articles and a citation frequency of 3357.

3.4 | Author statistics

Among the top 100 most-cited articles, Marcus Maurer was the most prolific, authoring 15 articles with a citation frequency of 3643. M.W. Greaves was second, publishing 12 articles with a citation frequency of 3643, and A.P. Kaplan ranked third with 10 articles and a citation frequency of 1912 (Table 3).

3.5 | Statistics of published journals

Analyzing the journals where urticaria studies were published, 84 articles appeared in the top 10 journals. Table 4 lists the leading journals in urticaria research. The Journal of Allergy and Clinical Immunology was the most frequent publication venue, with 31 articles and a total citation frequency of 6407. The British Journal of Dermatology ranked second with 13 articles and a total citation frequency of 3336. Allergy was third, hosting 10 publications and 1868 co-citations.

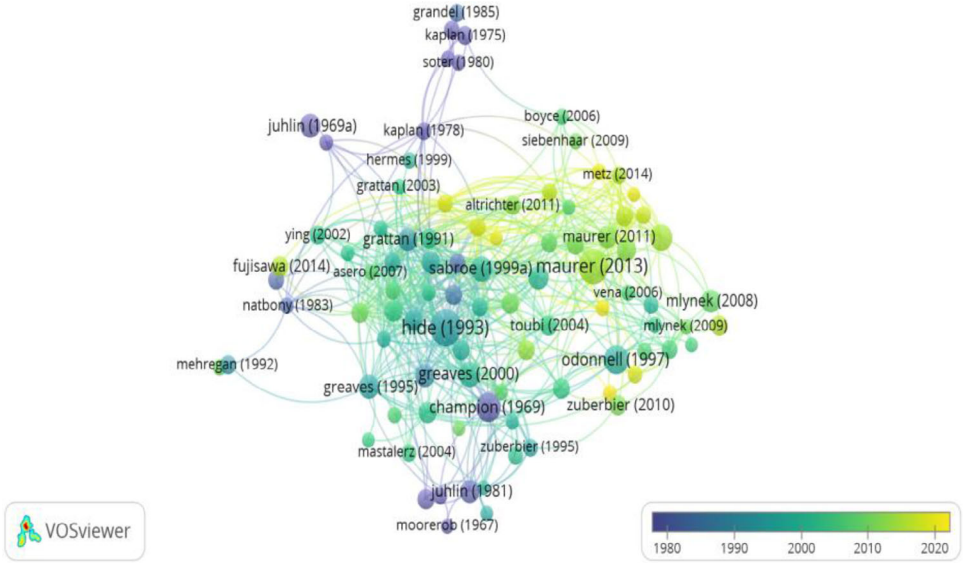

FIGURE 4 Time research trends in urticaria are analyzed based on 100 related articles. (The earlier the year, the more the node color tends toward blue-black, and vice versa).

TABLE 1 Top nine countries' publication and citation frequency statistics.

Rank	Countries	Documents	Citations
1	Usa	39	8787
2	Germany	26	5666
3	England	25	6660
4	Italy	9	1526
5	Spain	5	1422
6	Canada	5	1035
7	France	5	899
8	Poland	4	991
9	Switzerland	4	819

TABLE 2 Statistics of the top nine institutions' publication and citation frequency.

Rank	Organization	Documents	Citations
1	Charite	13	3357
2	The Medical University of South Carolina	11	3019
3	Charite Universitäts medizin Berlin	9	1658
4	St Thomas' Hospital	7	1532
5	Harvard University	6	989
6	Johns Hopkins Asthma and Allergy Center	4	1387
7	Genentech Inc.	4	1620
8	Univ Calif Los Angeles	4	924
9	Univ Milan	4	635

TABLE 3 Top 10 authors and citation frequency statistics.

Rank	Authors	Documents	Citations
1	Maurer, Marcus	15	3643
2	Greaves, MW	12	3643
3	Kaplan, AP	10	1912
4	Francis, DM	9	2663
5	Grattan, CEH	8	2393
6	Church, Martin K.	6	1149
7	Maurer, M.	6	1181
8	Metz, Martin	6	1124
9	Barr, RM	5	1220
10	Black, AK	5	1294

3.6 | Keywords analysis

VOSviewer software is used to analyze the co-occurrence of keywords to form a visual time view, and Pajek is used to further visualize the results to obtain keyword clustering view and density view, where circles and labels combine to form units, and units of different colors delineate separate clusters. These colors signify diverse research directions, with the size of the nodes representing the frequency of keyword occurrences. Keywords recurring more than five times were clustered, revealing four distinct groups (Figure 5). Cluster 1 focused on the quality of life and Omalizumab treatment in urticaria, featuring main keywords such as "management," "Omalizumab," and "quality of life." Cluster 2 dealt with the pathogenesis of urticaria, with key terms including "chronic idiopathic urticaria," "IgE receptor," "basophils," "FcεRIα," and so on. Cluster 3 centered on urticaria autoimmunity, highlighting "antibodies," "mast cells," "thyroid autoim-

TABLE 4 Top 10 published journals and citation frequency statistics.

Rank	Source	Documents	Citations
1	Journal of Allergy and Clinical Immunology	31	6407
2	British Journal of Dermatology	13	3336
3	Allergy	10	1868
4	New England Journal of Medicine	9	2885
5	Journal of the American Academy of Dermatology	6	1066
6	Archives of Dermatology	3	731
7	Journal of Investigative Dermatology	3	673
8	Clinical and Experimental Allergy	3	637
9	Journal of Clinical Investigation	3	568
10	Acta Dermato-Venereologica	3	440

munity," among others. Lastly, Cluster 4 explored urticaria treatment through antihistamines, with keywords like "antihistamines," "release." In the keyword time view (Figure 6), the earlier the keyword appears, the more the node color favors blue, the later the keyword appears, and the more the node color favors yellow. It can be seen that most of the literatures related to "IgE," "Omalizumab," and "CSU " were recently published. The keyword density view can be used to quickly observe the knowledge and research density of important fields and a certain field. The regional brightness is positively correlated with the frequency of keywords. In the keyword density view (Figure 7), "chronic idiopathic urticaria," "CU," "autoantibodies," and "FcεRIα" are the keywords with the highest salience intensity, reflecting that they are important areas of research.

4 | DISCUSSION

Urticaria represents a challenging condition within dermatology. As research progresses, the understanding of its etiology, pathogenesis, and treatment has improved. This study analyzed the top 100 English literature pieces related to urticaria with the highest citation frequency in the WOS core collection database from 1963 to 2023, utilizing the bibliometric software VOSviewer for visual analysis. Publication statistics revealed a unimodal upward trend in urticaria-related publications, suggesting sustained interest from researchers. The period between 1998 and 2002 saw the highest publication volume, totaling 19 articles, highlighting urticaria research as a focal area with significant potential for high-quality literature. Among the 100 most cited articles, pathogenesis and treatment emerged as dominant themes, discussed in 61 articles. In contrast, only 10 articles concentrated on the epidemiological and pathological aspects, with a primary focus on CU.

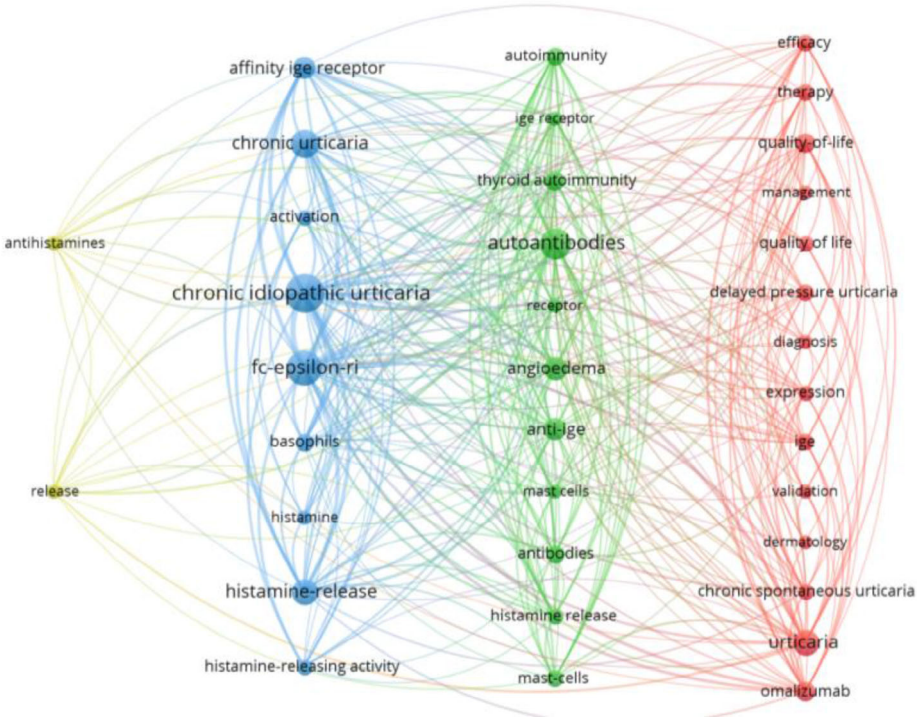

FIGURE 5 Analyze the scientometric diagram of keywords in the articles. (Cluster colors are as follows: Cluster 1 - Red, Cluster 2 - Green, Cluster 3 - Blue, Cluster 4 - Yellow.).

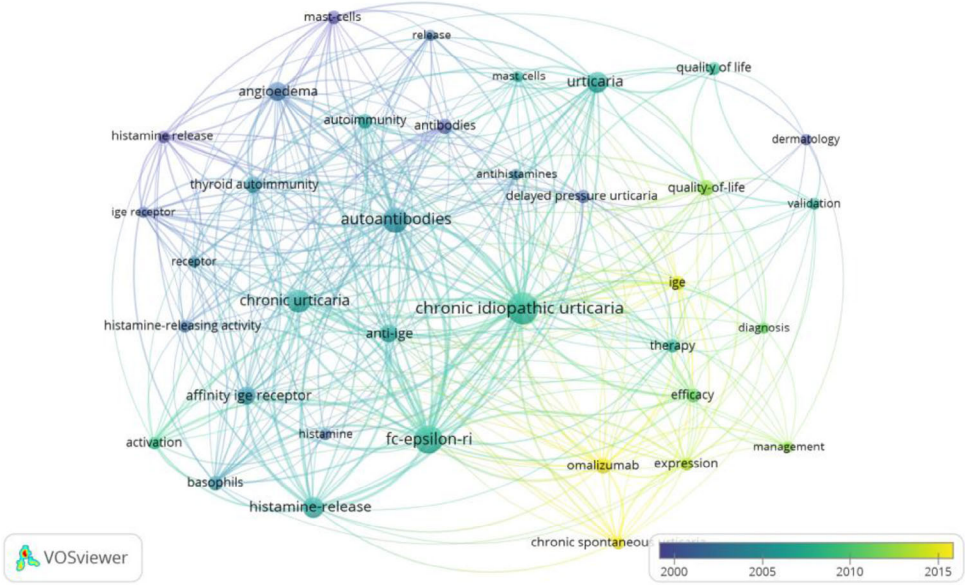

FIGURE 6 Keyword time view of urticaria research: Color ranging from blue to yellow indicates the timeline of keyword appearance from earlier to more recent.

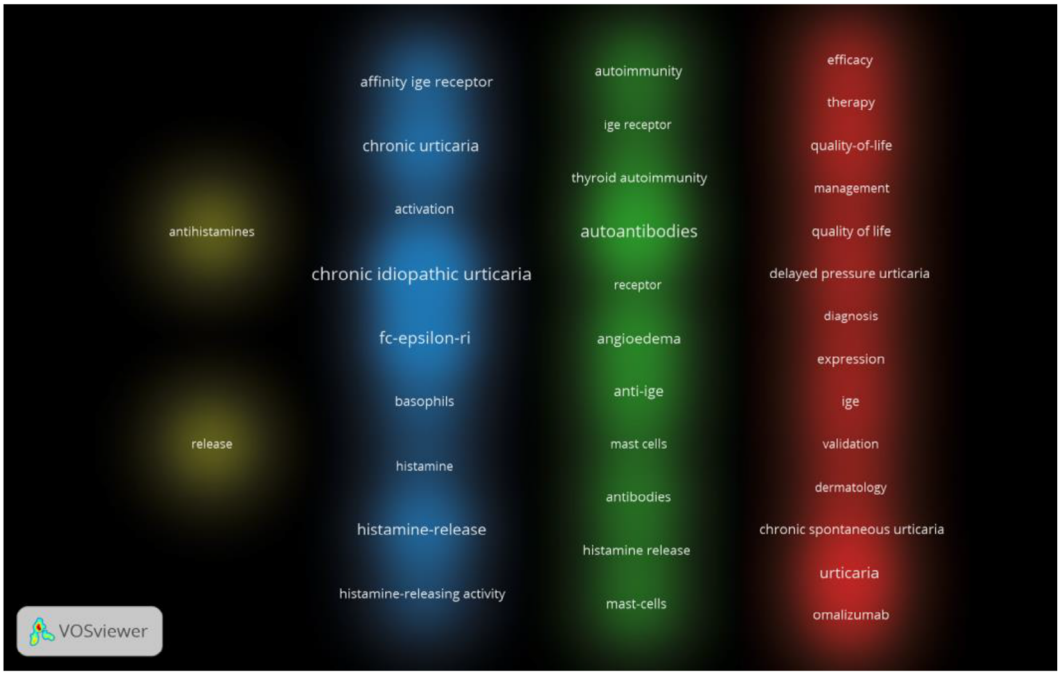

FIGURE 7 Brighter regions indicate higher intensities of keyword highlighting.

In the course of urticaria, susceptibility to allergens can lead to its chronicity, hence the emphasis on a deeper understanding and effective management of the condition. It is evident that a substantial portion of influential literature has concentrated on exploring the causes of CU and identifying treatment strategies. Research has indicated that IgE-mediated mast cell activation and degranulation, along with the release of histamine-based inflammatory mediators, play a crucial role in CU's pathogenesis.[46–48] This hypothesis has been supported by experiments showing elevated histamine levels in individuals with CU.[49–50] Recent findings also reveal that, besides anti-high-affinity IgE receptor α subunit (FcεRIα) and anti-IgE antibodies, the presence of anti-thyroid autoantibodies, anti-HP antibodies, and anti-FcεRIα antibodies in CU patients' circulation indirectly relates to the immune pathogenesis of CU.[25,51,52] Furthermore, urticaria is linked with vascular edema,[53,54] thyroid autoimmunity,[55,56] and its treatment drugs include cyclosporine.[57] For treatment-resistant urticaria, high doses

of levocetirizine and desloratadine may be considered.[17] Omalizumab has been shown to significantly alleviate pruritus in CU patients,[20,58] particularly in those who continue to experience symptoms after using H1 antihistamines.[26]

Through VOSviewer analysis, "management," "omalizumab," and "quality of life" emerged as keywords with significant density, highlighting the research focus on urticaria related to quality of life and omalizumab treatment. The Nottingham Health Profile (NHP) illustrates that CU impacts various aspects of patients' lives, including home management, personal care, entertainment and social interactions, mobility, emotional factors, sleep, rest, and work.[59] The disease activity of urticaria is evaluated by the Urticaria Activity Score (UAS) and Quality of Life (QoL), revealing a positive correlation between the UAS and QoL scores of CU patients.[60] Tools such as the Urticaria Control Test[61] and the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL)[62] are instrumental in enhancing the life quality of individuals with CU.

As a recombinant humanized anti-IgE monoclonal antibody, omalizumab can bind to free IgE and inhibit its binding to IgE receptors on mast cells, eosinophils, basophils, and other effector cells, thus preventing effector cell activation and blocking the IgE-mediated inflammatory response.[22] Omalizumab stands as the sole anti-IgE monoclonal antibody biological agent authorized for CSU with insufficient antihistamine response, demonstrating efficacy and safety.[27,28,63–65] Currently, research on biomarkers associated with omalizumab's efficacy in CU treatment is limited. New biological agents, including anti-IgE antibodies, IL-5 inhibitors, TNF-α inhibitors, IL-1 inhibitors, IL-17 inhibitors, BTK inhibitors, and dupilumab, are attracting interest, with Ligelizumab potentially succeeding omalizumab in CU treatment.[30]

Bibliometrics is extensively utilized in the medical domain. However, due to variations in literature coverage, there's inherent bias in literature selection, influenced by publication timing, authorship, and journal source. Thus, citation analysis may not fully capture an article's impact on its field, necessitating a nuanced interpretation of citation frequency.

5 | CONCLUSION

A systematic bibliometric analysis was performed on the 100 most frequently cited articles in the field of urticaria, spanning publications from 1963 to 2023. The majority of these articles focused on the mechanisms underlying urticaria, pharmacological interventions, and health management strategies for the condition. Biological agents represent the forefront of current treatments, particularly for spontaneous and treatment-resistant forms of urticaria, where their effectiveness is notably high. Furthermore, the exploration and therapeutic application of additional biological agent targets will be central to future research endeavors.

CONFLICT OF INTEREST STATEMENT

The authors declare that the research is conducted in the absence of any commercial or financial relationships. The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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