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Global Research Trends and Hotspots in Non-Eosinophilic Asthma: A Bibliometric and Visual Analysis

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ABSTRAK

Pendahuluan: Asma non-eosinofilik merupakan fenotipe asma yang mencakup hampir separuh kasus asma dan sering menunjukkan respons yang buruk terhadap terapi kortikosteroid. Meskipun memiliki implikasi klinis yang besar, hingga saat ini belum terdapat analisis bibliometrik yang secara khusus memetakan perkembangan penelitian mengenai asma non-eosinofilik. Penelitian ini bertujuan menganalisis tren publikasi global, pola kolaborasi ilmiah, serta hotspot penelitian pada bidang asma non-eosinofilik.
Metode: Penelitian ini merupakan studi bibliometrik menggunakan data dari basis data Scopus yang dikumpulkan pada 27 Juni 2025. Sebanyak 531 artikel berbahasa Inggris yang diterbitkan dalam jurnal dan memenuhi kriteria inklusi dianalisis. Analisis dilakukan menggunakan Scopus Analyze Results, Biblioshiny, dan VOSviewer 1.6.19 untuk mengevaluasi tren publikasi, sitasi, kolaborasi penulis dan negara, artikel paling berpengaruh, serta analisis ko-kemunculan kata kunci.
Hasil: Publikasi mengenai asma non-eosinofilik meningkat pesat sejak tahun 2008 dan mencapai puncaknya pada tahun 2022. China menjadi negara dengan produktivitas publikasi tertinggi, sedangkan Australia memiliki jumlah sitasi dan rata-rata sitasi tertinggi. Gibson PG merupakan penulis paling produktif sekaligus paling berpengaruh dalam bidang ini. Analisis kata kunci menunjukkan bahwa fokus penelitian terkini bergeser menuju mekanisme inflamasi non-T2, neutrofil, resistensi kortikosteroid, biomarker, mikrobioma, obesitas, serta pendekatan precision medicine.
Kesimpulan: Penelitian mengenai asma non-eosinofilik mengalami perkembangan yang pesat dengan pergeseran fokus menuju pemahaman mekanisme biologis dan pengembangan terapi yang lebih personal. Temuan ini memberikan gambaran komprehensif mengenai lanskap penelitian global serta dapat menjadi dasar dalam menentukan arah penelitian dan pengembangan terapi pada masa mendatang.

Kata Kunci: asma non-eosinofilik; inflamasi; tren penelitian; analisis bibliometrik

ABSTRACT

Introduction: *Non-eosinophilic asthma represents nearly half of asthma cases and is commonly associated with poor responsiveness to corticosteroid therapy. Despite its significant clinical burden, no bibliometric study has comprehensively mapped the global research landscape of non-eosinophilic asthma. This study aimed to analyze global publication trends, scientific collaborations, and emerging research hotspots in non-eosinophilic asthma.*
Methods: *A bibliometric study was conducted using the Scopus database, with data retrieved on June 27, 2025. A total of 531 English-language journal articles that met the eligibility criteria were included. Data were analyzed using Scopus Analyze Results, Biblioshiny, and VOSviewer 1.6.19 to evaluate publication trends, citation performance, collaboration networks, influential publications, and keyword co-occurrence.*
Results: *Research output on non-eosinophilic asthma increased markedly after 2008 and peaked in 2022. China was the most productive country in terms of publications, whereas Australia achieved the highest total and average citations. Gibson PG was identified as the most productive and influential author. Keyword analysis demonstrated a shift in research focus toward non-T2 inflammatory mechanisms, neutrophilic inflammation, corticosteroid resistance, biomarkers, microbiome, obesity, and precision medicine approaches.*
Conclusion: *Global research on non-eosinophilic asthma has expanded substantially, reflecting a transition from conventional eosinophilic-centered concepts toward a deeper understanding of disease heterogeneity and*

personalized therapeutic strategies. These findings provide a comprehensive overview of current research trends and may serve as a valuable reference for future investigations and therapeutic development.

Keywords: non-eosinophilic asthma; inflammation; research trend; bibliometric analysis

INTRODUCTION

Historically, since the time of the Greco-Romans and Hippocrates, asthma has been known as a disease of the respiratory system (Kapri et al., 2022). As a chronic inflammatory disease due to genetic factor and environmental triggers in the human respiratory tract, asthma is characterized by the emergence of various symptoms such as shortness of breath, coughing, chest tightness, and wheezing which are often complained of by sufferer (Hammad & Lambrecht, 2021; Gohal et al., 2024). It is estimated that there are around 300 million asthma sufferers worldwide and this number is predicted to increase to 400 million by 2025 (Dharmage et al., 2019; Yuan et al., 2025). All around the world, asthma has a significant negative impact on people's quality of life and causes a number of difficulties, such as psychological, medical, and financial ones (Yuan et al., 2025). According to research, people with asthma have a risk of experiencing depression or anxiety up to 6 times higher than people without asthma. In addition, people with asthma are more likely to experience panic disorders. Thus, asthma is associated with a decrease in a person's quality of life, disruption in social life, and decreased productivity leading to unemployment and financial problems (Stanescu et al., 2019). Asthma that is not well controlled can also increase the risk of lung infections and acute exacerbations of asthma which can be life-threatening (Mohammad & Brough, 2019). With the high number of people with asthma and the large burden of asthma today, this shows that asthma is not just about wheezing. Behind the seemingly simple symptoms, there is a biological complexity that reflects the uniqueness of each person with asthma. Asthma is not a single disease entity, but rather a collection of different phenotypes with their own characteristics (Pembrey et al., 2018; Kuruvilla et al., 2019; Borish, 2016; Bourdin et al., 2024).

Based on its phenotype, asthma is generally divided into eosinophilic asthma (Th2 asthma) and non-eosinophilic asthma (non-Th2 asthma). Eosinophilic asthma which is found commonly in childhood asthma is characterized by eosinophilic airway inflammation. Whereas, non-eosinophilic asthma which encompasses obesity-associated asthma, smoking-associated asthma, and very late onset asthma is characterized by either neutrophilic or paucigranulocytic airway inflammation. This latter phenotype is also considered to have a lack of response to steroid treatment (Kuruvilla et al., 2019). Current asthma therapy is widely developed to target eosinophilic asthma involving Th2 inflammatory pathways such as IL-4, IL-5, IL-13, and eosinophils. Meanwhile, regarding non-eosinophilic asthma therapy, it is still a challenge in clinical practice both in its diagnostic technique and appropriate treatment (Calhoun & Chupp, 2022; Hinks et al., 2021; Esteban-Gorgojo et al., 2018). Amidst the need for a more precise, personalized, and specific phenotype-based approach, mapping the direction and development of current scientific research on non-eosinophilic asthma is very important. This is supported by the fact that the number of non-eosinophilic asthma sufferers is estimated to be half of the total number of asthma sufferers today and 30-50% of severe asthma sufferers have a non-eosinophilic phenotype (Ricciardolo et al., 2021; Hinks et al., 2021).

One approach that can be taken to map the development of research on non-eosinophilic asthma is through bibliometric analysis. This bibliometric analysis allows us to evaluate the landscape of scientific literature quantitatively, identify publication patterns, find out research topic trends, find out collaborations between authors or institutions, and map the development of scientific concepts over time (Donthu et al., 2021; Passas, 2024; Öztürk et al., 2024). There are currently several bibliometric analyses that discuss asthma (Liye et al., 2024; Guo et al., 2024; Chen et al., 2022). However, none of

them specifically discuss non-eosinophilic asthma. Therefore, considering the relatively high number of cases of non-eosinophilic asthma at present, we decided to conduct a bibliometric analysis of non-eosinophilic asthma with the aim of mapping the development of research around non-eosinophilic asthma.

METHOD

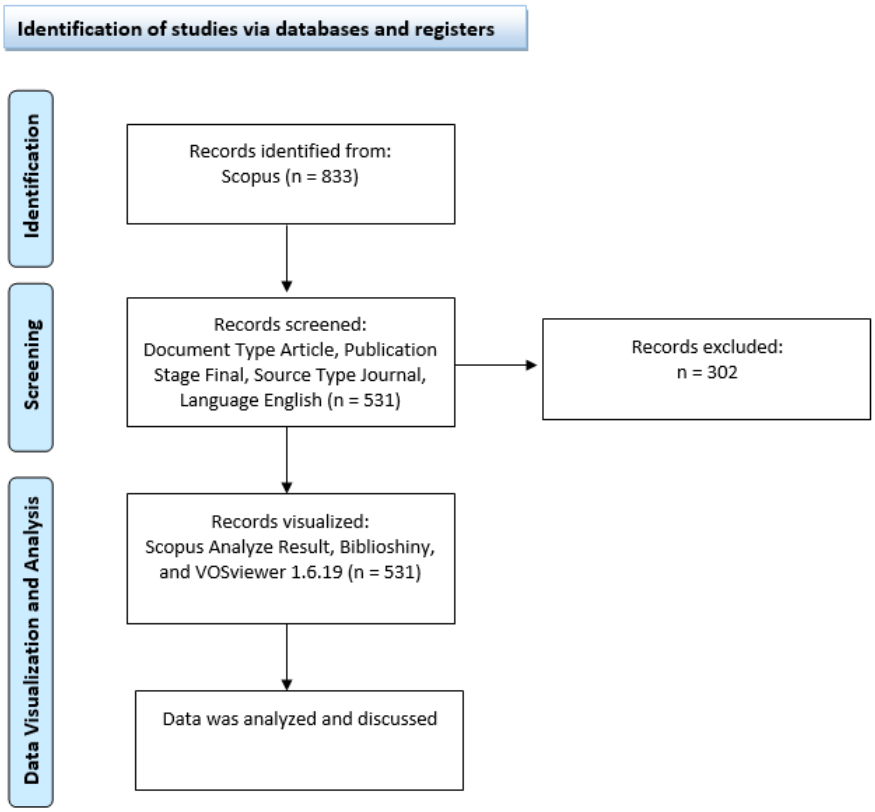

Figure 1. Identification of study on non-eosinophilic asthma using Scopus database

In order to find research on non-eosinophilic asthma, a broad search was conducted in the Scopus database on June 27, 2025, using the title, keywords, and abstract fields, as seen in Figure. 1. From the search on the Scopus database, a total of 833 documents were obtained in the period 1979 to 2025. The keywords we used in the search were TITLE-ABS-KEY ("non-Th2 asthma" OR "T2-low asthma" OR "Non-type 2 asthma" OR "Non-eosinophilic asthma" OR "neutrophilic asthma" OR "paucygranulocytic asthma" OR "mixed granulocytic asthma" OR "obesity-associated asthma" OR "smoking-associated asthma" OR "very late onset asthma" OR "corticosteroid-resistant asthma" OR "steroid-insensitive asthma"). After that, we applied some restrictions to our search results. We limited our search to document type article, publication stage final, language English, and source type journal. Our final search results yielded 531 documents. We then exported these 531 documents into CSV format and analyzed them using Scopus Analyze Result, Biblioshiny, and VOSviewer 1.6.19.

RESULT

Publication Growth

From Figure. 2a, it can be seen that publications on non-eosinophilic asthma began around 1979. Until 2008, publications on the topic appeared to be few and monotonous. This is likely because the research in that period focused on eosinophilic asthma. From 2008 to the present, publications on

non-eosinophilic asthma have grown rapidly, reaching a peak in 2022, with 70 documents published that year. This shows that research interest in non-eosinophilic asthma has grown quite drastically compared to the period 1979-2008. By mid-2025, 24 documents on non-eosinophilic asthma had been published. This number of publications could still increase in the next 6 months.

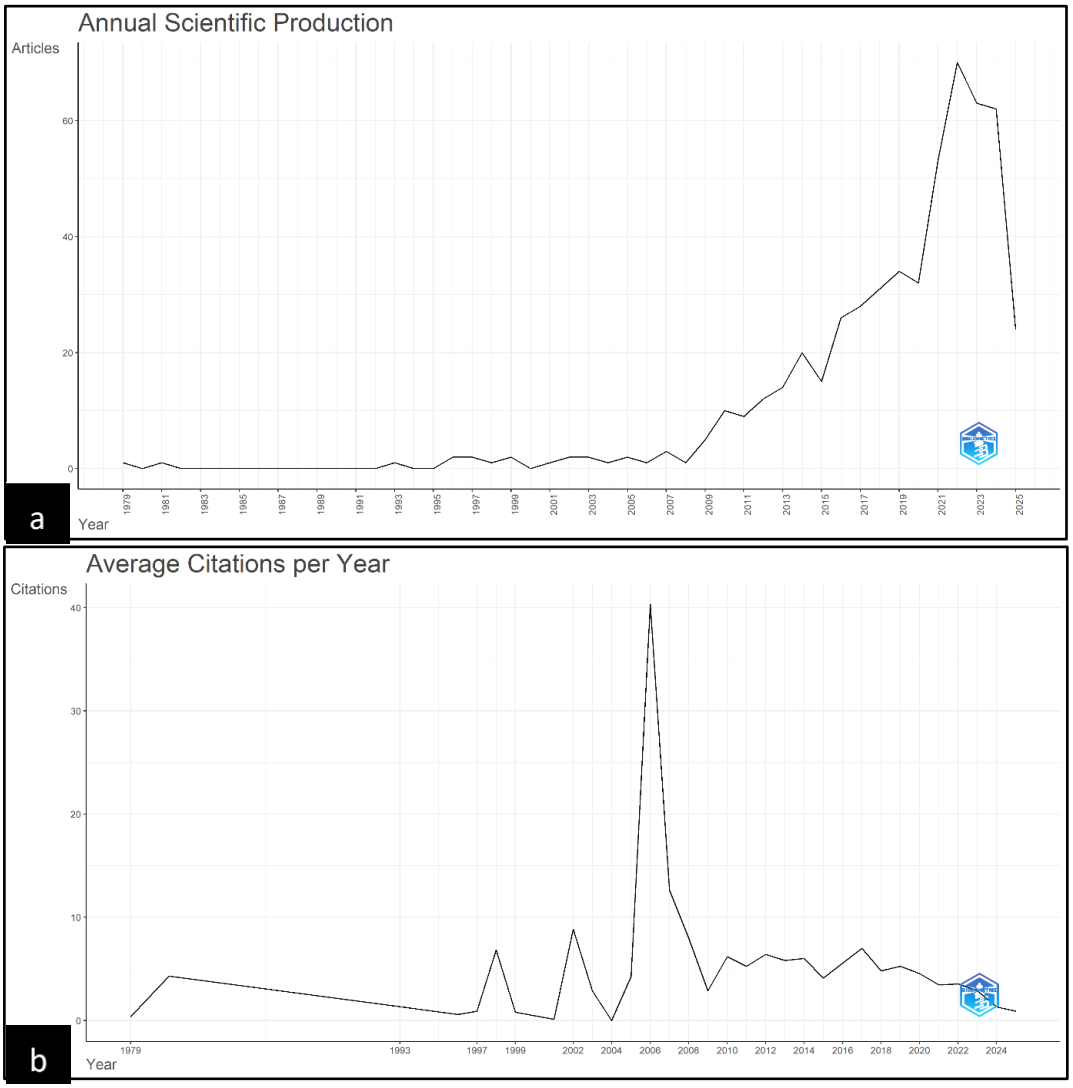

Figure 2. (a). Annual scientific publication of non-eosinophilic asthma. (b). Average citations per year of non-eosinophilic asthma

Based on Figure. 2b, the number of citations of publications on non-eosinophilic asthma fluctuates from year to year. The highest number of citations was in 2006 with the average citations per year 40.4. If we compare it with the low number of annual publications in 2006, this shows that it could be due to significant research or publication on non-eosinophilic asthma occurring in 2006 and this attracted the interest of many researchers to conduct research in the following years on non-eosinophilic asthma. In the following years, the number of citations decreased and fluctuated more or less the same as the period before 2006. This shows that the increase in the number of scientific publications is not necessarily proportional to the number of citations. This could be due to the increasing number of articles published on non-eosinophilic asthma after 2006 as shown in Figure. 2a, so that researchers in the following years were divided into many new references. This is a normal phenomenon which can be found in bibliometric analysis.

Network of Collaboration

Collaboration Network of Country

Table 1. Scientific production of countries

Country	Articles	Total Citations	Average Citations
China	1051	1927	15.30
United States of America	703	2736	42.80
Australia	450	5435	97.10
United Kingdom	376	1659	57.20
South Korea	299	502	13.60
Japan	254	813	33.90
Brazil	143	142	11.80
Italy	140	552	36.80
Germany	131	273	19.50
Spain	128	76	7.60

From Table 1, data is obtained on the 10 countries with the most published articles on non-eosinophilic asthma. The productivity level of each country is calculated using a full count based on the contribution of scientific article authors. China ranks first as the country with the most authors publishing research on non-eosinophilic asthma (n = 1051 articles). The second position is occupied by the United States (n = 703 articles), the third position is occupied by Australia (n = 450 articles), and the fourth position is occupied by the United Kingdom (n = 376 articles). Interestingly, the top four positions are occupied by 4 countries from different continents. However, the total citations and average citations are not in line with the productivity of authors in publishing articles. The country with the highest total citations as well as the highest average citations is occupied by Australia. Although China ranks first in the number of authors publishing articles, its average citation rate is ranked 7th.

Figure. 3 shows the co-authorship analysis based on countries. We set the minimum number of articles produced by each country at 5 articles and out of 71 countries, 24 countries meet the criteria. From the Figureure, the nodes represent the number of collaborative documents published by a country. Meanwhile, the number of lines and the thickness of the lines connecting the nodes indicate the intensity of cooperation between countries whose strength is measured quantitatively through the total link strength. Based on the analysis results obtained in Figure. 3, China emerged as the country with the largest number of international collaborative publications on non-eosinophilic asthma (n = 135 articles), indicated by the largest node size compared to other countries. However, the United States occupies a more central position in the inter-country collaboration network, reflecting its strategic role as the main link between various partner countries. This is indicated by the high number of published collaborative articles (n = 106 articles), the number of citations (n = 3612), and the total link strength (n = 76). This may indicate that China's collaborative productivity tends to be centered on certain countries (e.g. Singapore, Japan, Australia), while the United States collaborates more widely. Although the United Kingdom has the highest total link strength (n = 88), the United States' position at the center of the network also indicates that the United States has a more important role in bridging cross-country collaboration, while the United Kingdom forms more intense but more concentrated collaborative relationships. Australia's role is also no less important than the countries above. Australia plays a strategic role in the international scientific collaboration network with the highest number of citations to articles (n = 6424). Although the number of collaborative documents (n = 76 articles) and total link strength (n = 63) are lower than those of the United States and the United Kingdom, Australia's semi-central position in the network reflects Australia's considerable influence.

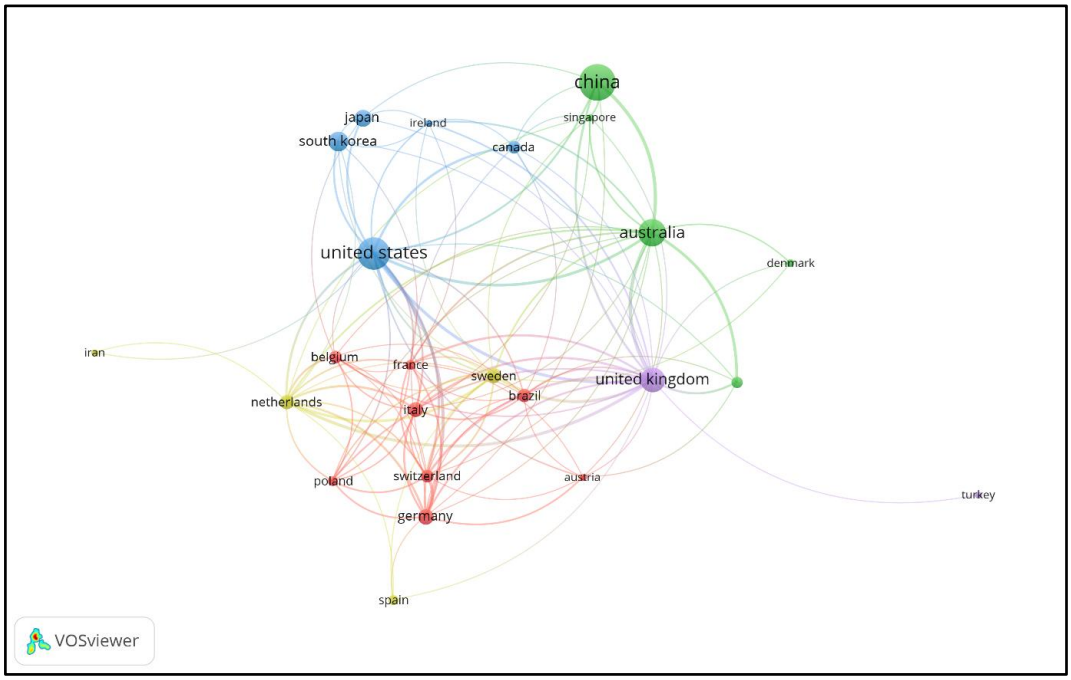

Figure. 3. Co-authorship analysis of country.

Collaboration Network of Authors

Table 2. Top 10 most productive authors

Authors	Documents	H-index	Total Citations
Gibson PG	56	36	5497
Simpson JL	43	30	4501
Baines KJ	25	21	2014
Zhang X	21	8	181
Hansbro PM	17	14	1453
Wood LG	16	16	1839
Chung KF	16	13	990
Adcock IM	14	10	965
Chen Z	11	10	106
Hodge S	11	10	1012

From Table 2, it is shown that Gibson PG is the most productive author on non-eosinophilic asthma research. It is known that Gibson PG is a clinical scientist and respiratory specialist who researches the causes and management of various pulmonary diseases including severe asthma. As a thought leader with more than 600 published journal articles, he has created novel strategies for treating refractory cough, researched airway biomarkers, neurogenic mechanisms, inflammatory subtypes of asthma and cough, and multidimensional assessment and therapy of complicated airway illnesses (Gibson et al., 2023). His highest H-index supports the fact that his published articles are of high quality and influence other researchers. Simpson JL and Baines KJ follow Gibson PG as the second and third most productive authors respectively. Their publications are also high quality as indicated by their high H-indexes.

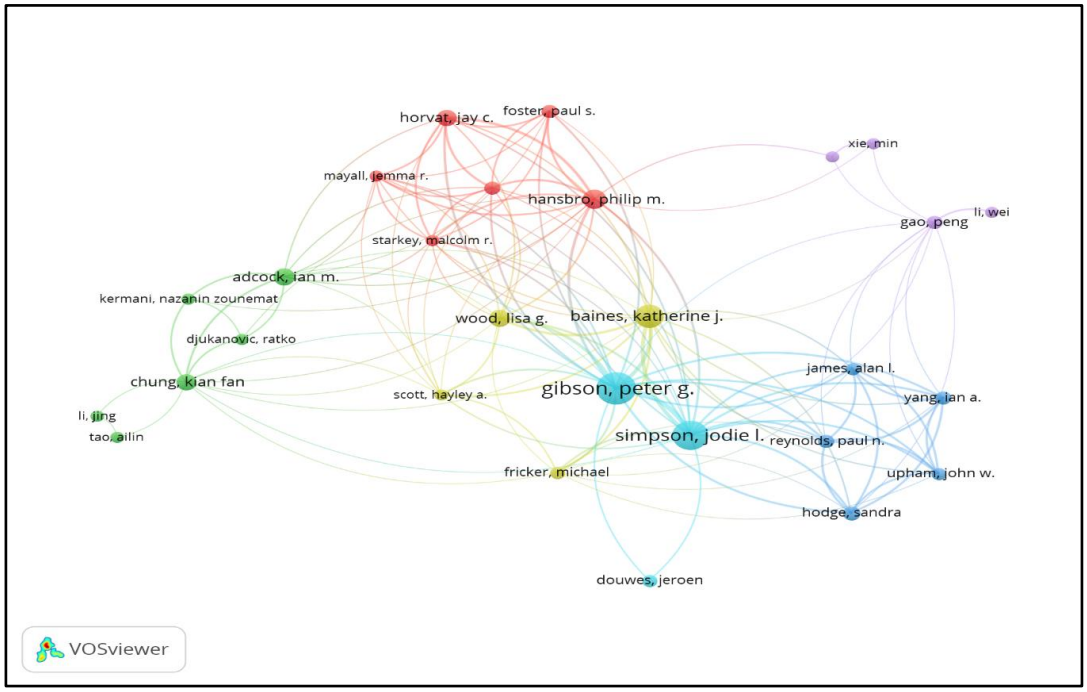

Figure. 4. Co-authorship analysis of authors

Figure. 4 shows co-authorship analysis based on authors. We set the minimum number of articles produced by each author at 5 articles and out of 3154 authors, 47 meet the criteria. The visualization of the author cooperation network depicts scientific interactions between researchers working in the same field, with each node representing an author and its size reflecting their level of scientific production or importance. Connecting lines represent the intensity of collaboration among authors, whereas different colors represent research clusters developed based on scientific partnership closeness. According to the map, Gibson, Peter G. and Simpson, Jodie L. hold a key position, serving as the primary link between clusters and having the most comprehensive collaboration network. The red cluster, led by Hansbro, Philip M. and Horvat, Jay C., represents a group of researchers with strong internal relationships, whereas the green cluster, centered on Chung, Kian Fan and Adcock, Ian M., represents a group with a specific research focus that is still linked to other clusters via connecting authors such as Wood, Lisa G. and Baines, Katherine J. Overall, this map depicts a strong and integrated collaborative structure, with numerous notable researchers playing critical roles in bridging communication and knowledge exchange between research groups, resulting in a dynamic and diversified research environment.

Most Cited Publications of Non-Eosinophilic Asthma

Table 3 shows most cited publications about non-eosinophilic asthma. It is demonstrated that the most cited article is “Inflammatory subtypes in asthma: Assessment and identification using induced sputum” published in “Respirology” Journal in 2006 (Total citations = 807). This study sought to assess a method for identifying and categorizing asthma patients into inflammatory subtypes using induced sputum analysis, notably for distinguishing non-eosinophilic asthma, which is less uniform in clinical practice. They intended to see if the proportion of eosinophils in sputum could be used to reliably distinguish between eosinophilic and non-eosinophilic asthma, and then identify inflammatory subtypes based on eosinophil and neutrophil counts in sputum. The findings of this study suggest that the proportion of eosinophils in produced sputum is a good indicator of eosinophilic asthma, with a repeatable definition. Non-eosinophilic asthma, on the other hand, is variable and can be classified into two categories based on neutrophil elevation: neutrophilic asthma and paucigranulocytic asthma. This classification is significant because it shows that the pattern of airway inflammation in asthma is not

uniform, and understanding these subtypes has clinical implications, including investigation, characterization, and potential personalized treatment of the patient's airway inflammation type (Simpson et al., 2006).

Table 3. Top 10 most cited articles of non-eosinophilic asthma

Rank	Title	Journal	Year	Total citations	Total citations per year
1.	Inflammatory subtypes in asthma: Assessment and identification using induced sputum	Respirology	2006	807	40.35
2.	Interleukin-17–producing innate lymphoid cells and the NLRP3 inflammasome facilitate obesity-associated airway hyperreactivity	Nature Medicine	2014	549	45.75
3.	Pathological features and inhaled corticosteroid response of eosinophilic and non-eosinophilic asthma	Thorax	2007	413	21.74
4.	p38 Mitogen-activated protein kinase–induced glucocorticoid receptor phosphorylation reduces its activity: Role in steroid-insensitive asthma	The Journal of Allergy and Clinical Immunology	2002	390	16.25
5.	Role for NLRP3 Inflammasome–mediated, IL-1β–Dependent Responses in Severe, Steroid-Resistant Asthma	American Journal of Respiratory and Critical Care Medicine	2017	349	38.78
6.	Thymic stromal lymphopoietin induces corticosteroid resistance in natural helper cells during airway inflammation	Nature Communications	2013	305	23.46
7.	Innate immune activation in neutrophilic asthma and bronchiectasis	Thorax	2007	282	14.84
8.	Effects of steroid therapy on inflammatory cell subtypes in asthma	Thorax	2010	269	16.81
9.	Airway inflammation is augmented by obesity and fatty acids in asthma	European Respiratory Society	2011	264	17.60
10.	Inflammatory phenotypes in patients with severe asthma are associated with distinct airway microbiology	The Journal of Allergy and Clinical Immunology	2018	263	32.88

The second most cited publication is “Interleukin-17–producing innate lymphoid cells and the NLRP3 inflammasome facilitate obesity-associated airway hyperreactivity” published in “Nature Medicine” journal in 2014. Interestingly, this is an article with the highest total citations per year. The study aimed to investigate the immunological mechanisms underlying the association between obesity and the development of airway hyperreactivity (AHR), a hallmark feature of asthma, with a particular focus on the role of IL-17-producing innate lymphoid cells (ILC3), the NLRP3 inflammasome, and the cytokine IL-1β. They employed a mouse model fed a high-fat diet to develop obesity, then tested the

effect of genetic impairment in Il17a or Nlrp3 on AHR and looked for ILC3s in individuals with asthma. Obesity by a high-fat diet causes AHR irrespective of the adaptive immune system, as evidenced by its persistence in Rag1-/- mice. AHR is dependent on IL-17A and NLRP3, as neither Il17a-/- nor Nlrp3-/- mice develop it. Obesity increases IL-1β production by macrophages in the lungs, which promotes the proliferation of IL-17A-producing CCR6+ ILC3 cells. In immunodeficient mice, adoptive transfer of ILC3 and IL-1β is sufficient to trigger AHR. Blocking IL-1β with an IL-1 receptor antagonist lowers AHR and reduces ILC3s. In addition, the study discovered ILC3-like cells in asthmatic patients' bronchoalveolar fluid. Therefore, NLRP3, IL-1β, and ILC3 are essential players in the inflammatory system that links obesity to AHR, opening the door for novel treatment strategies for asthma associated with obesity (Kim et al., 2014).

The latest most cited article is “Inflammatory phenotypes in patients with severe asthma are associated with distinct airway microbiology” published in “The Journal of Allergy and Clinical Immunology” in 2018. This study aimed to characterize the composition of the airway microbiota in adult patients with severe and stable asthma, then evaluate the relationship between the airway inflammatory phenotype and other clinical characteristics. The findings revealed that individuals with a neutrophilic asthma phenotype had a significantly different airway microbiota than those with an eosinophilic phenotype, with lower microbial diversity and more heterogeneous composition. The number of neutrophils in sputum was found to be a strong predictor of microbiome alterations. These findings suggest that differences in the airway microbiota may influence the response to antimicrobial and corticosteroid therapy, as well as the risk of pulmonary infections in severe asthma patients (Taylor et al., 2017).

Evolution of Topic on Non-Eosinophilic Asthma Throughout the Years

The word cloud shown in Figure. 4a indicates that current research focuses on the non-eosinophilic phenotype of asthma, as evidenced by the predominance of terms like “asthma” (n = 209), “neutrophilic asthma” (n = 67), “neutrophil” (n = 73), and “airway inflammation” (n = 33). The presence of the term "severe asthma" (n = 41) highlights the focus on severe asthma, which often has complex inflammatory characteristics, while the term "obesity" (n = 28) indicates the presence of comorbidities that contribute to phenotype variation especially in non-eosinophilic asthma. Overall, this word cloud reflects a research focus on understanding the inflammatory phenotype of asthma to support more personalized therapeutic approaches.

The evolution of research on non-eosinophilic asthma, as depicted in Figure. 4b, demonstrates a very interesting shift in research direction and reflects a new dynamic in the understanding of asthma pathophysiology. The scientific community started to challenge the shortcomings of the previous paradigm, which placed an excessive amount of emphasis on eosinophilic inflammation, starting in 2015 and 2016. Non-eosinophilic asthma is no longer merely a minor phenotype, but rather a major concern in contemporary asthma research, as seen by the steady increase in both the frequency and scope of publications since its debut. This upward trend coincides with an increase in studies on neutrophils, airway inflammation, biomarkers, and particularly corticosteroid resistance, suggesting that scientists are starting to identify a subset of patients with severe symptoms who do not improve with conventional steroid-based treatments. Research on non-eosinophilic asthma is advancing not just clinically but also mechanistically and molecularly, as seen by the inclusion of themes such innate immunity, T2-low asthma, and induced sputum. Interestingly, this research also coincides with increasing attention to comorbidities such as obesity, which is known to be a significant factor in the non-T2 phenotype. The presence of this term in research trends strengthens the argument that non-eosinophilic asthma is a multifactorial condition with a much more complex biological spectrum than the classic model of allergic asthma. Overall, Figure. 4b demonstrates a major transformation in the asthma research landscape: from a homogenous approach to an understanding that asthma is a highly

heterogeneous disease, requiring precise phenotypic characterization, and requiring truly personalized therapeutic strategies.

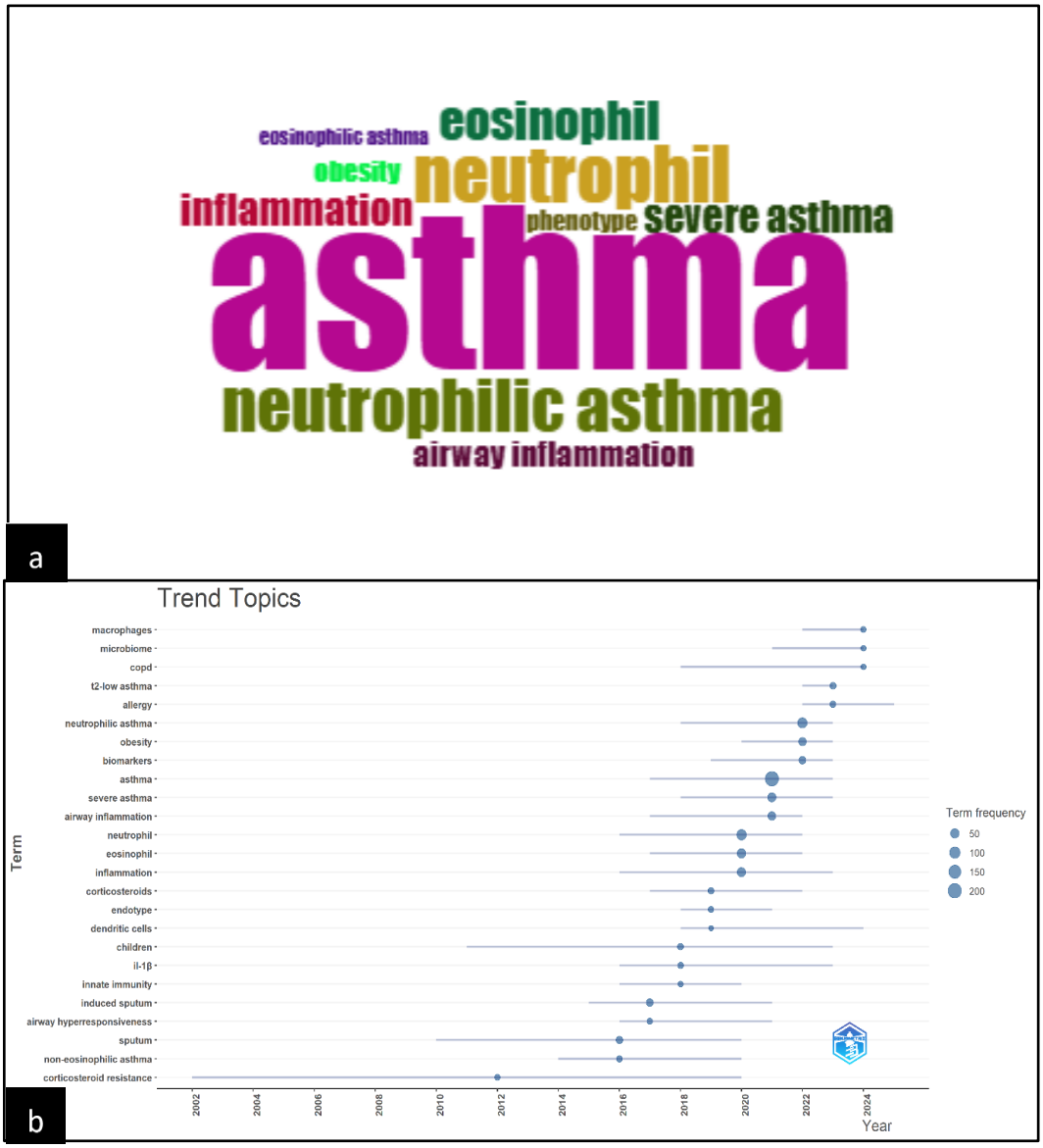

Figure. 4. (a). Top 10 authors' keywords used in publications. (b). Evolution of keywords around non-eosinophilic asthma since 2002.

Co-occurrence Analysis of Authors' Keywords

The keyword co-occurrence visualization as seen in Figure. 5a displays four main clusters that illustrate the intellectual structure of research on non-eosinophilic asthma. The green cluster indicates a focus on non-T2 inflammatory mechanisms dominated by the role of neutrophils, including IL-17 activity, IL-1β, the Th17 pathway, oxidative stress, NETosis, and macrophage contributions. This cluster illustrates the biological basis of steroid-resistant non-eosinophilic asthma and has become the focus of mechanistic research. Meanwhile, the red cluster reflects a clinical approach oriented towards characterizing phenotypes and endotypes, reflected by the proximity of keywords such as "severe asthma", "phenotype", and "endotype". This cluster is related to efforts to understand the clinical variations of non-eosinophilic asthma, especially in severe, difficult-to-treat asthma. On the other hand, the yellow cluster highlights omics and microbiota-based research, as seen through the

interconnectedness of terms such as “microbiome”, “sputum”, “biomarkers”, and “proteomics”, signaling the development of molecular approaches to more precisely map non-eosinophilic asthma phenotypes. Finally, the blue cluster serves as a conceptual framework integrating terms such as “non-eosinophilic asthma”, “phenotypes”, and “endotypes”, indicating a research focus on defining, classifying, and developing a multidimensional understanding of non-eosinophilic asthma heterogeneity. The close interaction between clusters emphasizes that non-eosinophilic asthma studies require a multidisciplinary approach that harmoniously combines biological, clinical, molecular, and conceptual aspects.

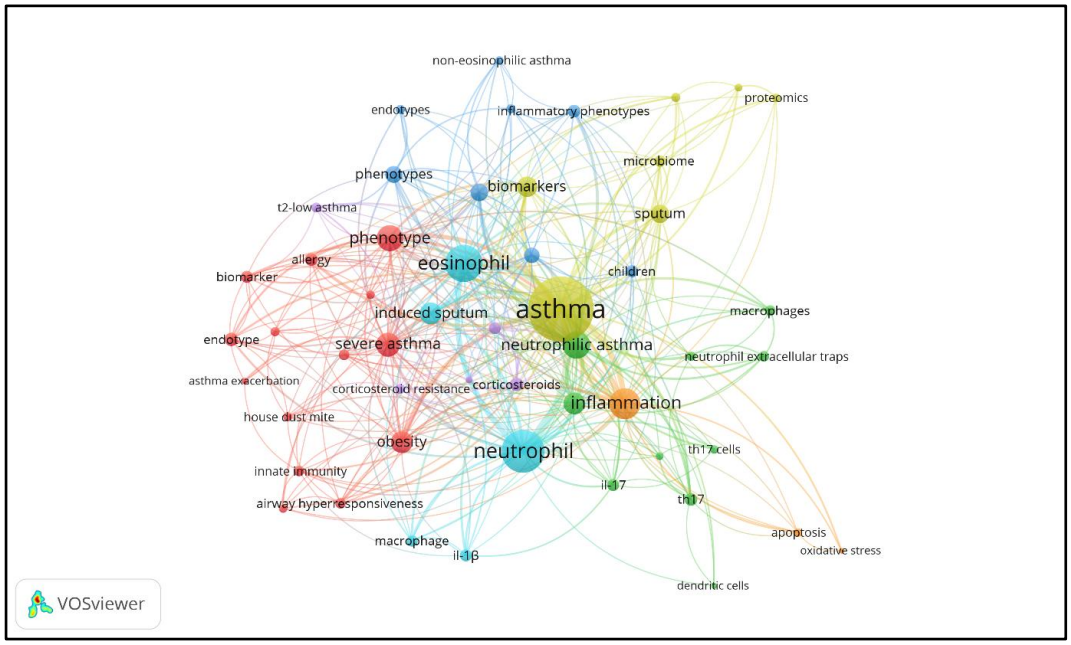

Figure. 6. Keyword co-occurrence visualization

DISCUSSION

This bibliometric analysis reveals that the asthma research landscape is undergoing a major conceptual transformation, marking a paradigm shift in asthma from a classical inflammatory approach toward a deeper understanding of type 2–low mechanisms and the dominance of the innate response. Publication trends demonstrate an acceleration inextricably linked to clinical dissatisfaction with standard corticosteroid-based therapies, which are highly effective in the eosinophilic phenotype but fail to provide meaningful benefit for the more than one-third of asthma patients who are found to have the non-eosinophilic phenotype (Esteban-Gorgojo et al., 2018; Kim et al., 2017; Nabe, 2020; Wang et al., 2016). This shift reflects the urgent need for the global community to address the blind spots that have long been a major challenge in modern asthma management.

Pathophysiologically, non-eosinophilic asthma exhibits a complexity that extends far beyond the definition of “non-eosinophilic” itself. The predominance of neutrophils in the airways reflects not only cellular variation but also a shift to more resistant, destructive, and difficult-to-modulate non-T2 inflammatory pathways. The activity of IL-17, IL-1β, TNF-α, and inflammasomes such as NLRP3 drive steroid-refractory inflammatory mechanisms, explaining why conventional therapies are often ineffective in non-eosinophilic asthma patients (Kim et al., 2017). The most frequently cited studies in this dataset demonstrate that these pathways are not only hallmarks of non-eosinophilic asthma but also key drivers of disease progression and therapy resistance. Therefore, the increasing research focus on biomarkers, innate immune pathways, and novel molecular candidates is not simply a scientific trend

but a direct response to the failure of the Th2-based approach that has dominated asthma management for decades.

Bibliometric findings also reveal another dimension of non-eosinophilic asthma that is gaining increasing attention: its interaction with metabolic comorbidities and the microbiota. Obesity, which consistently features in non-eosinophilic asthma-related research topics, has been shown to create a unique inflammatory microenvironment that drives the airways into a hyperresponsive pattern through adipokine and inflammasome activity (Tashiro et al., 2024; Miethe et al., 2020). This phenotype results in an IL-17-dominant inflammatory profile that is entirely independent of Th2, adding to the complexity of non-eosinophilic asthma's response to standard therapies (Olejnik & Kuźnar-Kamińska, 2024). This suggests that in many cases, non-eosinophilic asthma is not simply an airway disease, but rather a systemic manifestation of metabolic dysfunction that alters the character of airway inflammation. A growing body of published microbiota research also suggests the possibility that non-eosinophilic asthma has a distinct biological ecological basis from eosinophilic asthma, with lower microbiota diversity and a predominance of pathogenic bacteria that may amplify neutrophilic inflammation (Yang et al., 2018; Simpson et al., 2015). These findings point to the concept that some non-eosinophilic asthma subtypes may actually be “microbiome-driven” diseases, a new direction of thought that has the potential to transform future therapeutic approaches.

Collaboration analysis reveals fragmented research network structures within specific countries, which, while productive, tend to result in population bias. Nearly all non-eosinophilic asthma research originates from high-income countries with populations experiencing significantly different environmental exposures, dietary patterns, and healthcare access than populations in South Asia, Africa, or South America. A study shows that the prevalence of non-eosinophilic asthma is actually higher in developing countries such as Brazil, Uganda, and Ecuador. In low-income countries like Uganda, the high prevalence of neutrophilic asthma is thought to be related to environmental exposures that induce background neutrophilic inflammation, even in individuals without asthma. Factors such as indoor air pollution, chronic infections, endotoxin exposure, and contact with animals can increase the number of neutrophils in the airways, leading to a more prominent pattern of neutrophilic inflammation in these populations (Pembrey et al., 2023). The absence of significant contributions from these countries in global research networks creates a geographical research blind spot that must be addressed if non-eosinophilic asthma is to be understood as a global condition.

From a therapeutic development perspective, bibliometric data indicate that there are currently no truly effective treatments for non-eosinophilic asthma (Esteban-Gorgojo et al., 2018; Sze et al., 2020). This situation not only reflects a lack of therapeutic options but also reflects the inadequate understanding of the biological targets of non-eosinophilic asthma. Although extensive research highlights the IL-17, IL-1β, inflammasome, and neutrophil pathways as key candidates, clinical evidence for targeting these pathways remains very limited. Clinical trials of IL-17 inhibitors, for example, have consistently shown disappointing results in asthmatics, indicating that the pathophysiology of non-eosinophilic asthma is far more complex than the “IL-17–driven inflammation” model (Iwaszko et al., 2025). Thus, despite the rapid advancement of mechanistic research, a significant gap remains between basic biological findings and truly effective clinical applications for non-eosinophilic asthma.

The future of non-eosinophilic asthma research demands a more integrative and precise approach than current research strategies. A key priority is the development of reliable biomarkers to accurately identify the non-T2 phenotype, given the limitations of current methods such as unstable sputum neutrophil counts and their impracticality for widespread clinical implementation (Carr et al., 2018). Integrating multi-omics approaches including genomics, proteomics, metabolomics, and microbiome profiling is anticipated to be a crucial starting point for more comprehensively mapping non-eosinophilic asthma endotypes (Picado et al., 2025). Similarly, future research should increasingly

address the contribution of the airway microbiome to chronic neutrophilic inflammation, as preliminary evidence suggests that specific bacterial colonization and dysbiosis patterns may be key drivers of this condition (Pang et al., 2019; Campbell et al., 2023).

Furthermore, low- and middle-income countries need to be a focus of research because non-eosinophilic asthma has been shown to be more prevalent in these populations. Therefore, future studies should consider environmental factors such as biomass pollution, chronic infections, and endotoxin exposure that can shape non-eosinophilic inflammatory phenotypes (Pembrey et al., 2023). In the therapeutic realm, research needs to move away from the "one biological target fits all" model and toward targeted therapy strategies tailored to subphenotypes, including further exploration of neutrophil chemotaxis pathway inhibitors, inflammasome suppressors, immunomodulatory therapies such as long-acting macrolides, and novel approaches based on microbiome modulation. The development of more representative animal and in vitro models for non-eosinophilic asthma is also needed to bridge the gap between basic biological findings and effective clinical therapies. Finally, the integration of machine learning and precision medicine is expected to strengthen the endotyping process and predict therapeutic response, enabling personalized non-eosinophilic asthma treatment in the future. By combining in-depth biological exploration, environmental understanding, and technological innovation, future research directions have great potential to overcome the barriers that have hampered progress in the clinical management of non-eosinophilic asthma.

RESULT

This bibliometric study demonstrates that research on non-eosinophilic asthma is quickly developing and gaining increased attention from the global scientific community. Research has evolved from classical approaches that focused solely on eosinophilic inflammation and toward a more thorough knowledge of phenotypic variation, non-T2 inflammatory processes, and underlying biological and environmental variables. These findings highlight that non-eosinophilic asthma is a rapidly evolving scientific field with considerable clinical problems, notably in the areas of diagnosis, biomarker discovery, and the development of effective medications. As a result, future non-eosinophilic asthma care will require interdisciplinary research that integrates genetic, clinical, and precision technology methods.

LIMITATIONS

This study's limitations include the use of a single database, the restriction to English-language publications and article types, and the nature of the bibliometric analysis, which does not assess the methodological quality of each publication. Furthermore, the evolving literature may result in future changes in publication patterns, citations, and research hotspots.

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