Brief report

Bibliometric analysis of the trends and evolution in β-lactam allergy research

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Background: β-Lactams remain the most reported drug allergy globally, with the volume and diversity of related drug allergy research continuing to accumulate. Recognizing evolving research trends can help inform future directions and encourage synergistic collaborations.

Objective: We conducted a comprehensive bibliometric analysis of all publications relevant to β-lactam allergy, with a focus on longitudinal publication rates, international collaborations, and key word/trend analysis.

Methods: Meta-data from all original articles, letters, and reviews relevant to β-lactam allergy on the Web of Science Core Collection up until December 31, 2023, were analyzed.

Results: From 1966 to 2023, there were 4451 records (3536 articles, 631 reviews, and 284 letters) from 78 countries. There was an exponential increase in publications, especially during the past decade, with half of all publications on β-lactam allergy published during this time (50.6% [2252 of 4452]). Overall, 18.1% of the publications (805 of 4452) involved international coauthorships, with a significant increase since the previous decade (12.7% vs 23.3% [*P* < .001]). The most frequent key words in the first published half of articles were *skin testing* (84 of 1919), *IgE* (57 of 1919), and *anaphylaxis* (49 of 1919); in contrast to the key word *skin testing* (137 of 3351), the key words *drug provocation test* (121 of 3351), *antimicrobial resistance* (120 of 3351), and *antimicrobial stewardship* (118 of 3351) were the most frequent key words in the latter half.

Conclusion: There has been a surge in publications, international collaboration, and shifting paradigms in β-lactam allergy research. The field has evolved beyond focusing on *in vitro* tests or desensitization toward antimicrobial stewardship. However, there still seems to be relatively fewer collaborations with non-Western countries. Further international collaborations to harmonize delabeling strategies against the threat of mislabeled β-lactam allergy should be encouraged. (J Allergy Clin Immunol Global 2024;3:100328.)

Key words: *Allergy, β-lactam, bibliometric, drug, penicillin, research, trends*

INTRODUCTION

β-Lactams, especially penicillins, remain the most reported drug allergy, with a prevalence of 2% to 10% globally.[1-3] Unfortunately, many nonallergic adverse drug reactions are often misdiagnosed as allergies, with approximately 90% of β-lactam/penicillin allergy labels found to be incorrect following allergy evaluation.[4,5] Unverified, incorrect allergy labels can be dangerous and associated with a myriad of adverse outcomes, including obligatory use of less effective antibiotics and development of multidrug resistant microorganisms.[6,7] Removal of incorrect allergy labels (delabeling) has therefore become an important focus of β-lactam allergy research and integral part of antimicrobial stewardship programs worldwide.[4-8] Although the volume and diversity of β-lactam allergy research continue to accumulate, a comprehensive bibliometric analysis has not been performed.[9] Recognizing evolving research trends can help inform future directions and encourage synergistic collaborations into this globally important research field. Therefore, we conducted a comprehensive bibliometric analysis of all publications relevant to β-lactam allergy, with a focus on longitudinal publication rates, international collaborations, and key word/trend analysis.

All original articles, letters, and reviews relevant to β-lactam allergy on the Web of Science Core Collection up until December 31, 2023, were identified (details regarding the study methodology are summarized in Fig E1 [available in the Online Repository at www.jaci-global.org]). Duplicate and non-English records were excluded. Meta-data of eligible records (authors, countries, publication year and journal title, references, and key words), number of publications by year and country, most frequent key words (after a median split into 2 equally sized groups based on date), and trend topics were analyzed. A median split was chosen arbitrarily, as we did not identify any specific year or period with a surge in publications (ie, a steady increase throughout the analysis period). Different variations or synonyms of key words were manually reviewed and grouped for analysis (eg, delabelling and delabeling, direct

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Abbreviation used
TF: Term frequency

provocation test and challenge). Statistical analysis was performed by using R, version 4.3.1 (R Foundation, Vienna, Austria) using *Bibliometrix*.[9] Proportions of international coauthorship (articles involving authors from >1 country) were compared by using the chi-square test with IBM SPSS Statistics, version 28.0 (IBM, Armonk, NY). A *P* value less than .05 indicates statistical significance. Ethical approval was waived, as this study involves publicly accessible data only.

RESULTS AND DISCUSSION

From 1966 to 2023, a total of 4451 records (3536 articles, 631 reviews, and 284 letters) from 78 countries were analyzed. Collectively, these articles were cited 165,108 times with an h-index of 166 and an average citation count of 37.1 times per article. There was an exponential increase in the number of publications, especially during the past decade (2014-2023), with half of all publications on β-lactam allergy (50.6% [2252 of 4452]) published during this time (Fig 1, *A*). Overall, 18.1% (805 of 4452) involved international coauthorships, with a significant increase since the past decade versus before 2013 (12.7% vs 23.3% [$P < .001$]) (Fig 1, *B*).

A total of 4611 different key words were identified. The most frequent key words (including variations and synonyms) in the first published half of articles were *skin testing* (84 of 1919), *IgE* (57 of 1919), and *anaphylaxis* (49 of 1919); in contrast to the key word *skin testing* (137 of 3351), the key words *drug provocation test* (121 of 3351), *antimicrobial resistance* (120 of 3351), and *antimicrobial stewardship* (118 of 3351) in the latter (as depicted by word clouds [font size proportional to key word frequency] in Fig 2). Similarly, Fig E2 (see the Online Repository at www.jaci-global.org) shows the detailed recent 25-year trend analysis, demonstrating the most recent trends evolving from *delabeling* (term frequency [TF] = 51 in 2020-2023), *antibiotic prophylaxis* (TF =29 in 2018-2022), and *antimicrobial stewardship* (TF = 121 in 2018-2022).

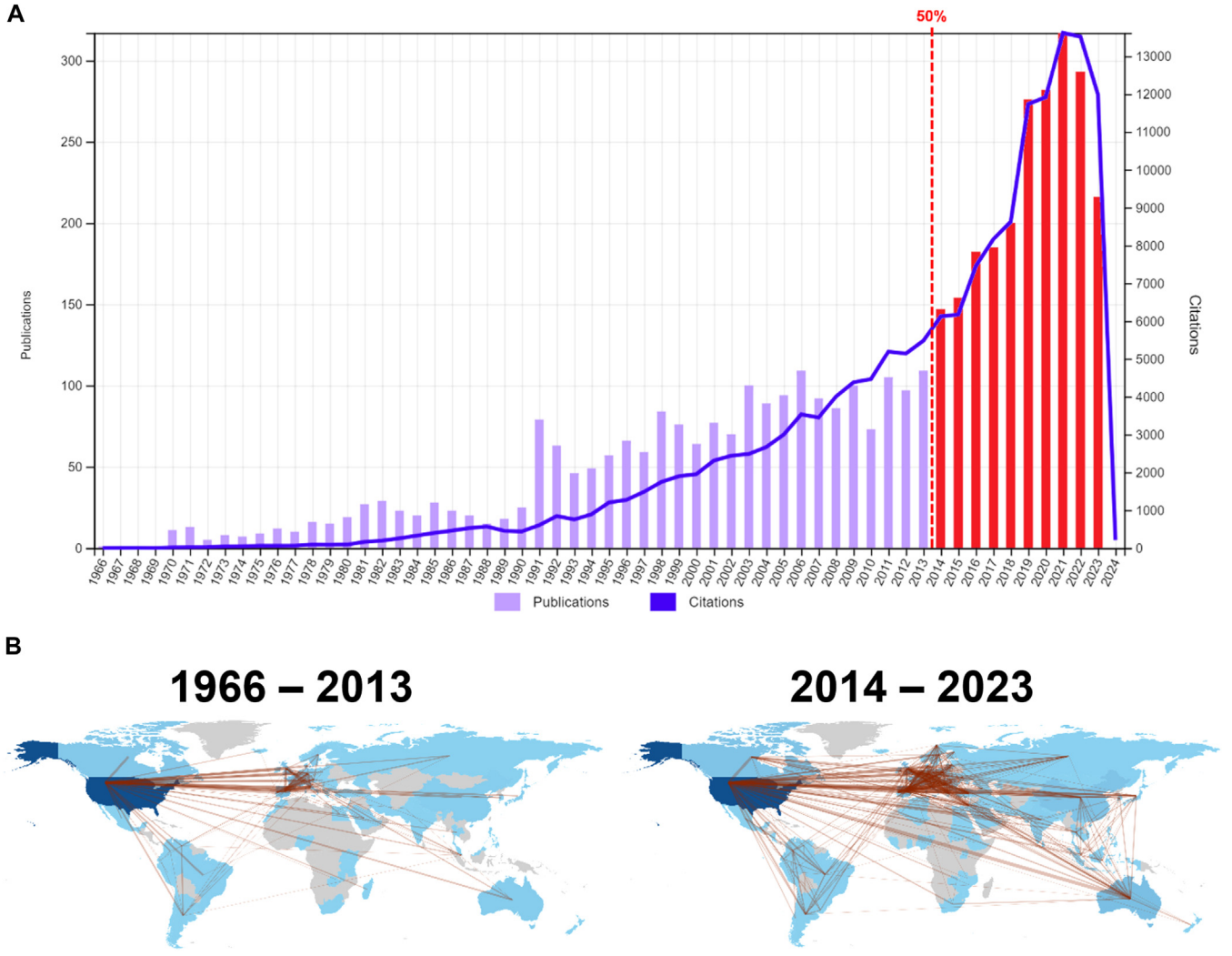

FIG 1. Trend of annual publications and citations (**A**) and international collaborations (**B**) of β-lactam allergy research between the periods 1966-2013 and 2014-2023.

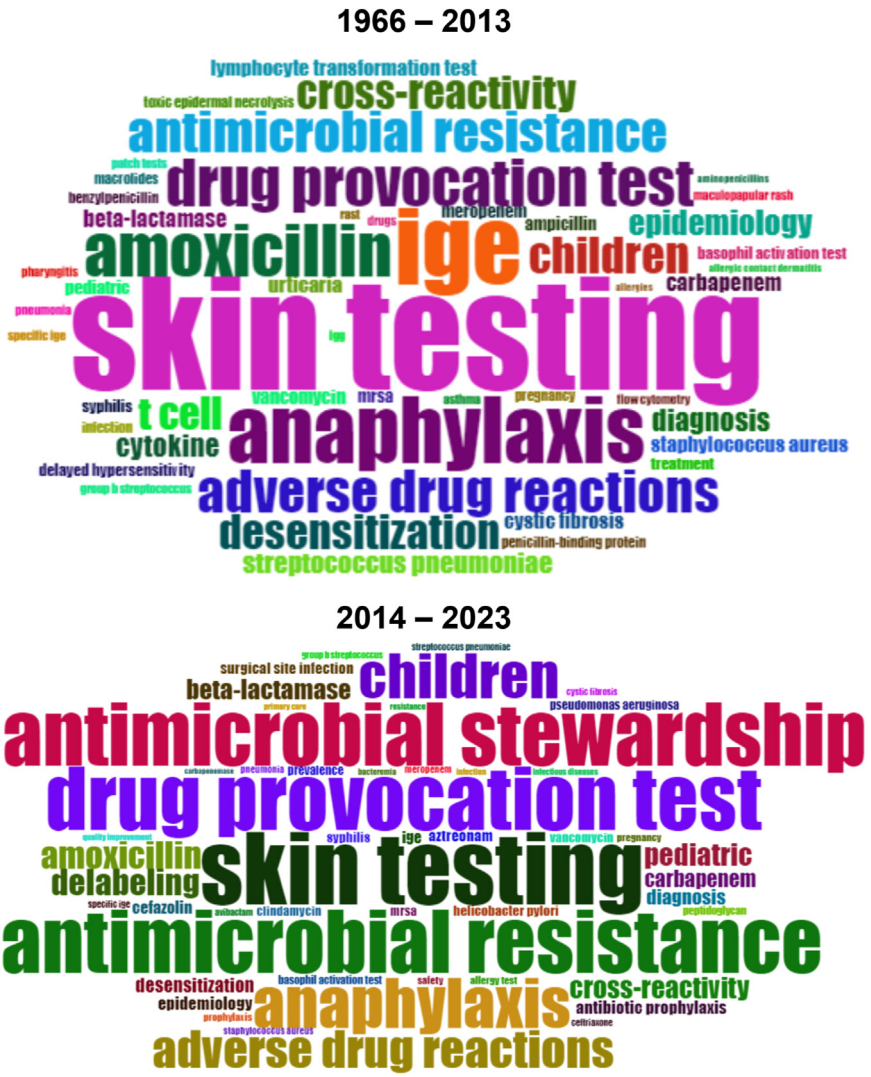

FIG 2. Word clouds in the periods 1966-2013 and 2014-2023 (by key word frequency).

Our bibliometric analysis demonstrates a sustained increase in publications on β-lactam allergy, with a dramatic upsurge in the recent decade (constituting half of all available literature). Antibiotic overuse and misuse are the key drivers of antimicrobial resistance, and β-lactam allergy delabeling has been recognized as being the cornerstone toward antimicrobial stewardship worldwide.[4-6,8] Although different regions will have differences in the epidemiology of drug allergy, sensitization patterns, cultural behaviors, prescription practices, and infrastructure, drug allergy (mis)labeling and antimicrobial resistance remain global health threats requiring combined solutions and teamwork.[2] The significant rise in international coauthorships in the past decade likely reflect the increasing global awareness of antimicrobial stewardship and need for collaboration.[7] However, the majority of collaborations were seen between Western countries of Europe and North America, with relative underrepresentation among countries in Africa or South America. Although there is a possibility of ascertainment bias owing to exclusion of non-English publications, the aforementioned underrepresentation at least emphasizes the relative lack of partnerships between Western countries and the rest of the world.

The analysis of key words and search trends also corroborated known paradigm shifts in the practice of β-lactam/penicillin allergy evaluation, with previously popular key words such as *desensitization* and *in vitro tests* being superseded by more effective delabeling strategies with a focus on antibiotic stewardship. Although the term *skin testing* remained the most popular key word throughout the entire study period, the popularity of the key word *drug provocation tests* has increased significantly in recent years. This is in line with "direct" provocation testing (without the need for prior *in vitro* or skin tests) becoming more favored for the overwhelming majority of low-risk individuals, especially in regions lacking sufficient specialist resources or support. With growing evidence from multicenter and multicountry collaborations, such novel strategies incorporating direct provocation testing among low-risk individuals have now started to be recognized and recommended internationally.[8] Having said that, skin testing remains an important modality (especially in the diagnosis of non–low-risk or severe reactions) and therefore likely remains a popular key word. Similarly, the need for desensitization (with significant inherent risk for individuals with true allergy) has likely decreased with the growing availability of alternative antibiotics as well as with the growing emphasis on accurate drug allergy diagnosis and delabeling.

This study was limited mainly by its observational nature, exclusion of non-English articles, single source of data, and absence of detailed manual screening of individual publications. For example, we were unable to further define skin testing (eg, skin prick, intradermal or patch test). It is also possible that the proportion of international collaborations was overestimated, as many missed non-English publications tend to be mononational. This further highlights the need to promote international collaborations and improve access to scientific publications; this is especially for international publications beyond those available and indexed in English databases.

In conclusion, this study highlights the recent surge in publications, international collaboration, and shifting paradigms in the field of β-lactam allergy research. However, there still seems to be a disparity in international collaborations, with relatively fewer collaborations with non-Western countries participating in collaborations, thus highlighting the urgent need for internationalization of drug allergy research. The β-lactam allergy research field seems to have evolved beyond focusing on *in vitro* tests or desensitization and toward antimicrobial stewardship, with more streamlined delabeling strategies such as direct provocation testing for the population of low-risk mislabeled individuals. In lieu of growing global interest in combating antimicrobial resistance, further international collaborations to harmonize delabeling strategies against the pervasive threat of mislabeled β-lactam allergy should be encouraged.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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