Bibliometric analysis of papers on inflammation in glaucoma from 2000 to 2025

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Abstract

● **AIM:** To perform a bibliometric analysis of publications focusing on inflammatory mechanisms in glaucoma, thereby comprehensively understanding the current research status and identifying potential frontier directions for future studies.

● **METHODS:** A systematic search was conducted in the Web of Science Core Collection (WoSCC) database to retrieve relevant literature published from January 1, 2000, to August 31, 2025 (data accessed on September 12, 2025). Multiple data visualization tools were employed to conduct in-depth analyses of the included publications, covering aspects such as publication quantity and quality, evolutionary trends of research hotspots, keyword co-occurrence networks, and collaborative patterns among countries/regions, institutions, and authors.

● **RESULTS:** A total of 3381 articles related to glaucoma inflammation were extracted from WoSCC. The analysis showed that the USA had the highest research output in this field (29.04%, *n*=982), followed by China (18.40%, *n*=622) and UK (6.01%, *n*=203). Based on citation frequency and burst intensity, the USA also ranked as the most influential country. Baudouin C and Sun X were identified as the most productive authors, while *Journal of Glaucoma* and *Investigative Ophthalmology & Visual Science* were the journals with the highest number of published relevant articles. Additionally, keyword analysis revealed that "neuroinflammation", "retinal ganglion cells (RGCs)", "pathophysiology", and "traditional Chinese medicine" are emerging research hotspots in the field of immune-inflammatory responses in glaucoma.

● **CONCLUSION:** This study presents a comprehensive bibliometric overview of research on glaucoma-related inflammation, indicating that this field has received extensive scientific attention with a steady upward trend in research activity. Furthermore, it establishes a theoretical basis for the development of neuroinflammation-targeted therapeutic strategies for glaucoma and emphasizes the necessity of strengthening interdisciplinary collaboration to promote the clinical translation of research findings.

● **KEYWORDS:** glaucoma; inflammatory mechanism; bibliometric analysis; data visualization; research hotspot; neuroinflammation

INTRODUCTION

Glaucoma, a group of neurodegenerative diseases affecting the optic nerve, is a leading cause of irreversible blindness[1]. The estimated number of individuals with glaucoma was between 76.0-79.6 million in 2020, with projections indicating an increase to over 111.8 million by 2040[2]. Pathological characteristics of glaucoma include optic disc atrophy, retinal thinning, and the progressive loss of retinal ganglion cells (RGCs)[3]. Glaucoma patients exhibit substantially compromised health-related quality of life compared to population controls. The incomplete elucidation of glaucomatous pathogenesis confines current intraocular pressure (IOP)-lowering therapies to suboptimal long-term outcomes, necessitating urgent mechanistic clarification and innovative therapeutic development targeting alternative pathways.

It has been postulated that inflammation and immune responses may significantly contribute to the pathogenesis of glaucoma. Several identified risk factors for glaucoma encompass biomechanical, vascular dysfunction, oxidative stress, and immune-mediated neuroinflammatory conditions[4]. It is noteworthy that inflammation serves as a common feature

in the pathological progression of all types of glaucoma[5]. Studies have confirmed that elevated fecal calprotectin may indicate underlying intestinal inflammation in glaucoma, which induces mitochondrial dysfunction and cellular apoptosis, thereby constituting a critical pathological mechanism driving glaucoma advancement[6]. Recent transcriptomic and proteomic studies have identified an upregulation of several molecules involved in inflammation pathways in both human donor eyes and animal models with glaucoma[7]. Glaucoma-related glial cell reactivity is marked by an increase in proinflammatory cytokines, like tumor necrosis factor (TNFα), interferon (IFNγ), interleukin (IL)-1, IL-2, IL-12, and chemokines[8]. Therefore, delineating the dynamic interplay between pro- and anti-inflammatory mediators in sustaining immune homeostasis becomes critical, not only for deciphering glaucoma's pathophysiological underpinnings but also for informing targeted immunomodulatory therapies.

In scientific research, analysis of bibliometric data was a useful tool for reviewing prominent publications, analyzing current research, and predicting research trends[9]. In recent years, bibliometric analysis has gained increasing traction across diverse biomedical fields, spanning immunotherapy, cardiovascular research, pharmacology, biomedical materials, and ophthalmic sciences. VOSviewer is a free tool that simplifies the creation and analysis of bibliometric maps[10]. An additional bibliometric tool for analyzing trends and hotspots in a knowledge domain is CiteSpace, which is widely used in bibliometric analysis[11]. To our knowledge, no systematic analysis exists regarding inflammatory mechanisms in glaucoma. This study provides the first bibliometric profiling of current research landscapes, delineating emerging trends and knowledge gaps within key domains. The findings are positioned to facilitate novel insights for guiding future investigations.

MATERIALS AND METHODS

Data Sources and Search Strategies　The search for publications was conducted using the Web of Science platform, which offers a wide array of high-value and high-impact literature resources. All publications were exported in the "Full Record and Cited References" format as plain text files. The search criteria utilized were as follows: [(TS=(glaucoma)) AND TS=(inflammatory OR inflammation OR inflammations)] AND DOP=(2000-01-01/2025-08-31) AND Document types=(Article OR Review) AND Language=(English). The document searches were performed simultaneously to prevent selection bias resulting from database updates. Two investigators (Chen WL and Zhang LX) independently executed literature retrieval, screening, and bibliometric analysis using datasets extracted from the Web of Science Core Collection (WoSCC). The literature search strategy and main framework elements are depicted in Figure 1.

This study was optimally designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[12]. The Institutional Review Board of the Affiliated Hospital of Wenzhou Medical University determined the protocol's exemption from ethical review based on non-involvement of personal identifiers.

Statistical Analysis　We performed a systematic literature search in the SCI-EXPANDED database of WoSCC, covering publications from January 1, 2000, to August 31, 2025, that investigated inflammatory mechanisms in glaucoma, we used "TS=[glaucoma AND (inflammatory OR inflammation OR inflammations)]" as the search term. The search was strictly limited to peer-reviewed articles published in English, with "Article" or "Review" designated as the sole publication type. Subsequently, the data was imported into various software programs including Microsoft Excel 2019, CiteSpace (version 6.3.R1), VOSviewer (version 1.6.20), the Bibliometric Online Analysis Platform, R (version 4.2.3), and RStudio (version 4.2.3) for bibliometric analysis. The parameters of CiteSpace were set as follows: time slicing (2000-2025), years per slice (1), term source (all selection), node type (choose 1 at a time), pruning (pathfinder) and visualization (cluster view-static, show merged network)[13].

To examine and visually represent country and regional postings, as well as collaborative postings, we utilized a free statistics website (https://bibliometric.com/) and SCImago Graphica 1.0.25 software (https://graphica.app/). The visualization map displays nodes as circles, with the size of each circle indicating the frequency of the corresponding label in the co-occurrence analysis. The color of each circle corresponds to the cluster of categories it belongs to[14]. The connections between nodes signify their association, with the thickness of the connecting lines reflecting the strength of this association.

RESULTS

General Information and Distribution of Publications by Year　The methodology utilized in this study involved a data retrieval strategy and collection process as illustrated in Figure 1. A total of 3381 documents meeting the inclusion criteria were obtained from the WoSCC public database, covering the period from January 1, 2000 to August 31, 2025. Of these, 2611 (77.23%) were categorized as "Articles" and 770 (22.77%) as "Reviews". The distribution of publications per year from 2000 to 2025 is depicted in Figure 2, with 2021 and 2024 standing out as the years with the highest publication counts in the WoSCC database. The sustained increase in glaucoma-related publications since 2000 demonstrates growing scientific interest in elucidating the inflammatory mechanisms underlying this ocular pathology.

Countries/Regions Analysis　The chord diagram employed illustrates scientific collaboration patterns, highlighting China

and the USA as central hubs within the global research network (Figure 3A). Specifically, the USA, UK, China, Germany, and Italy were identified as the most active participants in the publication of articles. These leading nations exhibit stronger levels of cooperation amongst themselves, while other countries demonstrate lower levels of collaboration. Additionally, Figure 3B provides an analysis of publication trends and growth patterns within the top 10 countries, as depicted through the online analysis platform of literature metrology. Following a delayed initiation, China's scholarly productivity in this domain surpassed global counterparts, attributable to sustained investment in research infrastructure and strategic prioritization of ocular innovation. Our analysis identified the participation of 87 countries in literature publication, and geospatial analysis reveals predominant research clustering in Europe, East Asia, and North America, with marked publication output disparities persisting across national boundaries.

Journal Analysis Table 1 displays the top 10 journals based on publication frequency and citation count, encompassing impact factors ranging from 1.4 to 4.9. The majority of these journals are positioned within the Q1 and Q2 categories of the Journal Citation Reports (JCR), comprising 80% of the total. Impact factor serves as a metric for assessing a journal's influence within its respective discipline. Remarkably, our examination indicates that journals with higher publication frequencies exhibited a greater propensity to accept research articles pertaining to inflammation in glaucoma compared to those with lower publication rates.

Additionally, the citation and co-citation networks of the journals were graphically represented using VOSviewer (Figure 4A, 4B). Each cluster is denoted by a point of consistent color, signifying a substantial level of collaboration among them. The co-citation network exhibits two prominent clustering groups, with the red clusters indicative of the ophthalmology field, encompassing journals like *Invest Ophthalmol Vis Sci* and *J Glaucoma*. The remaining scattered cluster comprises diverse journals, such as *PLoS One* and *Ocul Immunol Inflamm*, focusing on pathological mechanisms and ophthalmic disease topics. Furthermore, Citespace was utilized to visually represent the citation relationships between citing and cited journals. A dual-map overlay was conducted on journals pertaining to inflammation in glaucoma research, revealing two primary reference paths: an orange path and a tan primary reference path, as depicted in Figure 4C. Bibliometric analysis revealed concentration of glaucoma inflammation studies in neurology, sports science, and ophthalmology journals, whereas high-impact citations predominantly converged in molecular biology/genetics periodicals. This divergence suggests a research paradigm integrating clinical
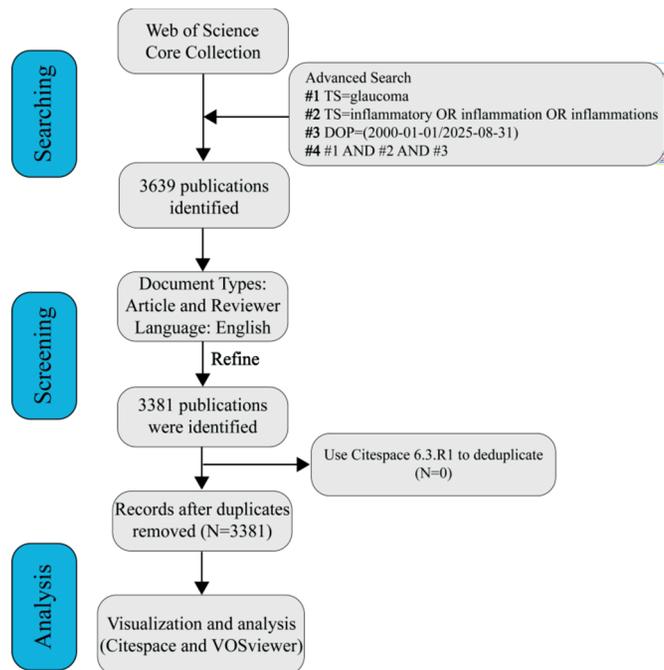

Figure 1 Flow diagram of the study identification and retrieval strategy.
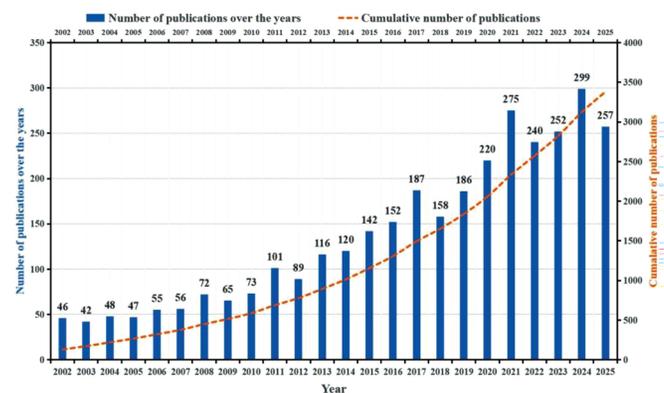

Figure 2 The number of documents published over the years.

observations with molecular pathogenesis investigations, where ophthalmic applications provide clinical validation while genomic approaches drive mechanistic discovery.

Author and Co-Cited References Analysis A total of 15 111 scholars published articles in the field of the inflammation research in glaucoma worldwide. The indicators of the top ten scholars as shown in Table 2. Totally 164 articles were published by the top ten scholars, four scholars were from the Spain and two were from France, the rest were from China, Italy, Denmark and Germany. Baudouin C (29 articles) at the Quinze-Vingts Hospital, Sun X (19 articles) at the Fudan University and Agnifili L (18 articles) at the University "G. D'Annunzio" of Chieti-Pescara were identified as the top three authors with the highest number of published articles. Baudouin C also ranked first in the total number of citations received and the H-index, while Brignole-Baudouin F ranked first in the average frequency of citations per paper. In general, these publications, academic values in this field were greatly
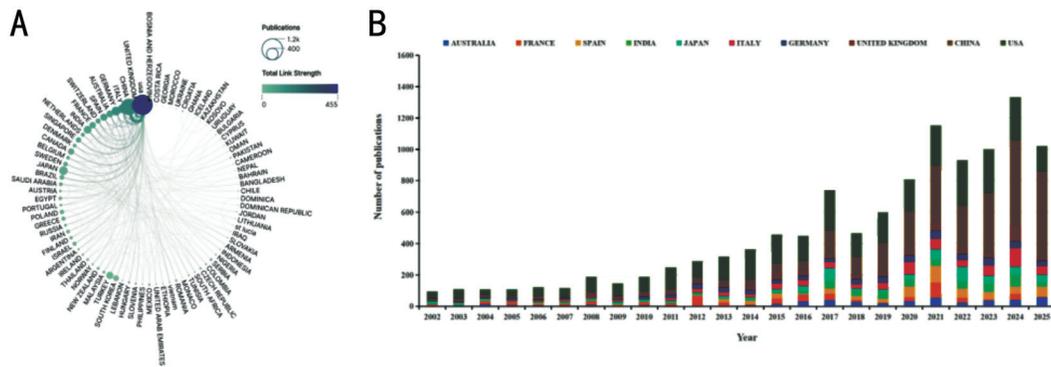
Figure 3 Countries/regions analysis on inflammatory in glaucoma A: Scientific collaboration networks among all countries/regions (The size of the circle is proportional to the number of published articles, and the thickness of the line indicates the intensity of cooperation between countries/regions). B: The number of annual publications and growth trends of the top 10 countries/regions.
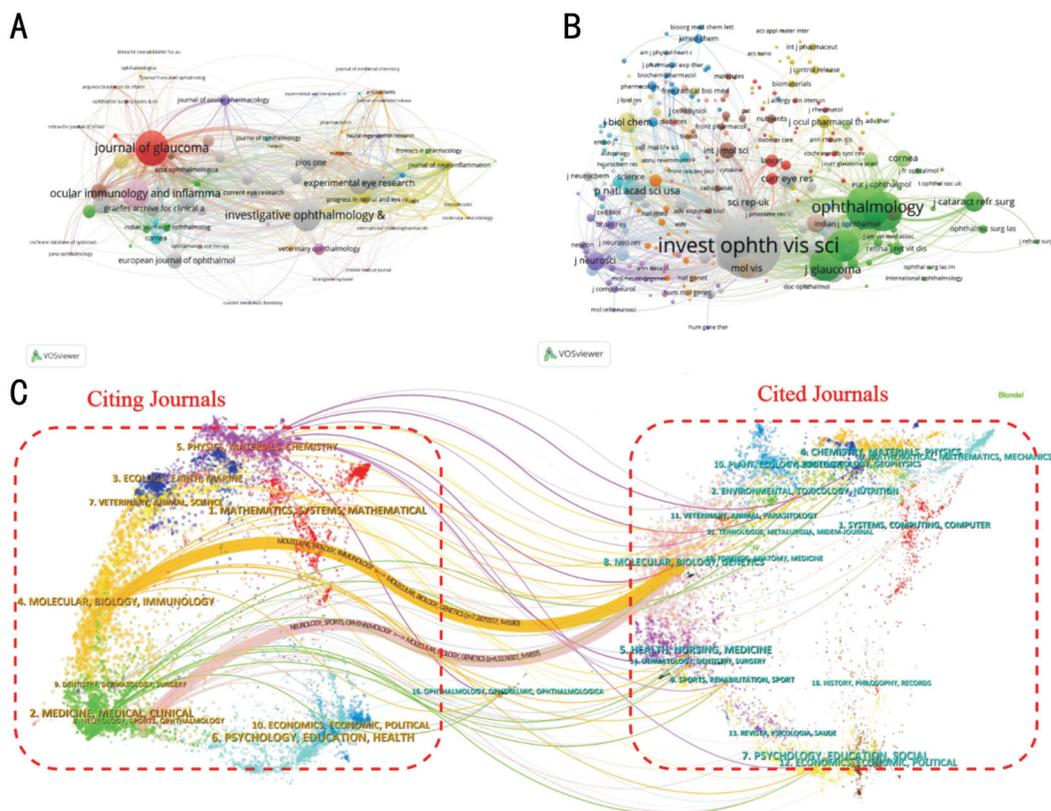

Figure 4 The relevance analysis of journal related to the inflammation research in glaucoma A: The citation sources network; B: The co-citation sources network; C: The dual-map overlay of WoSCC journals. WoSCC: Web of Science Core Collection.

accepted. Table 3 presents a summary of the 10 most frequently co-cited publications, and one of these is the publication titled "Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis" authored by Tham *et al*[2] with the highest quantity of co-citations (*n*=279). Notably, USA-affiliated researchers contributed 40% of the top-cited works (4/10), reflecting their intellectual dominance in advancing glaucoma-related inflammation research, as evidenced by citation impact scores exceeding global averages.

Figure 5A employs a scientometric bubble map to delineate temporal trajectories of scholarly productivity, quantifying both publication volume and citation impact indices for leading contributors in glaucoma inflammation research. For example, Baudouin C and Wang Y had a substantial number of publications and received a large number of citations in 2021. This trend suggests the introduction of new contributors, infusing fresh perspectives and promoting the development of the field. The collaborative network relationship between authors is shown in Figure 5B. There was a collaborative relationship between authors in each circle; the connecting line between the nodes represents this collaborative relationship, Baudouin C, Brignole-Baudouin F, and Labbé A comprised the authors with the most collaborations. Additionally, we generated single-country publications (SCP) and multiple-country publications (MCP) analyses for the top 10 countries,

Table 1 The top 10 journals ranked by publication and citation count

Journal	Number of publications[a]	Total times cited	IF 2024 (JCR)	Country/region	Journal	Number of publications	Total times cited[b]	IF 2024 (JCR)	Country/region
J Glaucoma	130	3114	1.8 (Q3)	USA	*Invest Ophthalmol Vis Sci*	113	5135	4.7 (Q1)	tUSA
Invest Ophthalmol Vis Sci	113	5135	4.7 (Q1)	USA	*Prog Retin Eye Res*	30	4692	14.7 (Q1)	UK
Ocul Immunol Inflamm	107	1621	2.0 (Q2)	the Netherlands	*Ophthalmology*	59	4382	9.5 (Q1)	USA
Exp Eye Res	83	2257	2.7 (Q2)	USA	*J Glaucoma*	130	3114	1.8 (Q3)	USA
Int J Mol Sci	80	1764	4.9 (Q1)	Switzerland	*Am J Ophthalmol*	65	2345	4.2 (Q1)	USA
Br J Ophthalmol	67	2084	3.5 (Q1)	UK	*Exp Eye Res*	83	2257	2.7 (Q2)	USA
Am J Ophthalmol	65	2345	4.2 (Q1)	USA	*Surv Ophthalmol*	25	2220	5.9 (Q1)	USA
PLoS One	62	1966	2.6 (Q2)	USA	*Br J Ophthalmol*	67	2084	3.5 (Q1)	UK
Eur J Ophthalmol	61	749	1.4 (Q3)	UK	*PLoS One*	62	1966	2.6 (Q3)	USA
Graefes Arch Clin Exp Ophthalmol	59	1200	2.3 (Q2)	USA	*Int J Mol Sci*	80	1764	4.9 (Q1)	Switzerland

JCR: Journal Citation Reports. Ranked by publications[a] and total time cited[b].

Table 2 Productivity, citations and H-index of the top ten authors of the inflammation research in glaucoma

Author	Country	Number of publications	Total citations	Average number of citations per paper	H-index
Baudouin C	France	29	2102	72.48	76
Sun X	China	19	519	27.32	48
Agnifili L	Italy	18	712	39.56	32
Pfeiffer N	Germany	16	451	28.19	63
Brignole-Baudouin F	France	15	1395	93.00	44
de Hoz R	Spain	14	790	56.43	28
Ramírez JM	Spain	14	790	56.43	29
Kolko M	Denmark	13	642	49.38	29
Salazar JJ	Spain	13	776	59.69	32
Salobrar-Garcia E	Spain	13	639	49.15	23

Table 3 Top 10 co-cited references concerning the research of inflammatory mechanisms of glaucoma

Co-cited reference	First author (y)	Journal	Total citations	Corresponding author's country
Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis	Tham YC (2014)	*Ophthalmology*	279	Singapore
The number of people with glaucoma worldwide in 2010 and 2020	Quigley HA (2006)	*Br J Ophthalmol*	264	USA
The pathophysiology and treatment of glaucoma: a review	Weinreb RN (2014)	*JAMA*	222	Singapore
Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop	Jabs DA (2005)	*Am J Ophthalmol*	156	USA
Inflammation in Glaucoma: From the back to the front of the eye, and beyond	Baudouin C (2021)	*Prog Retin Eye Res*	110	Germany
The molecular basis of retinal ganglion cell death in glaucoma	Almasieh M (2012)	*Prog Retin Eye Res*	108	Canada
Early microglia activation in a mouse model of chronic glaucoma	Bosco A (2011)	*J Comp Neurol*	93	USA
TNF-alpha and TNF-alpha receptor-1 in the retina of normal and glaucomatous eyes	Tezel G (2001)	*Invest Ophthalmol Vis Sci*	93	USA
Glaucoma	Jonas JB (2017)	*Lancet*	87	Germany
Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial	Heijl A (2002)	*Arch Ophthalmol*	85	Sweden

revealing that American scholars have published more articles and hold a leading position in this research field (Figure 5C).

Institutional Analysis In the field of the inflammation research in glaucoma, a total of 541 institutions are involved. Visual analysis indicates that Harvard University secured the top position with 127 articles, followed by Harvard Medical School (107 articles), Harvard University Medical Affiliates (101 articles), and University of London (82 articles), with the highest centrality observed at University College London (0.14; Figure 6A). The closeness of institutional cooperation reflects the differences in the level of communication and influence among different institutions in this field. The network of co-authorship organizations sharing the same color signifies their close collaboration in related fields. Surprisingly, Harvard Medical School, Singapore National Eye Center, Sun Yat-Sen University, and Harvard University exhibit significant co-authorship with other institutions (Figure 6B). Additionally, the citation-organizations network, comprising 145 nodes, highlights the Harvard University (cited 3037 times), Quinze Vingts National Ophthalmology Hospital (cited 2242 times), and Singapore National Eye Center (cited 2236 times) as the most influential institutions in this domain (Figure 6C). While disparate academic institutions exhibit substantial publication volume, the attenuated citation impact underscores methodological gaps in specialized research domains, necessitating enhanced scientific rigor and cross-disciplinary validation frameworks.
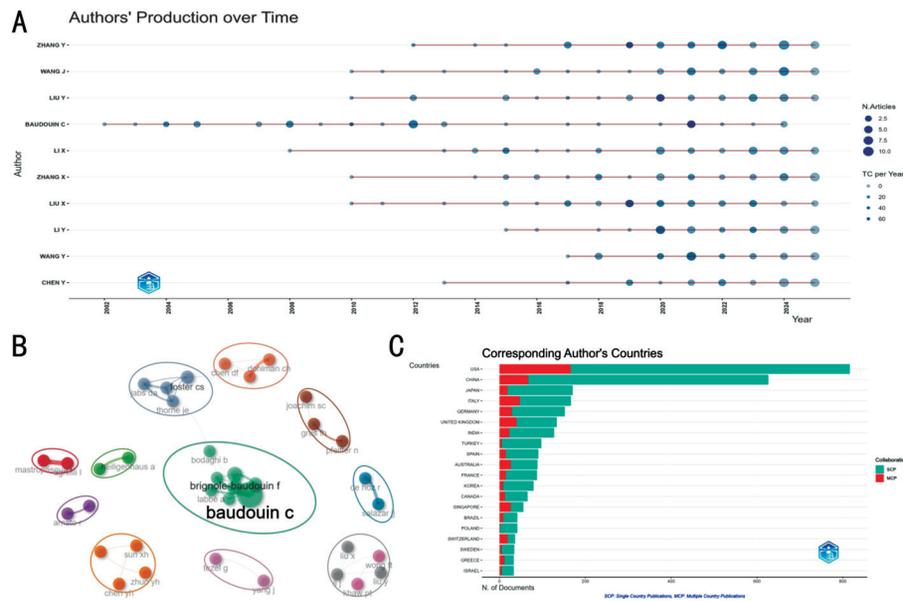
Figure 5 The analysis of authors　A: The authors production over time that with the most publications; B: The collaborative connections among authors; C: The distribution of corresponding author's countries. MCP: Multiple-country publications; SCP: Single-country publications; TC: Total citation.
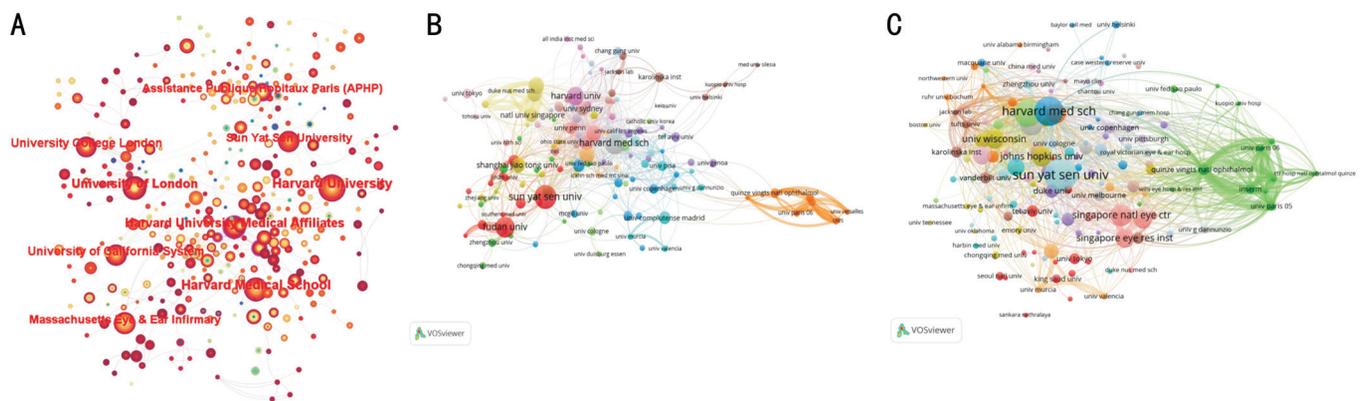

Figure 6 Institutional analysis in studies of inflammatory mechanisms of glaucoma　A: Collaboration network of institutions; B: The co-authorship organization network; C: The citation-organizations network.

Keywords Analysis　The keywords extracted by VOSviewer served as a representation of the central themes of the article, enabling a comprehensive analysis of the advancements in knowledge within the research field. Among the 6125 keywords identified, Figure 7A highlighted the top 25 keywords with the most significant citation bursts. Notably, surgery exhibited the highest burst strength at 14.73, followed by filtering surgery at 14.49 and follow up at 12.93. Over the past decade (2013-2025), research hotspots included optic nerve head, *in vivo* studies, apoptosis, human trabecular meshwork, injury, optical coherence tomography, and phacoemulsification. Using Vosviewer, a visual network diagram (Figure 7B) and an overlay diagram (Figure 7C) were created. Network analysis revealed that key terms grouped into 9 categories, with IOP being the most frequently mentioned and having the highest total link strength (Figure 7B and 7C). The overlay visualization revealed an evolutionary paradigm

shift, with early research domains dominated by clinical terminologies (including management, IOP, and therapy) progressively transitioning toward mechanistic explorations encompassing oxidative stress, neuroinflammation, and microglia activation pathways.

Figure 7D demonstrates longitudinal trends in glaucoma-related inflammatory mechanisms research (2000-2025 timeframe) through bibliometric analysis with annual keyword thresholds (5 terms/year), identifying 69 high-frequency themes. Circle diameters proportionally represent keyword frequencies. Key findings include: 1) 2015's clinical focus on therapy (81), *in vitro* models (79), and mitomycin-C applications (77); 2) 2020's mechanistic shift toward oxidative stress (168), cellular activation pathways (120), and murine models (117); 3) 2023's emerging neutrophil biology (7), kinase signaling (7), and therapeutic formulations (6) as frontier domains.
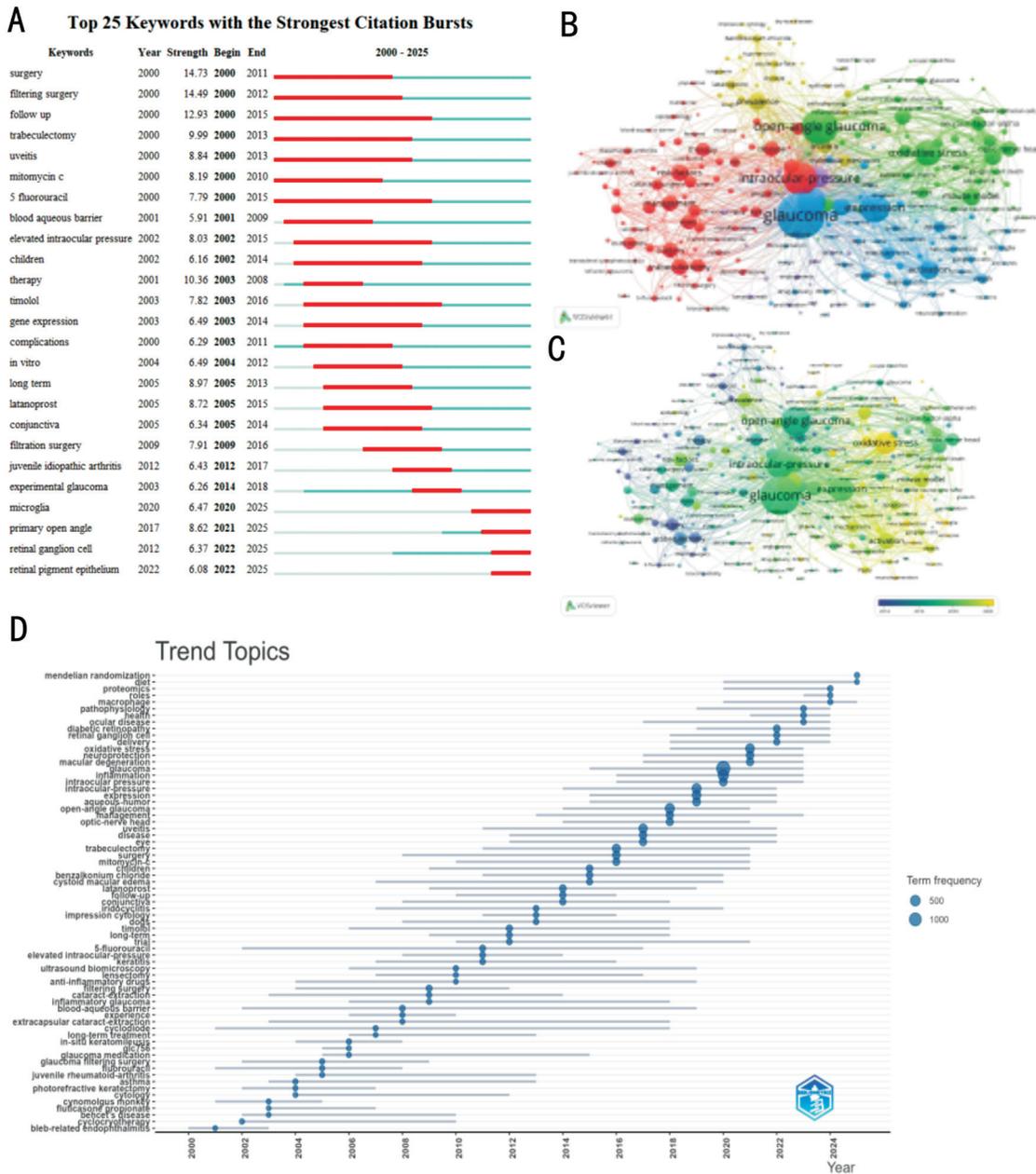
Figure 7 Visual mapping of keywords in the research of inflammatory mechanisms of glaucoma A: The top 25 keywords with the strongest citation bursts; B: Clustering view of keywords co-occurrence analysis; C: Temporal overlay visualization mapping of keyword co-occurrence networks in the period of 2000-2023; D: Trend topics analysis of keywords by Bilbliometrix package.

DISCUSSION

Bibliometric analysis constitutes a scientometric assessment framework that systematically assesses the scholarly impact of knowledge entities ranging from institutional portfolios to individual publications, while simultaneously enabling the mapping of intellectual landscapes through detection of emerging frontiers and quantification of scholarly influence metrics (*e.g.*, citation velocity). Over time, bibliometrics has gained prominence in assessing scientific achievements within particular academic fields over a specified period, as well as in gauging the advancements and progress within various research domains[15]. This longitudinal bibliometric investigation (2000-2025) delineates the therapeutic translation of neuroinflammatory pathways in glaucoma pathogenesis, employing scientometric indicators to establish predictive frameworks for targeting ocular inflammasomes and resolving current knowledge asymmetries.

General Information The research on the inflammatory mechanism in glaucoma experienced a slow development prior to 2010, with an annual publication rate of fewer than 100 papers. A gradual increase in publications began in 2011, and after 2016, the number of papers exceeded 150 per year, with a growth rate of over 100 papers annually. By 2020, the annual publication count had surpassed 200 (Figure 2), indicating a rapid expansion in the field. The top five countries in this area collectively contributed more than 1500 articles,

representing over 60% of the total publications worldwide. This finding highlights a notable disparity in research activity across countries in the field, with one leading country holding a distinct advantage over others. Collaborations among nations are depicted in Figure 3A and 3C, revealing significant levels of cooperation between China and the US, as well as close partnerships between Germany and the UK, Italy, and other European countries. Multivariate analysis reveals geopolitically clustered collaboration patterns, with robust intracontinental partnerships contrasting with constrained intercontinental knowledge transfer, where linguistic barriers significantly impede cross-regional epistemic integration.

In the field of authorship, the top 10 active authors have each made a minimum of 13 contributions, with Professor Baudouin C leading the group with 29 publications. Additionally, the collective works of these top 10 cited authors have received a minimum of 45 citations, indicating their significant impact on research related to inflammation in glaucoma. Baudouin C, with 2102 citations, holds the top position, followed by Brignole-Baudouin F (1395 citations) and de Hoz R (790 citations). Baudouin et al[16] is particularly recognized for his groundbreaking discovery of an aggressive anti-inflammatory regimen that shows promise as a clinical treatment for glaucoma. The *J Glaucoma* has the highest volume of publications within the field, while *Invest Ophthalmol Vis Sci* is noted for having the journal with the most citations.

Knowledge Base The knowledge base comprises a compilation of referenced sources frequently cited within a specific academic discipline, aiding researchers in understanding fundamental concepts and principles within a novel area of study[17]. By examining the relevant co-cited references, researchers can gain insight into significant research discoveries and primary issues.

Table 3 presents the most frequently co-cited references. Tezel et al[18] showed that the upregulation of TNF-alpha and its receptor-1 in the glaucomatous retina indicates the involvement of TNF-alpha-mediated cell death in the neurodegeneration process of glaucoma. The most cited paper in 2014 was an original research article titled "Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis" published in *Ophthalmology*[2]. Epidemiologic imperatives underscore the urgency of scaling investments in glaucoma clinical management, particularly given the disease's female predominance and unmet therapeutic needs, necessitating sex-specific pathophysiologic investigations to optimize evidence-informed precision health initiatives. Subsequent research has examined the obstacles and possibilities in glaucoma research, emphasizing the involvement of inflammatory mechanisms in the disease's pathological advancement. Bosco A[19]

conducted a study in which 6-week-old DBA/2J mice were treated with minocycline for 25wk. The researchers found that the reduction in microglial activation was associated with a notable enhancement in RGCs axonal transport, as assessed through neuronal retrograde tracing from the superior colliculus. These findings indicate that in glaucoma, the activation of microglia in the retina and optic nerve head may contribute to the initial impairment of optic nerve function and its subsequent degeneration. The review paper entitled "The pathophysiology and treatment of glaucoma: a review[20]" emerged as the most frequently cited scholarly article, drawing upon a comprehensive analysis of existing literature sources. Notably, it was observed that IL-6 exhibited peak expression levels in RGCs following optic nerve injury, as opposed to IOP, and was subsequently transported through axons to the site of damage[21]. The research findings of Almasieh et al[22] align with and reinforce previous research perspectives established in 2012.

In conclusion, the synthesized evidence from this review systematically elucidates key etiological factors and pathological consequences in glaucoma-related inflammation research. Critical appraisals encompass epidemiological trends, prognostic modeling of disease progression, and mechanistic links between microglial activation and retinal neuroinflammation. Collectively, these analyses provide actionable insights for advancing clinical management strategies while deepening our understanding of the molecular pathophysiology underlying glaucomatous inflammation.

Emerging Topics In accordance with scholarly sources, keyword analysis serves as a valuable tool for pinpointing focal areas within a research domain, thereby facilitating the anticipation of forthcoming trends in that particular field. Notably, the terms "5-fluorouracil" and "filtering surgery" have emerged as prominent keywords during the nascent phase of this field (Figure 7A). Additionally, keyword clustering analysis reveals predominant research foci in glaucoma-associated inflammatory pathology, with high-frequency terms including "intraocular pressure", "gene expression profiling", "neuroinflammatory pathways", and "oxidative stress markers". This semantic pattern demonstrates concordance with prior bibliometric assessments while quantitatively delineating current mechanistic investigation priorities in the field (Figure 7B).

Recent advances in glaucoma research have undergone a paradigm shift toward elucidating neuroinflammatory pathogenesis through integrated translational approaches. This evolution is characterized by methodological convergence on three investigative dimensions: molecular mechanisms (oxidative stress signaling, RGC apoptosis), experimental models (*in vitro* neuronal degeneration systems), and pathophysiological validation (gene expression dynamics,

cytokine-mediated inflammatory cascades). Thematic analysis of keyword trends as an additional research method demonstrates that the field maintains a focus on topics such as "pathophysiology", "neuroinflammation", "formulations", "herpes-simplex-virus", "microglia", and "oxidative stress" (Figure 7D), indicating sustained interest in these subjects and their potential as leading areas of study. Current research priorities include investigating mechanisms related to "neuroinflammation", "oxidative stress", and "apoptosis", as well as therapeutic research on "glaucoma", "retinal ganglion cells", and "ocular hypertension".

Hence, contemporary studies underscore the importance of targeting the retinal microenvironment, specifically by seeking to modify retinal inflammation, improve the axonal transport capacity of RGCs, and revert the inflammatory suppressive microenvironment to facilitate the adaptation of RGCs to stress stimuli.

Numerous stimuli, such as chronic mechanical stress resulting from elevated IOP, hypoxia/ischemia, and oxidative stress, in conjunction with a lack of neurotrophic factors, have been implicated in the dysfunction and death of RGCs, particularly in the aging retina[4]. Emerging evidence implicates chronic stress in microglial-mediated immune dysregulation, wherein sustained complement system activation triggers a neurodegenerative cascade characterized by progressive neuroinflammation and axonal degeneration[23]. Prolonged exposure to oxidative stress over an extended period is hypothesized to lead to an increased level of chronic para-inflammation[24]. In conditions such as glaucoma, this para-inflammation response becomes dysregulated and progresses into harmful inflammation. Human histological research has demonstrated that the activation of glial cells and subsequent intense inflammatory reaction are linked to nerve damage in glaucoma[25]. Recently, there have been reports of elevated protein levels of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-8, and IFN-γ) in human glaucomatous retinal tissue, along with increased levels of various inflammasome components such as NOD-like receptor pyrin (NLRP) 3, caspase 1, and caspase 8 in glaucomatous eyes compared to normal eyes[26]. Surprisingly, these findings align with the observed retinal inflammation in animal models of glaucoma.

Several researchers have noted that therapeutic interventions targeting the modulation of immune and inflammatory responses represent promising strategies for mitigating optic nerve head damage and RGCs loss in glaucoma[27]. Animal studies have demonstrated the capacity of various drugs to regulate the reactivity of glial cells and their inflammatory reactions. Nevertheless, despite the observed neuroprotective effects in rodent models, numerous drugs that have exhibited promise in experimental settings have not translated to successful outcomes in clinical trials. Surprisingly, our research also revealed that the utilization of natural products possessing antioxidant, anti-inflammatory, and anti-apoptotic properties could potentially offer therapeutic benefits in the management of glaucoma[28]. Pharmacological disruption of NLRP3 inflammasome-mediated crosstalk between Müller glia and retinal microvascular endothelium demonstrates 68% RGC survival improvement in preclinical models, positioning inflammo-resolution as a viable disease-modifying strategy for progressive glaucomatous optic neuropathy.

Future Research Directions The study delineates emerging research frontiers in glaucoma pathophysiology, highlighting four pivotal domains: neuroinflammatory pathways, retinal ganglion cell degeneration, oxidative stress modulation, and traditional Chinese medicine-based immunoregulation. Preclinical studies demonstrate therapeutic potential in targeting chronic neuroinflammation and redox imbalance, while translational gaps persist in human clinical validation. Notably, traditional Chinese medicine (TCM)-derived compounds are gaining traction as novel modulators of ocular immune-inflammatory cascades.

Limitations This study acknowledges three principal limitations. First, exclusive reliance on WoSCC data, while recognized as a gold-standard source for bibliometric analyses, may not encompass all relevant publications, resulting in possible database coverage constraints. Second, the predominance of English-language articles introduces potential geographical/ institutional bias in research representation. Third, temporal variations in institutional nomenclature conventions could lead to data inconsistencies across different chronological strata.

In conclusion, this study represents the inaugural bibliometric analysis of research on inflammation in glaucoma to our knowledge. The field of glaucoma inflammation research is currently experiencing rapid growth, characterized by extensive collaboration among academic institutions globally. USA and China are prominent contributors to this field, serving as hubs for research activities. Harvard University has emerged as the leading institution in terms of publication output, while Baudouin C has made significant contributions to advancing knowledge in this area. The majority of research output in this domain is disseminated through ophthalmology-related journals. The investigation of the retinal inflammation microenvironment and the mechanisms of microglia are becoming prominent areas of interest and potential future research directions in the field. Overall, irrespective of the specific therapeutic interventions being explored, the manipulation of a conducive inflammatory microenvironment is identified as a crucial strategy for enhancing the restoration of optic nerve functionality in studies related to the pathophysiology of glaucoma.

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