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REVIEW

Hotspots and Trends in Allergic Rhinitis Nasal Mucosa Studies: A Bibliometric Analysis (2010-2024)

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Purpose: This study aims to conduct a bibliometric and visual analysis of the research on the nasal mucosa in allergic rhinitis (AR) and to explore its emerging trends, hotspots, and future development.

Methods: We comprehensively searched the Web of Science Core Collection (WoSCC) for literature related to the nasal mucosa in AR published between 2010 and 2024. Bibliometric and visual analyses were performed using CiteSpace, VOSviewer, and the R language.

Results: A total of 1124 relevant articles were included in this study, and the analysis showed that the number of articles in this field has been increasing year by year. China dominated the article output, followed by South Korea and Japan. American Journal of Rhinology & Allergy (69 articles) topped the list of publications; keyword analysis showed that "immune response", "inflammatory response", "autophagy", "NLRP3 inflammasome", and "miRNAs" are hotspots in this field.

Conclusion: Over the past decade, research related to the nasal mucosa in AR have gained growing interest. This study is the first to use visualization software and data mining information to conduct a bibliometric analysis in this particular field, thereby providing fresh perspectives on the research terrain.

Keywords: autophagy, NLRP3 inflammasome, miRNAs, CiteSpace, visualization

Introduction

AR is a common allergic disease that primarily affects the nasal mucosa. The main symptoms include nasal itching, paroxysmal and continuous sneezing, watery rhinorrhea, and nasal congestion.[1] It is caused by an abnormal immune response to certain foreign substances (allergens). Over the past few decades, epidemiological studies have indicated that the incidence of AR has been increasing annually with the advancement of industrialization.[2,3] AR is now considered a predominant chronic inflammatory disease of the upper respiratory tract, impacting approximately 10–40% of individuals globally.[2] Although not life-threatening, AR poses a major challenge to global health as it has a significant impact on quality of life and the considerable socio-economic burden it brings.[4,5]

In AR, the immune and inflammatory response mechanisms of the nasal mucosa are multifaceted. When AR patients' immune systems encounter specific allergens, they generate allergen-specific IgE antibodies. These IgE antibodies then bind to mast cells within the nasal mucosa, initiating an immune response.[6] Epithelial cells and innate immune cells like dendritic cells (DCs) on the nasal mucosa can recognize allergens through pattern recognition receptors (PRRs). This recognition triggers the activation of signaling cascades and amplifies inflammatory responses.[7] In AR, the activation of the NLRP3 inflammasome is intimately linked to the impairment of nasal mucosa epithelium.[8] Cezmi A. Akdis summarized the epithelial barrier damage hypothesis for allergic diseases like AR, stating that the damage of the nasal mucosa barrier is one of the characteristic pathological changes in AR and is involved throughout the whole process of pathogenesis.[9] The disruption of tight junction proteins, dysregulation of epithelial cell function such as apoptosis and pyroptosis,[10] and the action of inflammatory mediators all lead to the impairment of the nasal mucosa epithelial barrier.

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Over the past decade or so, there has been an explosion of research related to the AR and nasal mucosa, leading to a corresponding increase in the relevant literature. However, there has been no systematic survey of this field using bibliometric to gain insight into the literature and identify research focus and academic frontiers. Bibliometrics was first introduced by Pritchard in 1969.[11] It involves quantitative analysis of literature through statistical, mathematical, and computer techniques to reveal intrinsic connections and patterns in the literature.[12] Its focus is on the process of statistical analysis, assessment, and evaluation of literature and scholarship, including a variety of metrics such as the number of documents, authors, keywords, countries, institutions, citation frequency, and journal impact.[13] Recently, the integration of bibliometric and visual analysis tools such as CiteSpace, VOSviewer, and Bibliometrix has made the presentation of literature data more vivid and intuitive, helping researchers to present their analysis in chart form, enhancing the readability and persuasiveness of reports.[14,15]

Hence, the aim of this paper is to employ bibliometric and visual analysis techniques to investigate the emerging trends and hotspots in the field of nasal mucosa within the context of AR spanning from 2010 to 2024. This assessment of the scholarly accomplishments in terms of quality and volume will enable a holistic overview of the evolution and shifts in scientific research emphasis. It will enhance our comprehension of the nasal mucosa-related mechanisms in AR, shed light on current focal points and vanguard issues, keep us informed about the pulse of research progress, and aid in devising more directed research strategies.

Methods

Search Strategy and Data Collection

In this study, we opted for the WoSCC as our primary data source, specifically leveraging the Science Citation Index Expanded and the Social Sciences Citation Index. Web of Science is renowned for its comprehensive coverage of literature across a diverse array of research disciplines.[16] Widely accepted among researchers for its quality, it stands as a premier digital repository for scholarly literature and is widely regarded as the most appropriate resource for bibliometric analysis.[17]

We concentrated on English-language articles and review documents since 2010. The search queries are as follows: ((((TS=("Nasal Mucosa")) OR TS=("Nasal Epithelium")) OR TS=("Nasal Epithelial")) OR TS=("Schneiderian Membrane")) AND TS=("Allergic Rhinitis"); Publication date: from 2010–01-01 to 2024–06-30. In total, 1304 studies were retrieved, and the data were downloaded on July 19, 2024. The search and screen procedures are presented in Figure 1.

Two independent reviewers evaluated the titles and abstracts of these 1304 studies identified by our search queries to screen for eligible studies. Any discrepancies that emerged during the screening were resolved through consultation with a third reviewer, ensuring a consensus was reached. Only those publications that received affirmation from both independent reviewers were deemed valid for inclusion in our study.

Bibliometric Analysis and Visualization

The data obtained from the WoSCC were exported in "plain text file" format, utilizing the "Full Record and Cited References" feature. For the bibliometric and visual analysis, we employed the widely recognized software tools CiteSpace 6.3.R1, VOSviewer, and R 4.4.1. Additionally, we utilized the R package to download Bibliometrix, a valuable tool for further data analysis.[18] This comprehensive approach ensures a thorough and insightful examination of the research data.

CiteSpace is a Java application that excels in bibliometric analysis developed by Chen.[19] It employs Kleinberg's algorithm to detect emerging research trends and Freeman's betweenness centrality to flag possible paradigm shifts,[20] offering a clear view of a field's progression and trends over time. For our study, we tailored CiteSpace to generate visualizations of co-occurrences for authors, countries, institutions, journals, references, and keywords. We also performed cluster and emergence analyses for the keywords. CiteSpace was set with annual time slices from January 2010 to June 2024, while other parameters remained default.

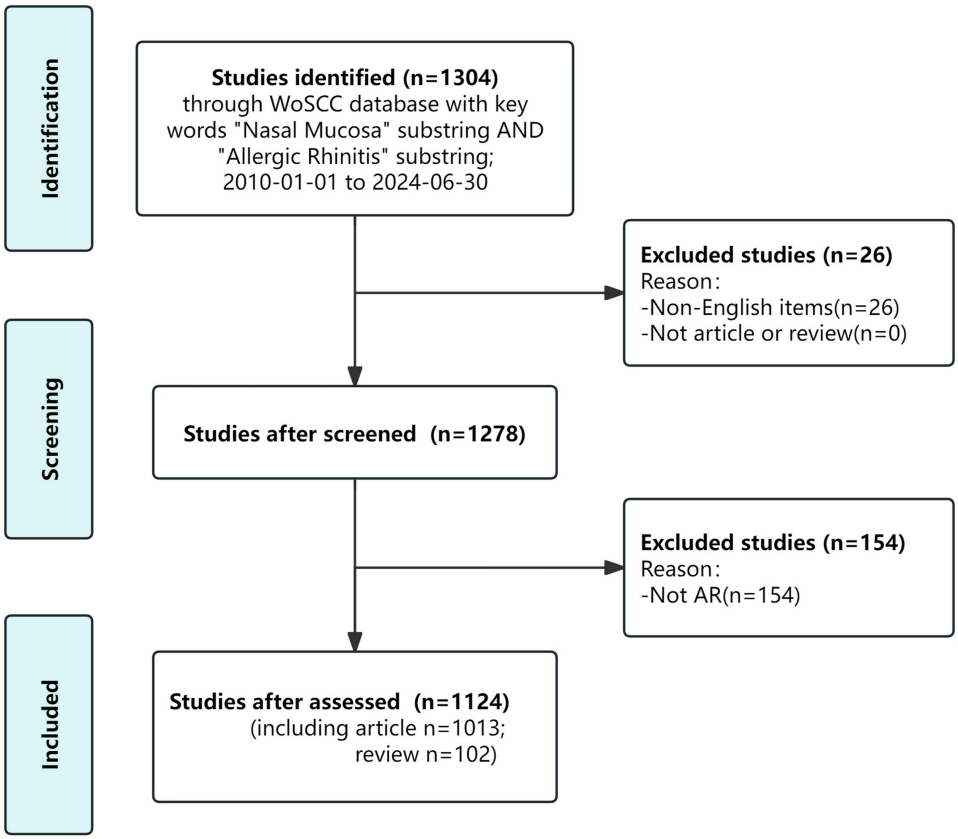

Figure 1 Search and screen procedure in this study.

VOSviewer, crafted by Eck and Waltman, facilitates the creation and visualization of bibliometric maps.[21] It provides diverse visual perspectives on co-authorship, co-occurrence, and co-citation, encompassing network, overlay, and density visualizations, known for their clarity and aesthetic appeal.

Using these sophisticated tools, we visualized 1124 studies across several critical dimensions, offering a detailed scholarly landscape overview. The analysis outlined individual author contributions, research distribution by country, and institutional collaborations. It also highlighted key journals, co-cited references, and core focus keywords. Burst word detection revealed emerging concepts and trending topics. This visualization provides a comprehensive snapshot of the research ecosystem.

Results

Main Information Description and Growth Trends of the Literature

The 1124 documents that form the basis of this study were collected over a period spanning January 1, 2010, to June 30, 2024 (Figure 2). These documents represent the collaborative efforts of 5355 authors affiliated with 1278 organizations across 61 countries. They have been disseminated through publications in 347 prestigious journals and have garnered attention by citing a substantial body of work, comprising 30044 documents from an extensive range of 4303 journals. This extensive network of scholarly communication highlights the globally collaborative and interdisciplinary character of research within this field.

Between 2010 and 2023, the WoSCC documented a significant body of work, totaling 1070 English-language publications, focused on AR and nasal mucosa. Over the past ten years, there has been a marked escalation in the output of scholarly research in this domain, with 332 distinct sources contributing to this corpus. The field has shown a robust annual growth rate of 8.96%, with a particularly notable surge in publication volumes post-2020. Since 2021, the annual output has not only witnessed a sharp rise but also reached a plateau, exceeding 100 publications each year. The

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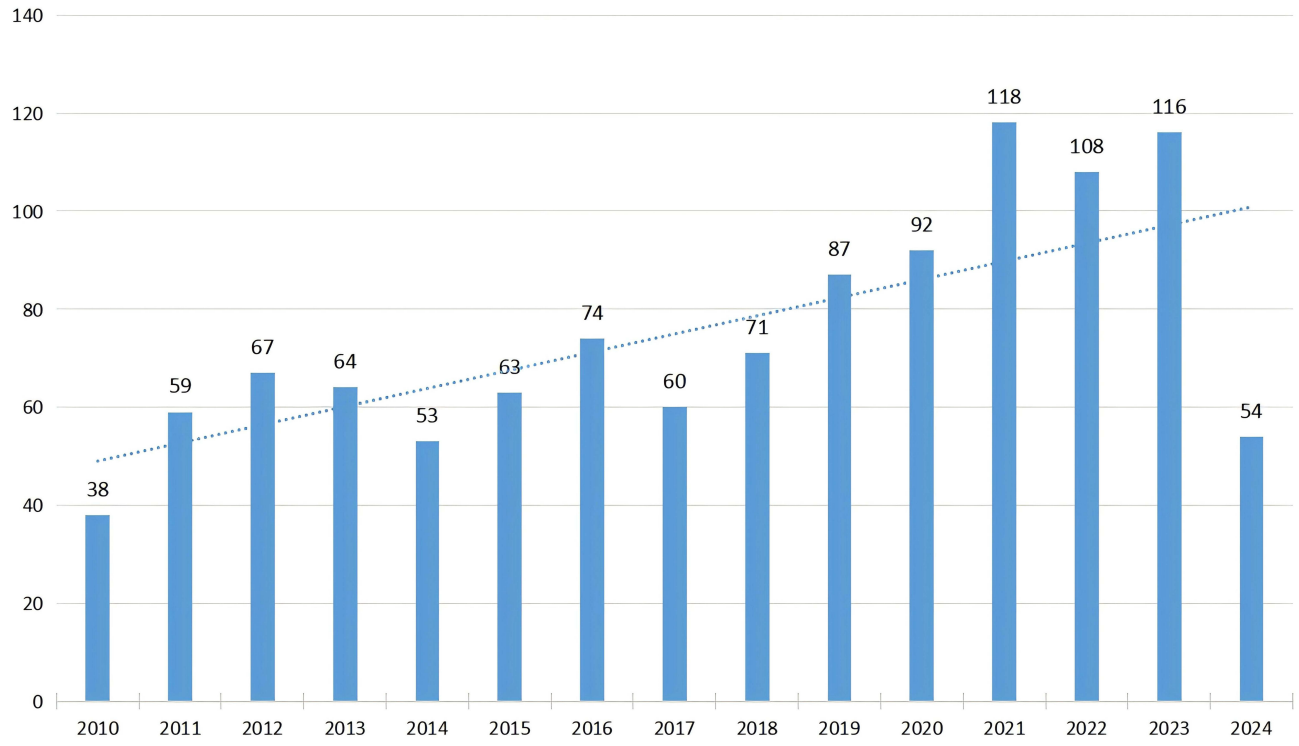

Figure 2 Growth trends and annual production of documents from 2010 to 2024.

zenith was reached in 2021, with a record 118 articles published (Table 1). Furthermore, from January 1 to June 30, 2024, the WoSCC has already indexed 54 relevant publications, surpassing the full-year total of 53 publications from 2014. This upward trajectory suggests a burgeoning interest among academic researchers in AR and nasal mucosa, signifying that this area is emerging as a focal point for investigation within the AR research community.

Table 1 Main Information Description From 2010 to 2023

Description	Results
Timespan	2010:2023
Sources (Journals, Books, etc)	332
Documents	1070
Annual Growth Rate %	8.96
Document Average Age	6.38
Average citations per doc	16.63
References	28473
Keywords Plus (ID)	2326
Author's Keywords (DE)	2325
Authors	4443
Authors of single-authored docs	10
Single-authored docs	10

(*Continued*)

Table 1 (Continued).

Description	Results
Co-Authors per Doc	6.59
International co-authorships %	15.23
Article	971
Review	99

Author Analysis

Lotka's Law is a cornerstone principle in the field of bibliometrics, illuminating the distribution of research output as measured by the number of papers written by researchers within a defined timeframe. This law serves as a metric for assessing both the productivity and the scholarly influence of researchers, as originally postulated by Lotka in 1926.[22] This principle underscores the concentration of research impact within a small cohort of prolific writers (Figure 3).

Price's Law, proposed by the eminent scholar Derek J. de Solla Price,[23] suggests that a significant proportion of the papers on a specific subject are authored by a group of notably prolific writers. This group's size is roughly equivalent to the square root of the total number of authors contributing to the field. Mathematically, this can be expressed as:

$$\sum_{m+1}^{I} n(x) = \sqrt{N}$$

Where *n(x)* represents the number of authors who have published *x* papers, and $I=n_{\max}$ represents the number of papers written by the most prolific authors in the field ($n_{\max}=19$ according to VOSviewer). The total number of authors is *N*, and *m* is the minimum number of publications required to be considered a core author. In accordance with Price's Law, $m=0.749\times m = 0.749 \times \sqrt{n_{\max}} \approx 3.26$. Consequently, we defined authors with 4 or more publications as core authors. This criterion identified 206 core authors in our study (Figure 4). Table 2 lists the top 5 authors with the highest

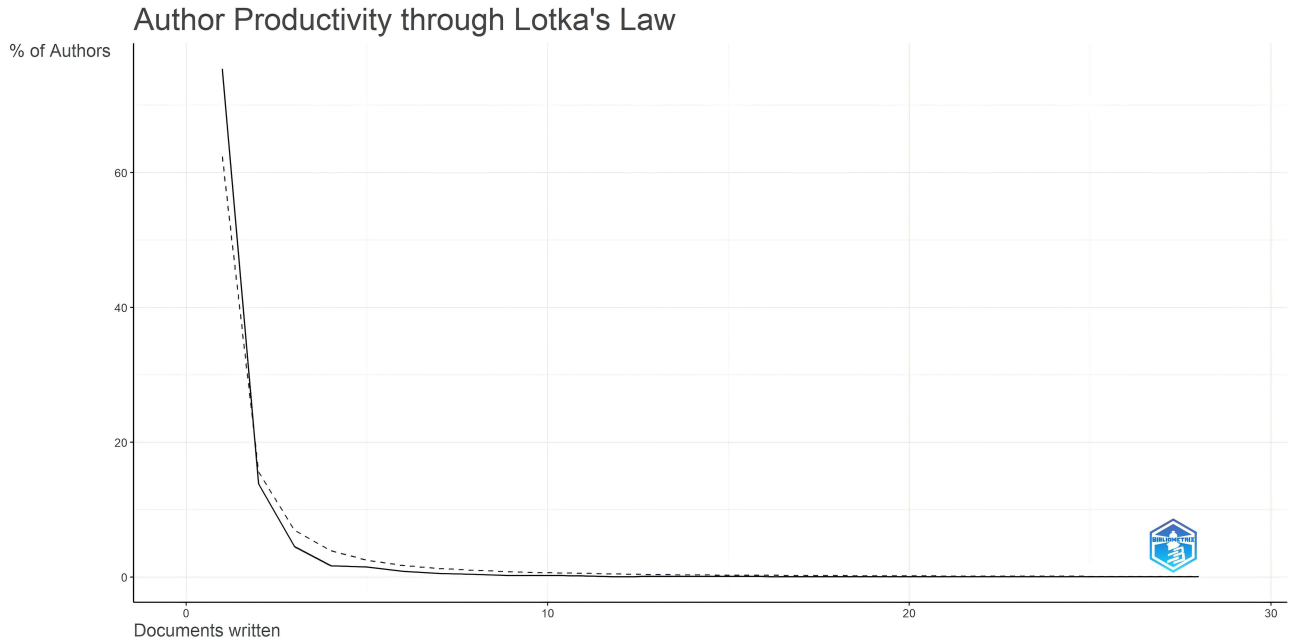

Figure 3 Author productivity through Lotka's Law in the field of AR and nasal mucosa.

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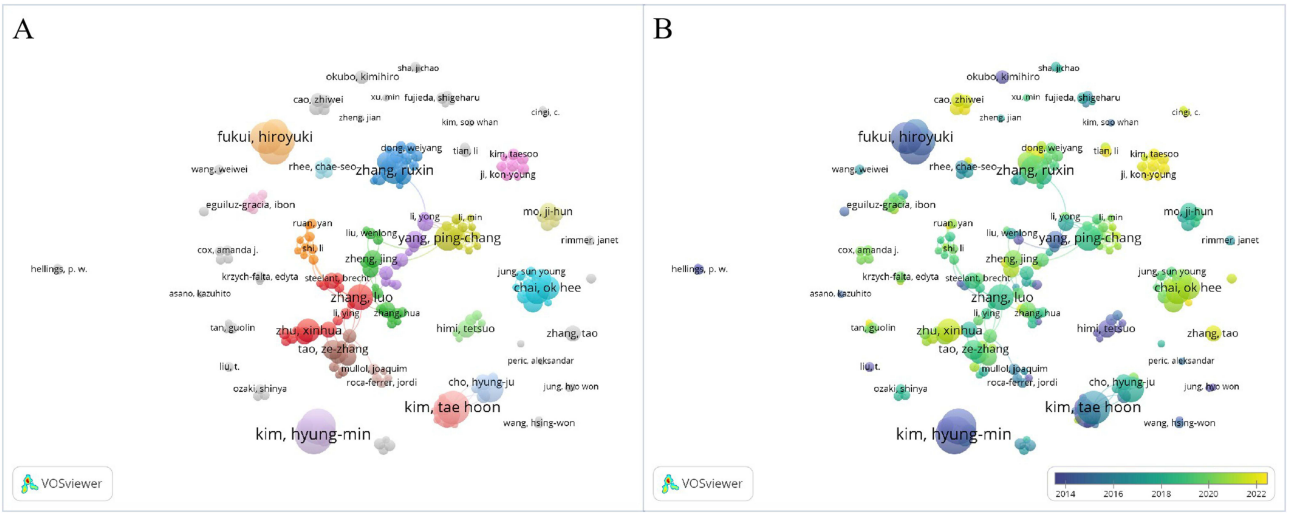

Figure 4 Author analysis. (**A**) Network visualization of core authors; (**B**) Overlay visualization of core authors.(Size of circles stands for the number of documents.).

publication counts in this field. Among these high-productivity authors, Kim Hyung-Min is the most prolific, followed by Jeong Hyun-Ja and Kim Tae-Hoon.

Countries/Regions Analysis

To gain insights into the countries with illustrious contributions to the field of studies related to AR and nasal mucosa, we conducted an analysis of the publication volume across 61 countries included in this study. Utilizing VOSviewer, we visualized the publication data for countries with four or more publications (Figure 5A). This analysis revealed that China (510 papers), South Korea (139 papers), Japan (115 papers), the USA (70 papers), and Italy (45 papers) were the top five most productive countries, a finding that aligns with the statistics generated by CiteSpace (Figure 5B). However, due to algorithmic differences, Bibliometrix statistics identified China, South Korea, Japan, the USA, and Turkey as the top five most productive countries. A closer look at the annual publication trends indicates that China has seen a remarkable increase in output since the start of 2018, solidifying its leading position in this research domain (Figure 5C).

Table 2 Top 5 Authors With the Most Publications

Rank	Author	Affiliation	Documents	Citations	Average Citation/ Publication
1	Kim, HM	Department of Pharmacology, College of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea	19	468	24.63
2	Jeong, HJ	Department of Food Science and Technology and Research Institute for Basic Science, Hoseo University, Chungnam, Republic of Korea	18	402	22.33
3	Kim, TH	Ludwig Institute for Cancer Research, 9500 Gilman Drive, La Jolla, CA 92093–0653, USA	17	207	12.18
4	Fukui, H	Department of Molecular Studies for Incurable Diseases, Institute of Biomedical Sciences, Fujii Memorial Institute of Medical Science, Tokushima University Graduate School, 3–18-15 Kuramotocho, Tokushima, 770–8503, Japan	16	215	13.44
5	Mizuguchi, H	Department of Molecular Pharmacology, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, 770–8505, Japan	16	215	13.44

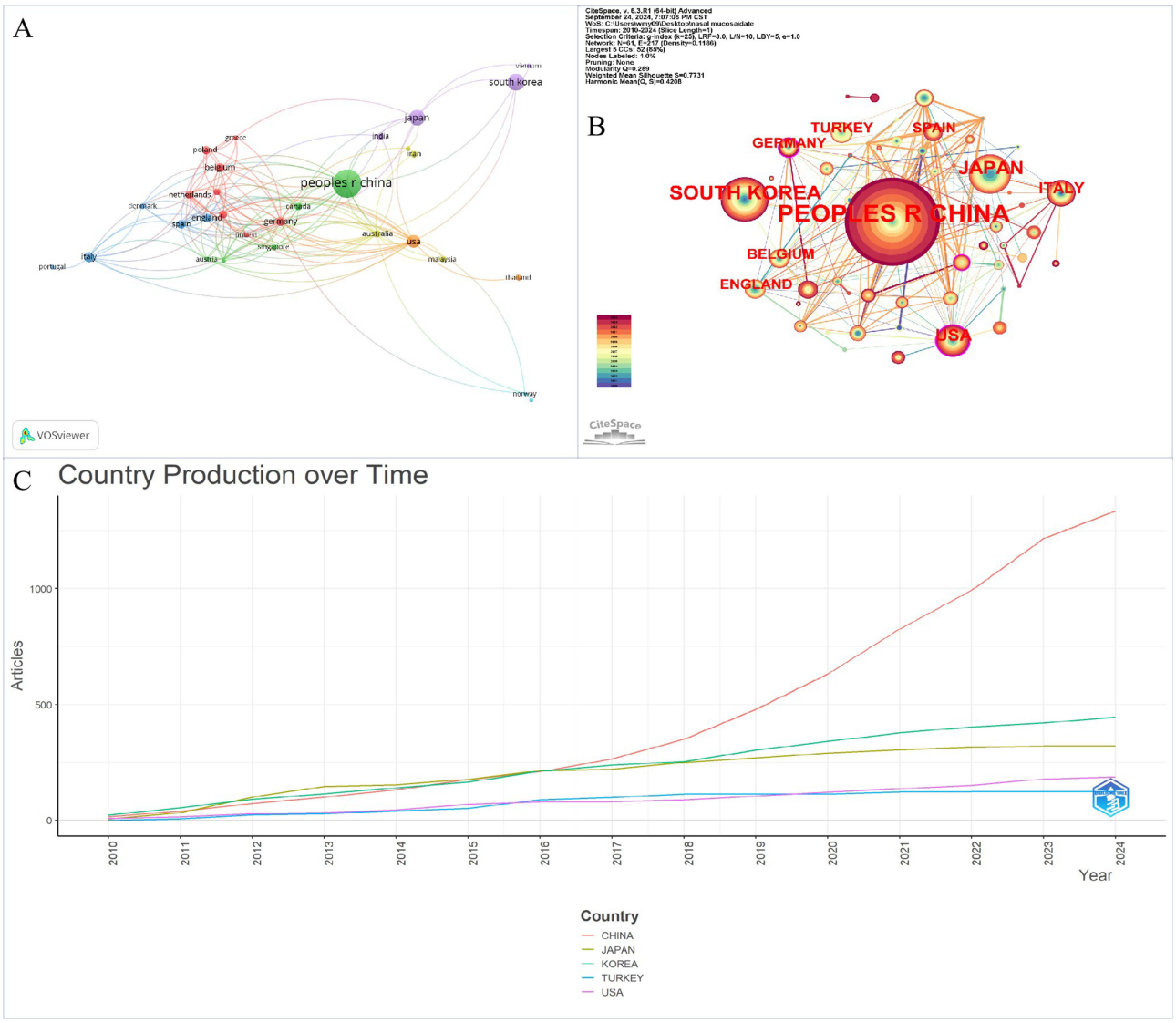

Figure 5 Countries/regions analysis. (**A**) VOSviewer's visualization map; (**B**) Citespace's visualization map; (**C**) Countries' production over time.

Institutions Analysis

After conducting a statistical analysis of the production institutions for the 1124 documents included in this study, it was found that the top ten producing institutions are all universities (Table 3). Fudan University leads with 34 documents, followed by Kyung Hee University with 29 and Sun Yat-sen University with 26. In terms of average citations per

Table 3 Top 10 Organizations in the Field of AR and Nasal Mucosa

Rank	Institution	Country	Centrality	Documents	Citations	Average Citation/Publication
1	Fudan University	Peoples r china	0.02	34	633	18.6176
2	Kyung Hee University	South korea	0.01	29	576	19.8621
3	Sun Yat Sen University	Peoples r china	0.09	26	521	20.0385
4	Korea University	South korea	0.00	26	327	12.5769

(*Continued*)

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Table 3 (Continued).

Rank	Institution	Country	Centrality	Documents	Citations	Average Citation/Publication
5	Nanchang University	Peoples r china	0.00	25	234	9.36
6	Shanghai Jiao Tong University	Peoples r china	0.03	22	227	10.3182
7	Seoul National University (SNU)	South korea	0.01	22	535	24.3182
8	Capital Medical University	Peoples r china	0.06	21	383	18.2381
9	China Medical University	Peoples r china	0.00	21	218	10.381
10	Wuhan University	Peoples r china	0.00	19	282	14.8421

publication, Sun Yat-sen University ranks first, with Kyung Hee University and Fudan University coming in second and third, respectively.

Cluster analysis using CiteSpace software revealed that in the field of AR and nasal mucosa-related research, specific collaborative groups of institutions have formed. For instance, in China, Fudan University, Sun Yat-sen University, Capital Medical University, Shanghai Jiao Tong University, Nanchang University, and Guangzhou Medical University; and in South Korea, Kyung Hee University, Korea University, Hoseo University, and Korea University Medicine (KU Medicine) have demonstrated a clear trend of collaboration in this area of research. However, most of these collaborations are primarily domestic, with international cooperation still being limited (Figure 6).

Sources Analysis

Bradford's Law is a fundamental concept in information science that helps in categorizing journals and identifying core journals in specific areas. Journals in the core zone are considered to be the most significant, as they contain a concentrated amount of information on the subject. It was introduced by British chemist and documentation scholar S. C. Bradford in 1948. This method is based on a mathematical formula that represents the distribution of articles across journals, typically following a $1:n:n^2$ ratio, where the number of journals decreases as the article frequency increases.[24] The core journals are listed in Table 4. We searched these journals in Journal Citation Reports (JCR) for their 2023 Impact Factors (IF) and quartile.

Analysis reveals that the American Journal of Rhinology & Allergy (69) published the highest number of papers, followed by International Immunopharmacology (42) and International Archives of Allergy and Immunology (35). The most influential journals are Allergy (IF_{2023}=12.6, H=19) and the Journal of Allergy and Clinical Immunology (IF_{2023} =11.4, H=19) (Figure 7).

References and Co-Cited Analysis

The phenomenon of co-citation refers to the simultaneous citation of two journals in one or more publications, signifying a scholarly connection. In CiteSpace, nodes exhibiting mediation centrality above 0.1 are identified as key points.[25] Analyses of co-cited authors using CiteSpace and VOSviewer reveal that Professor Jean Bousquet is the most frequently cited author (Figure 8). His article "Allergic Rhinitis" in Nature Reviews Disease Primers[26] is the most highly cited document (Table 5). Additionally, his contributions to the field of AR and nasal mucosa research are significant, with notable articles including "Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen)" published in Allergy[27] and "Allergic rhinitis: a disease remodeling the upper airways?" in the Journal of Allergy and Clinical Immunology.[28]

The overlay maps visualization illustrates the distribution of academic disciplines. The left side indicates the citing journals, while the right side indicates the cited journals. The colored paths illustrate the citation relationships, with the labels representing the disciplines that the journals encompass. Four particularly notable pathways are visible. The two

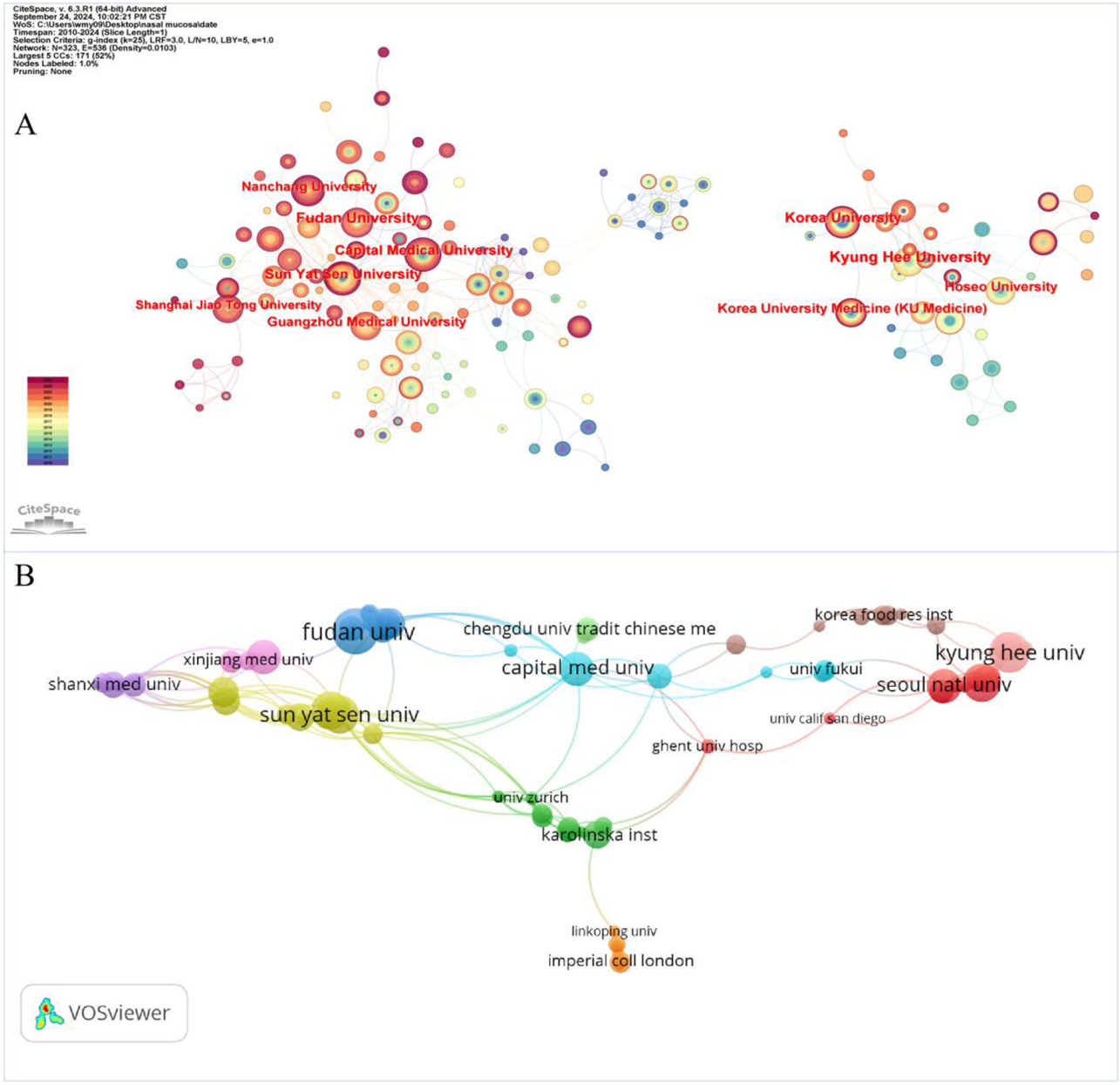

Figure 6 Institutions analysis. (**A**) Citespace's visualization map; (**B**) VOSviewer's visualization map.

yellow citation paths indicate that researches from journals in Molecular, Biology, Genetics and Health, Nursing, Medicine are often cited by those in Mathematics, Systems, Mathematical and Molecular, Biology, Immunology. The green citation path shows that researches from Molecular, Biology, Genetics journals are consistently referenced by

Table 4 Core Sources in the Field of AR and Nasal Mucosa

Rank	Sources	Documents	IF_{2023}	JCR Quartile	H
1	AMERICAN JOURNAL OF RHINOLOGY & ALLERGY	69	2.5	OTORHINOLARYNGOLOGY Q1	18
2	INTERNATIONAL IMMUNOPHARMACOLOGY	42	4.8	IMMUNOLOGY Q2	17
3	INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY	35	2.5	ALLERGY Q3	12

(*Continued*)

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Table 4 (Continued).

Rank	Sources	Documents	IF_{2023}	JCR Quartile	H
4	INTERNATIONAL FORUM OF ALLERGY & RHINOLOGY	34	7.2	OTORHINOLARYNGOLOGY Q1	13
5	ALLERGY	31	12.6	ALLERGY/IMMUNOLOGY Q1	19
6	JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY	24	11.4	ALLERGY Q1	19
7	CLINICAL AND EXPERIMENTAL ALLERGY	22	6.3	ALLERGY Q1	13
8	EUROPEAN ARCHIVES OF OTO-RHINO-LARYNGOLOGY	18	1.9	OTORHINOLARYNGOLOGY Q2	8
9	PLOS ONE	17	2.9	MULTIDISCIPLINARY SCIENCES Q1	11
10	ALLERGOLOGIA ET IMMUNOPATHOLOGIA	16	2.5	ALLERGY Q3	9

journals in Medicine, Medical, Clinical. Lastly, the grey citation path reveals that studies from Molecular, Biology, Genetics journals are regularly cited by journals in Dentistry, Dermatology, Surgery (Figure 9).

Keywords and Burst Analysis

Keywords serve to accurately summarize the themes of academic literature, describing the core content and research areas of a paper. In this study, keyword analysis was conducted on 1124 articles, yielding a total of 4342 keywords. The keywords that appeared with higher frequency include “asthma” (301, 10%), “expression” (261, 9%), “inflammation” (189, 6%), “cells” (146, 5%), “allergic rhinitis” (136, 5%), “nasal mucosa” (118, 4%), and “activation” (96, 3%) (Figure 10A). We utilized VOSviewer to conduct a co-occurrence analysis of keywords, setting the minimum number

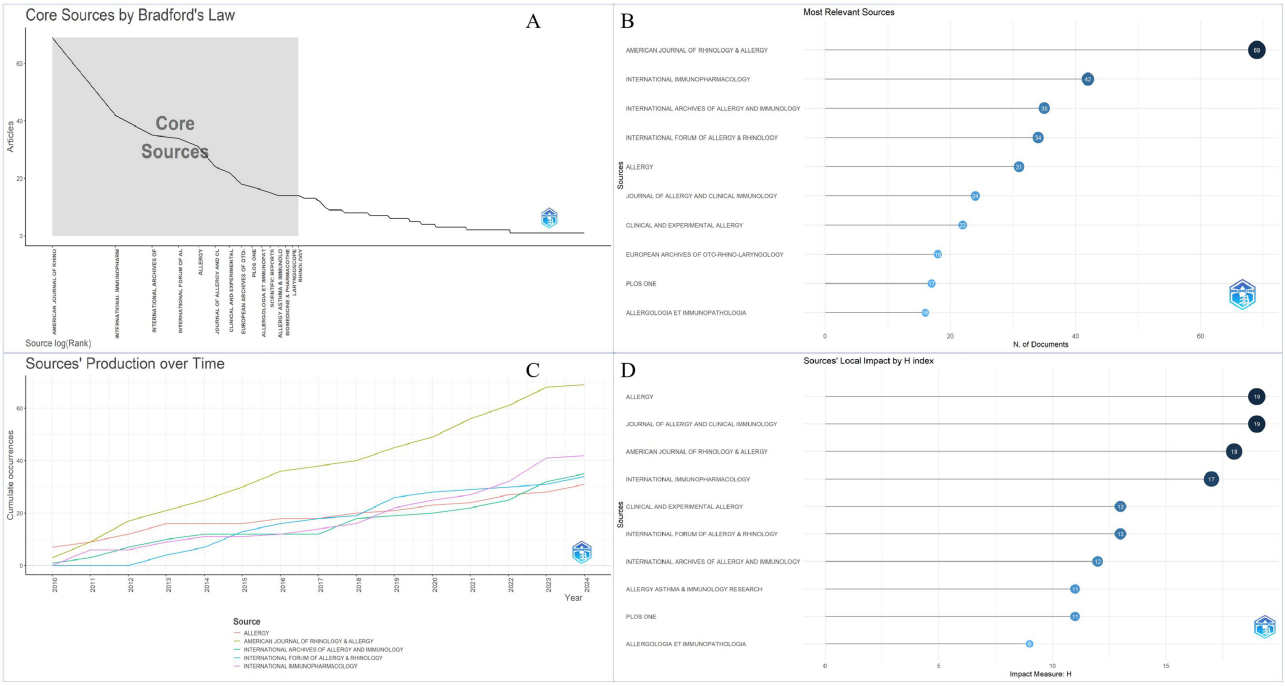

Figure 7 Sources analysis. (**A**)Core sources by Bradford’s law; (**B**)Most relevant sources; (**C**)Sources’ production over time; (**D**)Sources’ local impact by H index.

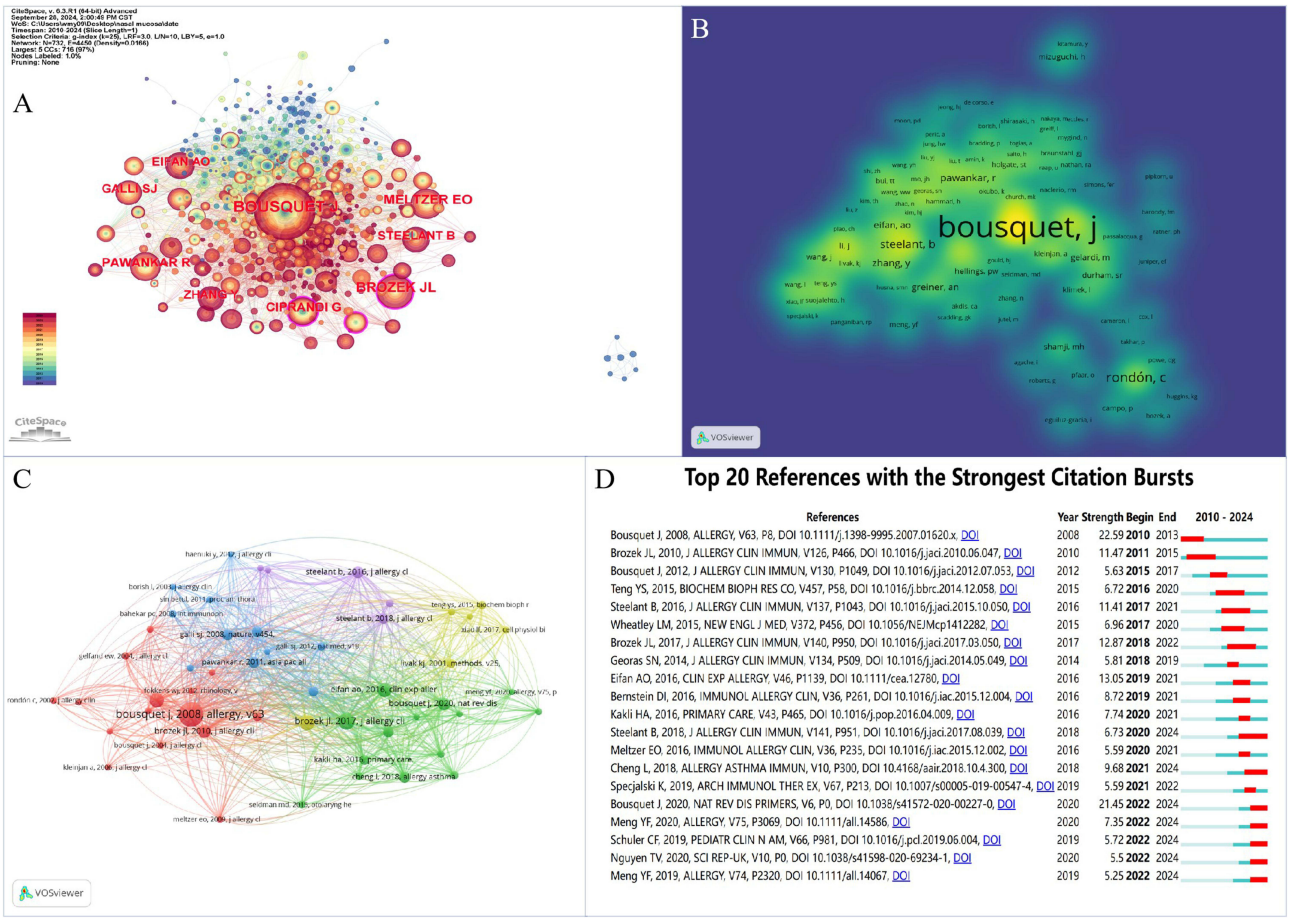

Figure 8 Citation analysis. (**A**) Author co-citation network; (**B**) Density visualization of author co-citation; (**C**) References co-citation network; (**D**)Top 20 references with strongest citation bursts.

of occurrences of a word to 20, which resulted in 76 keywords reaching the threshold. We calculated the total strength of co-occurring links between each of these 76 keywords. The keywords co-occurrence network diagram demonstrates that the thicker the connections between nodes, the more frequently two keywords appear at the same time (Figure 10C). These keywords form four distinct clusters, each representing a primary research direction in the fields of nasal mucosa and AR.

Table 5 Top 10 Cited References of Publication in the Field of AR and Nasal Mucosa

Rank	Frequency	Centrality	Author	Source	Title	Publication Year
1	63	0.01	Bousquet J	Nat Rev Dis Primers	Allergic rhinitis	2020
2	60	0.05	Brozek JL	J ALLERGY CLIN IMMUN	Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision	2017
3	46	0.01	Cheng L	ALLERGY ASTHMA IMMUN	Chinese Society of Allergy Guidelines for Diagnosis and Treatment of Allergic Rhinitis	2018

(*Continued*)

Table 5 (Continued).

Rank	Frequency	Centrality	Author	Source	Title	Publication Year
4	42	0.23	Bousquet J	ALLERGY	Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen)	2008
5	38	0.09	Eifan AO	CLIN EXP ALLERGY	Pathogenesis of rhinitis	2016
6	36	0.08	Steelant B	J ALLERGY CLIN IMMUN	Impaired barrier function in patients with house dust mite-induced allergic rhinitis is accompanied by decreased occludin and zonula occludens-1 expression	2016
7	33	0.03	Steelant B	J ALLERGY CLIN IMMUN	Histamine and T helper cytokine-driven epithelial barrier dysfunction in allergic rhinitis	2018
8	24	0.17	Kakli HA	PRIMARY CARE	Allergic Rhinitis	2016
9	24	0.24	Brozek JL	J ALLERGY CLIN IMMUN	Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision	2010
10	23	0.00	Zhang Y	ALLERGY	Advances and highlights in allergic rhinitis	2021

Cluster analysis of keywords is instrumental in delineating the structural framework of related research domains. By leveraging CiteSpace for clustering and analyzing keywords, we employed the Log-Likelihood Ratio (LLR) method to categorize these clusters, resulting in the generation of both cluster and timeline views (Figure 10D and E). An analysis of keywords from relevant articles spanning over a decade revealed that these primary keywords coalesced into seven significant clusters, numbered from 0 to 6, with the smaller numbers indicating clusters with a higher volume of

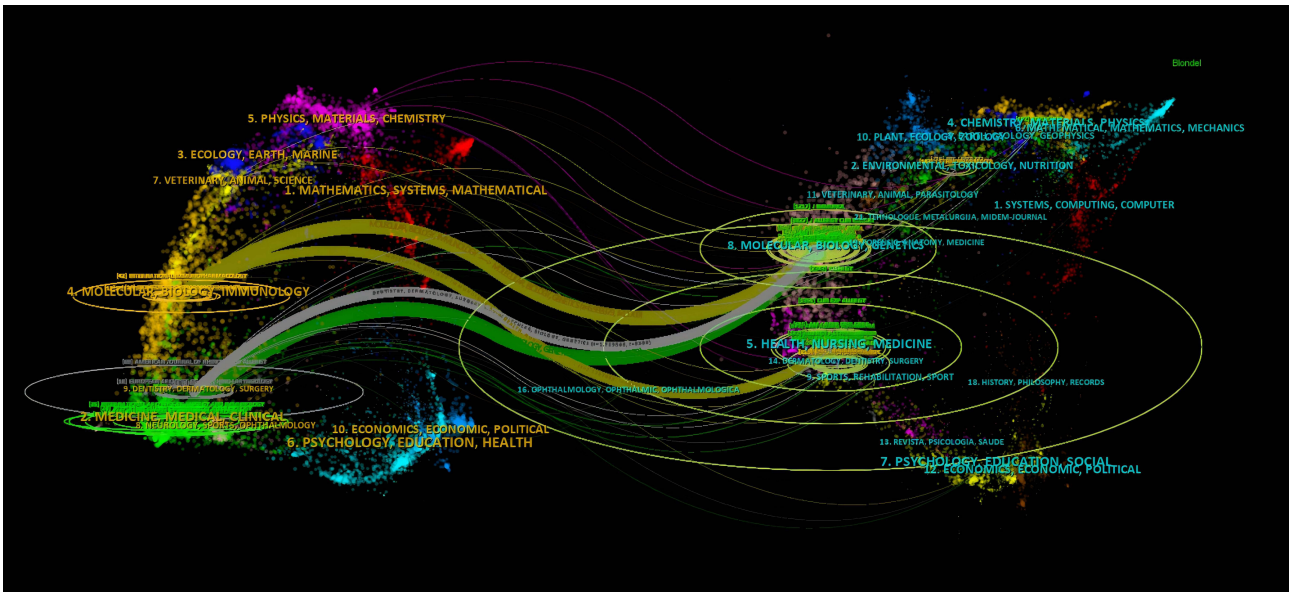

Figure 9 Overlay maps.

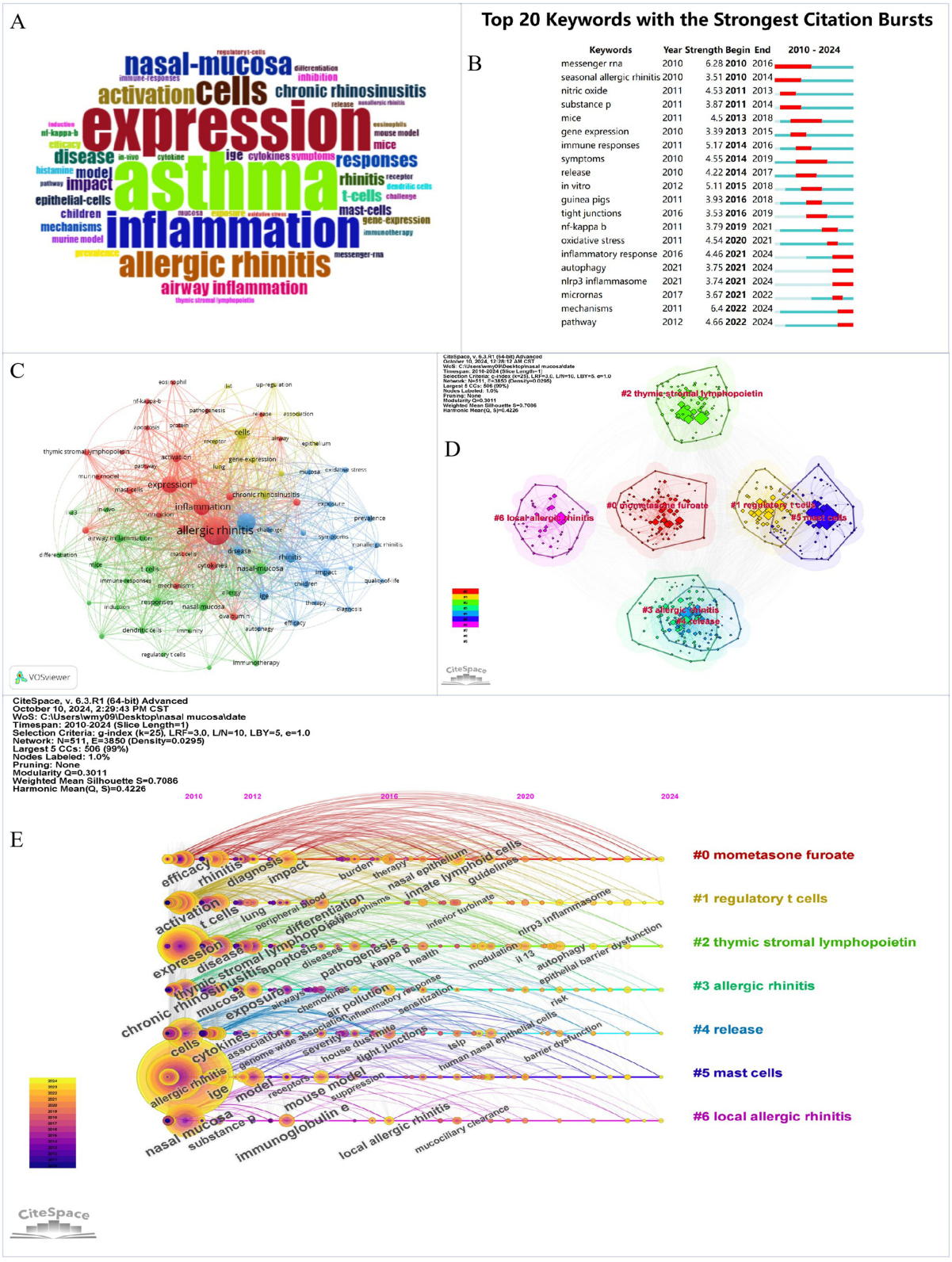

Figure 10 Keywords and burst analysis. (**A**) WordCloud; (**B**) Top 20 keywords with the strongest citation bursts; (**C**) Keywords co-occurrence network; (**D**) Keywords clustering map; (**E**) Timeline view of keywords.

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keywords. The presence of several overlapping clusters in the keyword co-occurrence diagram signifies their close interrelation. Each cluster represents a distinct research theme, and by assigning the same color to these clusters, we not only clearly demonstrate their interconnections but also reinforce the visual impression that they point to similar research areas. Moreover, the timeline view of the cluster diagram visualizes when each cluster was formed and its interconnections, presenting the dynamic evolution of research hotspots over time. In this timeline view, the X-axis represents the publication year and the Y-axis corresponds to the cluster numbers. Our cluster analysis identified key research hotspots in AR and nasal mucosa, encompassing "(#0) mometasone furoate", "(#1) regulatory T cells", "(#2) thymic stromal lymphopoietin (TSLP)", "(#3) allergic rhinitis", "(#4) release", "(#5) mast cells", and "(#6) local allergic rhinitis".

Kleinberg's burst detection algorithm is a fundamental computational approach for recognizing abrupt changes in events, widely used to detect the sudden emergence of research hotspots within specific domains. Keywords that exhibit explosive growth may signal key directions in growing trends. Based on a co-citation network of keywords, we conducted a burst detection analysis. We report the top 20 keywords with the highest citation burst in nasal mucosa and AR. As shown in Figure 10B, the blue line signifies the chronological sequence, with red segments highlighting the detected surges, noting the starting and concluding years and the duration of these abrupt increases. This visualization method provides us with an intuitive tool for identifying and tracking key trends and turning points within the research field. With a strength of 6.4, the keyword "mechanisms" leads the list, followed by "messenger RNA" (6.28) and "immune responses" (5.17). Emerging keywords that began to appear in 2020, such as "oxidative stress", "inflammatory response", "autophagy", "NLRP3 inflammasome", and "microRNAs", suggest that these subjects represent current research hotspots within the field. The emergence of these keywords may indicate new trends and key directions for development in the field, warranting further exploration.

Combining keywords analysis and burst detection, we have identified that "regulatory T cells", "thymic stromal lymphopoietin (TSLP)", "mast cells", "oxidative stress", "autophagy", "NLRP3 inflammasome", and "microRNAs" may emerge as potential future research priorities in the mechanisms of AR and nasal mucosa. These areas of focus could lead to significant advancements in understanding and treating AR, as well as provide insights into the complex interactions between the immune system and upper respiratory health.

Discussion

General Information

In recent years, AR has become significantly more prevalent, severely impacting patients' quality of life and creating a considerable health burden. As the exploration of the pathogenesis of AR continues, the role of nasal mucosa in the disease process is increasingly gaining attention. Accordingly, a systematic analysis of studies on AR and nasal mucosa was conducted using bibliometric techniques in this study, with the goal of gaining a thorough comprehension of the field's developmental trends and emerging research focal points.

In this study, we analyzed 1124 documents in the field of AR and nasal mucosa, using three bibliometric tools—VOSviewer, CiteSpace, and Bibliometrix—to showcase the advancements and key focal points in this field over the past decade. We quantitatively analyzed annual publication volumes, authors, countries/regions, institutions, journals, and keywords. The analysis of annual publication volumes indicates an increasing number of scholarly outcomes in this field, suggesting its promising and potential nature.

Drawing from the statistical analysis of publication counts by various countries and institutions, we are able to pinpoint the principal countries and institutions contributing substantially to the body of published literature on AR and the nasal mucosa, as well as determine their collaborative relationships. China, South Korea, and Japan are the main contributors to the publication of documents in this field, likely due to ample research funding and strategic prioritization of allergic disease research. Among the top ten institutions, all are universities, with 7 from China and 3 from South Korea. Yet, the lack of extensive international collaboration with other countries and regions underscores the necessity for strengthening the global trend of interdisciplinary and academic exchanges. It is imperative for nations at the academic core to spearhead the formation of a worldwide academic collaborative network to facilitate

extensive epidemiological studies and large-scale, multicenter clinical trials, along with a variety of other research endeavors.

From the perspective of authors, Hyung-Min Kim stands out as the most prolific author, dedicating his research to the impact of caspase-1/NF-κB signaling cascade on TSLP in AR.[29–31] In terms of cited literature, Professor Jean Bousquet is the most frequently cited author. Professor Jean Bousquet is a renowned expert in the field of allergic diseases. He is an honorary professor of pulmonary medicine at Montpellier University, France, and a pulmonary disease specialist with an MD, PhD degree. He has been involved in numerous research projects related to allergic diseases and respiratory diseases,[32–34] including the impact of allergic diseases in different environments, the impact of air pollution on respiratory diseases and digital transformation in healthcare.[35–37] His outstanding contributions to the study of the mechanisms of allergic diseases, along with over 1000 published papers, make him one of the most influential authors in allergic diseases.

Journals serve as tools for disseminating articles to the wider scientific community. Due to the allure of high IF journals within the scientific sphere, a journal's IF is, to some extent, one of the most powerful citation indicators. Articles with high citation rates are typically published in journals with a high IF. Among the top 10 journals in this field, the American Journal of Rhinology & Allergy stands out as the most prolific journal in the AR and nasal mucosa domain in terms of publication output. Allergy (IF_{2023}=12.6, H=19) and the Journal of Allergy and Clinical Immunology (IF_{2023}=11.4, H=19) are the most influential ones. Eight of these journals are classified as Q1 or Q2 in the JCR category, indicating a relatively high standard of quality for publications in AR and nasal mucosa-related research journals. Thus, this field of study possesses considerable importance within the broader global research landscape.

Emerging Trends and Hotspots

The analysis of high-frequency keywords sheds light on the focal points within specific research areas. Through the application of keyword co-occurrence and clustering analysis, we have pinpointed the principal directions and hotspots in the realm of AR and nasal mucosa, as well as the evolution and transformation of their thematic structures. Using Bibliometrix, VOSviewer, and CiteSpace for the visualization analysis of keywords, we found that the popular terms in this research field were primarily "asthma", "expression", "inflammation", "activation", "regulatory T cells", "thymic stromal lymphopoietin (TSLP)", "mast cells", "oxidative stress", "autophagy", "NLRP3 inflammasome", and "microRNAs". The emergence of novel keywords and their thematic evolution further validate these findings. Notably, the keyword frequency analysis has shown that "asthma" surpasses "AR" in frequency, potentially due to AR being an important risk factor for asthma.[5] The "one airway, one disease" hypothesis put forth by Grossman[38] encapsulates the pathogenic link between AR and asthma, suggesting that the interplay between AR and asthma is a vital area ripe for further investigation.

The array of keywords highlights several terms pertinent to the mechanisms of AR within the nasal mucosa, encompassing "NF-kappa-B", "regulatory T cells", "thymic stromal lymphopoietin (TSLP)", "mast cells", "cytokine", "oxidative stress", "autophagy", "NLRP3 inflammasome", and "microRNAs". The analysis of keyword bursts reveals an evolving emphasis within the research dedicated to understanding the nasal mucosa mechanisms in AR. Between 2010 and 2019, the scientific community prioritized keywords like "messenger RNA", "nitric oxide", "substance P", "immune responses", "tight junction (TJ)", and "NF-kappa-B". Since the onset of 2020, there has been an escalating trend of interest in "oxidative stress", "inflammatory response", "autophagy", "NLRP3 inflammasome", "microRNAs", "mechanisms", and "pathway". Notably, the enduring impact of "inflammatory response", "autophagy", and "NLRP3 inflammasome" on contemporary research underscores the most recent trends in the domain, signifying the frontiers of investigation in this scientific arena.

Immune and Inflammatory Response

It is well recognized that AR is an IgE-mediated immune response. In AR, there is an increase in the activation of Th2 cells, which in turn leads to the production of additional cytokines like IL-4, IL-5, and IL-13. These cytokines promote the synthesis of IgE and draw eosinophils to the inflammatory site.[39] Additionally, nasal epithelial cells play a role in the

pathogenesis of AR. Upon exposure to allergens, these cells can recognize allergens through TLRs,[7] activate downstream signaling pathways such as NF-κB,[40] and promote inflammatory responses. ILC2s, a newly identified group of lineage-negative cells, initiate type 2 allergic inflammation, typically relying on cytokines derived from epithelial cells for their activation.[41] IL-25, IL-33, and TSLP can induce Th2 cell immune responses, leading to allergic diseases, while also stimulating ILC2s to secrete Th2-type cytokines under the regulation of the transcription factor GATA-3, participating in inflammatory responses.[42] Myeloid dendritic cells (mDCs) from the nasal mucosa of patients with AR can activate ILC2s by secreting IL-33 via the IL-33/ST2 pathway.[43] Studies focusing on gene sets related to inflammatory responses are capable of identifying diagnostic characteristics, molecular subtypes, and potential therapeutic agents for AR. The pathways involved include chemokine and TNF signaling pathways, with NFKBIA, HIF1A, MYC, and CCRL2 being identified as characteristic genes related to the inflammatory response in AR.[44] These mechanisms work together to cause the onset and development of AR and are the main targets for AR treatment strategies.

Autophagy

Autophagy is a physiological cellular phenomenon where cells use their lysosomes to degrade and recycle damaged organelles, protein aggregates, and other unwanted components. This process is crucial for maintaining cellular homeostasis, organelle turnover, and responding to cellular stress.[10] Autophagy is also essential for the homeostasis of the epithelial TJ proteins.[45] When human nasal epithelial cells are treated with the dust mite allergen Derp1, the expression levels of autophagy-related proteins LC3 II/I and Beclin-1 increase, while the expression of TJ proteins Occludin, Claudin-1, ZO-1, and JAM-A at both mRNA and protein levels are suppressed. These effects are reversed by 3-MA, an autophagy inhibitor, indicating that enhanced autophagic activity in epithelial cells impairs epithelial barrier function. Exposure to Derp1 increases the expression and activation of CXCR4, subsequently upregulating the expression of miR-125b, which leads to the downregulation of Foxp3, thereby enhancing autophagy and damaging the epithelial barrier. Analysis conducted in vivo verifies the significance of the CXCR4/miR-125b/Foxp3 pathway in the compromised epithelial barrier associated with AR.[46] In the nasal mucosa of mice with AR, the expression of LC3II and ATG5 were significantly upregulated, while 3-MA suppressed their expression. This indicates that there is a substantial autophagic response in the nasal mucosa of AR mice. OVA-induced bone marrow-derived dendritic cells (BMDCs) autophagy can influence the differentiation of $CD4^{+}$T cells and the levels of related cytokines. However, the addition of 3-MA significantly reversed the imbalances in Th1/Th2/Th9/Th17/Treg/Tfh cell immunity. These results suggest that allergens are capable of inducing autophagy in CD11cDCs in a dose-dependent fashion, thereby promoting a pro-inflammatory phenotype among downstream T cell immune imbalances.[47]

NLRP3 Inflammasome

In recent years, significant attention has been given to the role of the NLRP3 inflammasome in allergic diseases. In AR, this inflammasome is capable of recruiting and activating caspase-1, which in turn stimulates the production of IL-1β and IL-18. The subsequent release of these inflammatory cytokines results in an amplified inflammatory response, ultimately contributing to the progression of AR.[48] The activation of the NLRP3 inflammasome may contribute to AR inflammation by inducing pyroptosis in nasal epithelial cells[49] and macrophages.[50]

Exposure to industrial chemicals and fine particulate matter can exacerbate AR nasal mucosal damage through NLRP3-mediated pyroptosis. For instance, in an OVA-induced AR mice model, the addition of nonylphenol (NP) leads to a significant increase in the expression of IL-6 and TNF-α in the nasal mucosa, aggravating the inflammatory response in AR nasal mucosa. Moreover, mice exposed to NP show increased expression of NLRP3, caspase-1, and ASC in the nasal mucosa, along with high expression of IL-1β/18, pro-IL-1β/18, GSDMD, and GSDMD-N. The data suggest that NP promotes NLRP3 inflammasomes and enhances GSDMD-mediated pyroptosis during the development of AR in mice.[51] Exposure to PM2.5 has also been shown to intensify AR symptoms in mice, with increased serum IgE secretion and significantly upregulated protein expression of NLRP3, caspase-1, GSDMD, and IL-1β in nasal mucosal tissue. Therefore, PM2.5 exposure exacerbates the development of AR through NLRP3 inflammasome-mediated pyroptosis of nasal epithelial cells.[52]

Olfactory dysfunction (OD), affecting the sense of smell, can result from recurrent episodes of AR. Zhou's research[53] indicated that 52.5% of AR mice models exhibited OD, characterized by notably higher expression levels of pyroptosis-associated proteins NLRP3, caspase-1, and GSDMD, along with pro-inflammatory cytokines related to pyroptosis, including IL-1β and IL-18, in the olfactory bulb tissue of the OD group; treatment with the pyroptosis inhibitor CY-09 significantly reduced the expression levels and markedly improved olfactory damage.

MicroRNAs

MicroRNAs (miRNAs), which are highly conserved small non-coding RNAs across species, act as essential epigenetic regulators. They participate in various biological processes, including their involvement in initiating and advancing inflammatory diseases, which significantly contributes to the pathogenesis of AR.[54]

Research has indicated that miRNAs are closely associated with AR through their involvement in innate immunity, adaptive immunity, and epigenetic factors.[55] Specific changes in miRNA expression are related to the pathogenesis of AR, offering potential as biomarkers for guiding the establishment of diagnostic and therapeutic strategies. For instance, in children with AR, miR-21 is downregulated within peripheral blood mononuclear cells and may become a potential indicator for the early prediction of AR.[56] Additionally, the role of miRNAs in regulating immune responses is gaining increasing attention, particularly their impact on the Th1/Th2 balance and cytokine production. MiR-21 restricts the activation of the IL-12/IFN-γ pathway, the polarization towards Th1, and the severity of delayed-type hypersensitivity in immune responses in vivo.[57] In AR, the abnormal expression of miRNAs may affect the regulation of inflammatory factors. For example, the study by Suojalehto suggests that in nasal biopsy tissues from AR patients, Th2 cytokines are upregulated, and the levels of miR-155, miR-205, and miR-498 are increased, while the level of let-7e is decreased. Additionally, they noticed that the presence of asthma concurrently had a minimal impact on the miRNA profile in AR.[58]

Overall, research on miRNAs in allergic rhinitis reveals their potential roles in the disease's onset and development, offering new targets for precision medicine in the treatment of AR.

Advantages and Limitations

Our research offers several unique strengths. Primarily, this is the inaugural systematic analysis of the relationship between AR and nasal mucosa, serving as a comprehensive guide for academics in this domain. Additionally, by employing a trio of widely used bibliometric tools—R language, VOSviewer, and CiteSpace—we ensure a high level of objectivity in our data analysis. Moreover, our bibliometric approach provides a more holistic view of research hotspots and vanguard trends compared to traditional narrative reviews.

However, this study also has several inherent limitations. Firstly, in our pursuit of conducting a high-quality bibliometric analysis, we chose to rely solely on the Web of Science database, thus not incorporating other databases like PubMed and Scopus. Secondly, by focusing solely on English-language publications, we may have disregarded significant contributions from non-English sources. Thirdly, due to varying citation practices across different disciplines, some fields may be more inclined to cite the latest research, while others might cite classic literature more frequently. This can affect the outcomes of citation analysis. High citation counts may be due to the pioneering nature of a study, but they can also arise from controversial aspects or other non-academic factors. Lastly, bibliometrics exhibits a degree of lag, relying primarily on published literature data, which fails to fully capture the scope of ongoing and unpublished research outcomes. Moreover, the most recent research findings may not have garnered sufficient citations, potentially impacting the accurate assessment of current research trends. Although these limitations may exert some influence on our research findings, we can still discern the evolutionary trends in AR and nasal mucosa-related fields, identify emerging hotspots, and speculate on future developmental directions.

Conclusion

This study presents a bibliometric analysis of the AR and nasal mucosa field, assessing the scholarly contributions across different years, authors, countries/regions, institutions, and journals, while also examining the progression of themes and emerging focal points for future research.The literature on AR and nasal mucosa has demonstrated a consistent upward trend in publication output over the past decade. Key areas of interest within the current research landscape include the inflammatory and immune mechanisms associated with AR, as well as the programmed cell death within the nasal

mucosa epithelium. Autophagy, NLRP3 inflammasomes, and microRNAs stand out as cutting-edge topics that are gaining momentum in the field. In summary, this bibliometric analysis offers a retrospective and prospective view of the research on AR and nasal mucosa, underscoring the significance of sustained global and interdisciplinary collaboration in unraveling the complexities of AR mechanisms.

Disclosure

The authors report no conflicts of interest in this work.

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