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Short Communication

A scientometric study on research characteristics and trends of amyloidosis involving the oral cavity

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Received 4 December 2024; Final revision received 10 December 2024

Available online 29 December 2024

KEYWORDS

Amyloidosis;
Bibliometrics;
Early diagnosis;
Macroglossia;
Oral;
Tongue

Abstract *Background/purpose:* Oral involvement often constitutes the first sign of amyloidosis as a life-threatening disease that can lead to multiple organ impairment. The purpose of this study was to analyze the scientometric characteristics and research trends of amyloidosis involving the oral cavity.

Materials and methods: All the papers on oral involvement of amyloidosis were comprehensively retrieved from the Scopus database. The years of publication were divided into before 2015 and 2015–2024 in the analysis of research trends.

Results: There were 2540 relevant papers on amyloidosis involving the oral cavity, with total citations of 73,896 and the *h* index of 119. The related disorders were light chain amyloidosis,

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transthyretin amyloidosis, amyloid A amyloidosis, heart/cardiac amyloidosis, cardiomyopathy, kidney amyloidosis, and multiple myeloma. The trend of drug aspect, e.g. prednisone, colchicine, corticosteroid, doxorubicin, and vincristine before 2015 has changed to monoclonal antibody, daratumumab, tafamidis, proteasome inhibitor, carfilzomib, ixazomib, patisiran, pomalidomide, diflunisal, and doxycycline. Besides, the trend of clinical aspect has changed to complication, quality of life, risk factor, diagnostic imaging, prospective study, and early diagnosis after 2015. Herein, we highlight the awareness of early diagnosis and improve the access to care for amyloidosis, since oral involvement frequently constitutes the first sign of this disease.

Conclusion: This scientometric study elucidated the current scenario and research trends of amyloidosis, underpinning that stomatologists can play roles in providing early recognition and timely diagnosis of amyloidosis when it involved the oral cavity.

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Introduction

Amyloidosis is a rare group of diseases caused by extracellular deposition of insoluble fibrillar proteins, which can involve any tissue and organ including the heart, kidney, and liver.¹ Amyloidosis can be categorized into localized and systemic types. Although it is generally a benign condition, systemic amyloidosis is actually a fatal disease owing to it finally leading to organ failure and eventual death.¹ According to the type of deposited amyloid, amyloidosis is mainly subdivided into immunoglobulin light chain (AL, primary), amyloid A (AA, secondary), β_2 microglobulin (β_2M , also known as dialysis-related amyloidosis), and transthyretin (ATTR, hereditary/familial) subtypes.¹ Reportedly, oral involvement was the first sign of this disease in 67.0 % of cases, with tongue being the most common involved site.^{2,3} The typical clinical presentation of oral amyloidosis is macroglossia, and it can also manifest as granular, papules, nodules, multiple blood blisters, mucosal petechiae or ecchymoses, as well as abnormal color change in the oral cavity as the initial and only clinical findings.^{4–10}

Despite progress in the management and treatment of amyloidosis in the past decades, this disease remains fatal, especially in advanced patients. The pathogenesis and development of amyloidosis, particularly AL and ATTR amyloidosis, are still not fully clear.^{11,12} Emphasis is placed on understanding the mechanisms underlying amyloid aggregation and deposition to mitigate organ involvement. Oral mucosal specialists and oral and maxillofacial surgeons can play roles in providing early recognition and timely diagnosis of amyloidosis when it involved the oral cavity. Scientometrics is a useful tool that utilizes citation and bibliometric data to measure scientific output and research trend of a specific research field.^{13–15} The bibliometric analyses on AL amyloidosis and cardiac amyloidosis have been reported previously,^{16,17} but there is little relevant analysis on oral involvement of amyloidosis. Therefore, the purpose of this study was to analyze the scientometric characteristics and research trends of all the papers on amyloidosis involving the oral cavity, in order to highlight the awareness of early recognition and timely diagnosis and improve the access to care for this disease.

Materials and methods

As per the methodology described previously,^{13–15} all the papers on amyloidosis in the Scopus database were retrieved on 18 Nov 2024. In literature search, we used medical subject terms “amyloidosis” in the Title and “oral OR intraoral OR mouth OR tongue OR buccal OR lip OR labial OR gingival OR palate OR head” in all fields of the papers. There was not restriction to paper type and year of publication, but language was restricted to the English as an international knowledge-exchange language. The scientometric characteristics of all the eligible papers were recorded for the following information: title, keyword, citation count, publication year, journal of publication, authorship, affiliation, and country/region of origin. Data search and extraction were performed independently by two investigators, and any discrepancy of results was resolved in a consensus symposium. The years of publication were divided into before 2015 and 2015–2024, so that the number of papers can be to some extent compared in the analysis of research trends. Microsoft Office Excel 365 was used for index model building, and the Bibliometrix Biblioshiny R-package software was used for bibliometric statistics. In this descriptive study, variables were presented as numbers and percentages. No comparisons were made, and thus no *P*-values were set.

Results

Citation characteristics

With the search strategy algorithm, a total of 2540 papers on amyloidosis involving the oral cavity were retrieved in the Scopus database. As presented in Fig. 1A, the most type of papers on amyloidosis was article ($n = 1822$), followed by review ($n = 446$) and letter ($n = 101$). The total citation count (after removal of self-citations) was 73,896 (63,996) and the *h* index was 119 (111) for all the papers. To further concretize the trends of scientific output, we assessed the annual number and accumulated citations of the papers during 2004–2023 (Fig. 1B). The annual number of the

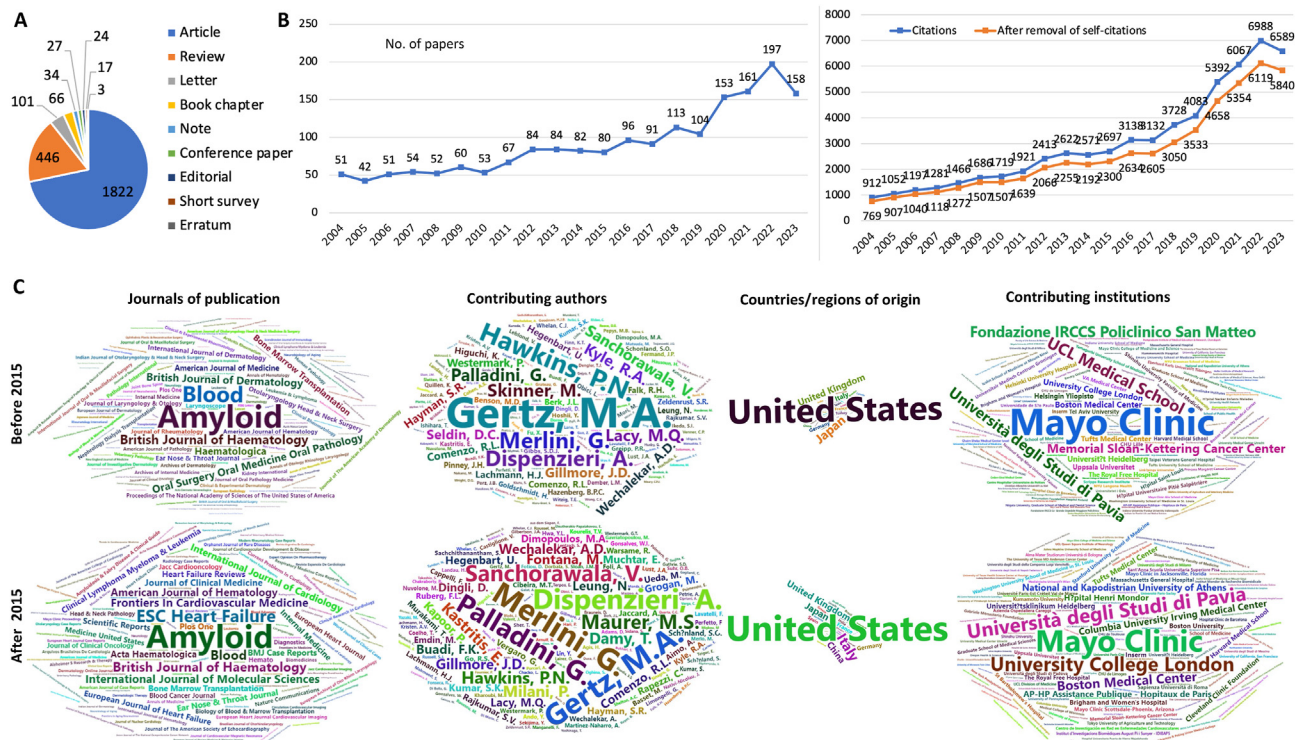


Figure 1 Bibliometric characteristics of the papers on amyloidosis involving the oral cavity. (A) The numbers of different paper types. (B) The annual number and accumulated citations of the papers during 2004–2023. (C) Cloud graphs of journal of publication, contributing authors, countries and institutions of origin regarding amyloidosis publications before 2015 and after 2015. The font size indicates the number of papers; a larger size means more papers in the cloud graphs.

papers on amyloidosis stably raised from 51 to 197 during 2004–2022. The accumulated citations (after removal of self-citations) of the papers steady increased from 912 (769) to 6988 (6119) during 2004–2022. The detailed information on publication year, authors, title, abstract, journal of publication, citation count, institutions, and keywords of the 100 most-cited papers are presented in [supplementary Tables S1](#).

Bibliometric characteristics

Fig. 1C displays cloud graphs of journals of publications, contributing authors, institutions, and countries/regions of origin of the papers on amyloidosis involving the oral cavity, which were divided into before 2015 (1243 papers) and after 2015 (1297 papers), so that the number of papers can be to some extent compared in the analysis. Before 2015, the journal of publication, contributing author, institution and country of origin with largest number of papers was *Amyloid* ($n = 47$), Gertz, M.A. ($n = 62$), Mayo Clinic ($n = 78$) and United States ($n = 417$), respectively. After 2015, the journal of publication, contributing author, institution and country of origin with maximum number was *Amyloid* ($n = 39$), Merlini, G. ($n = 45$), Mayo Clinic ($n = 39$) and United States ($n = 442$), respectively. [Table S2](#) presents the journals, contributing authors, institutions, and countries/regions with largest number of papers (rank, 1–10).

Research characteristics

Based on the frequency of the keywords in all the papers on amyloidosis involving the oral cavity (**Fig. 2A**), the study designs, amyloidosis-related disorders, drugs, and research keywords were identified. For study design, the most common design was case report, followed by controlled study, clinical article, retrospective study, animal experiment, cohort analysis, clinical trial, follow-up studies. The related disorders of oral involvement of amyloidosis were AL, ATTR, AA and A β 2M amyloidosis, heart/cardiac amyloidosis, cardiomyopathy, kidney amyloidosis, multiple myeloma, Alzheimer disease, familial amyloidosis, nephrotic syndrome, carpal tunnel syndrome, dyspnea, macroglossia, fatigue, diarrhea, dysphagia, hypertension, and plasma cell dyscrasia (**Fig. 2B**). For drug research, the most frequent drug was melphalan, followed by dexamethasone, bortezomib, cyclophosphamide, thalidomide, lenalidomide, prednisone, daratumumab, tafamidis, colchicine, pomalidomide, doxorubicin, doxycycline, and vincristine (**Fig. 2C**).

Based on the keywords of papers on amyloidosis published in different years (**Fig. 2D**), the more common keywords can basically reflect research trends. Before 2015, kidney amyloidosis-related diseases, hemodialysis, spleen, laryngeal diseases, dysphagia, mouth, tongue diseases, skin diseases, rheumatoid arthritis, nephrotic syndrome, and peripheral neuropathy were more frequent keywords

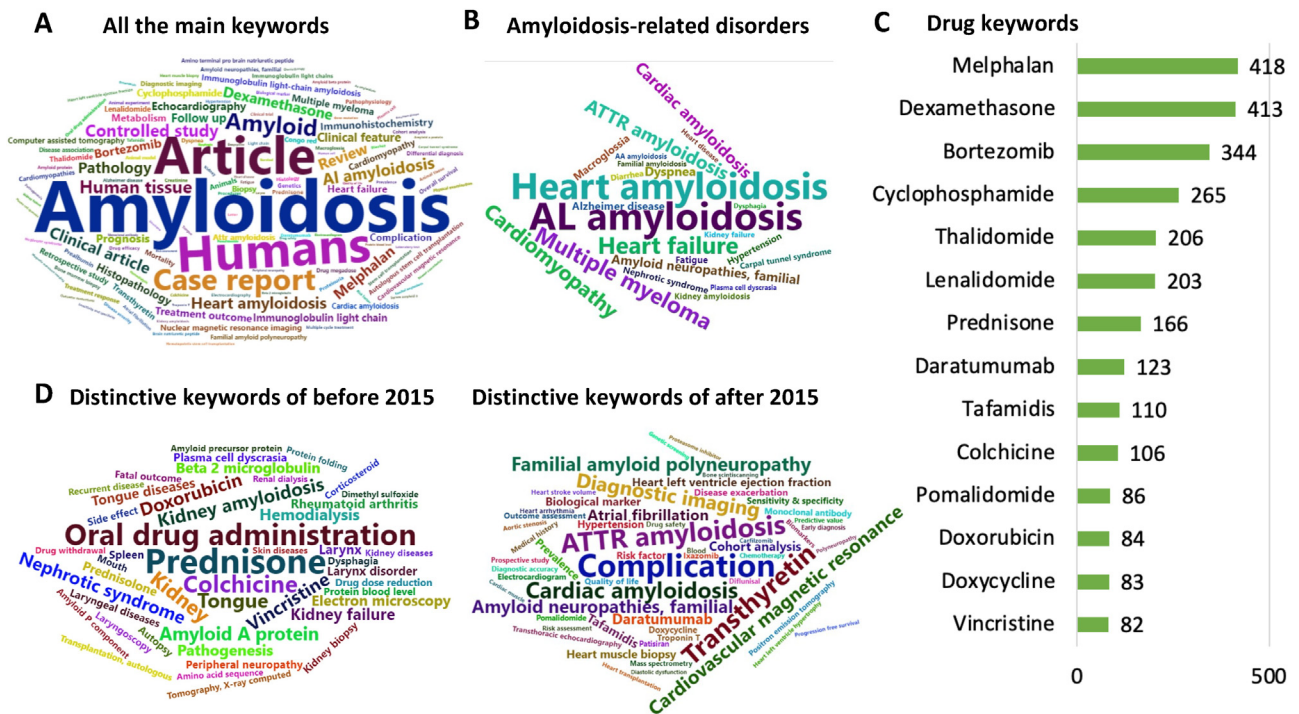


Figure 2 Research characteristics of the papers on amyloidosis involving the oral cavity. (A) The related keywords of differential diagnosis of amyloidosis. Cloud graphs of (A) all the keywords and (B) amyloidosis-related disorders. (C) The frequency of drug keywords. (D) Cloud graphs of distinctive keywords of papers published before 2015 and after 2015. The font size indicates the number of papers; a larger size means more papers in the cloud graphs.

regarding amyloidosis-related disorders. Drug withdrawal, drug dose reduction, prednisone, prednisolone, corticosteroid, colchicine, vincristine, and doxorubicin were more common keywords of drug research. After 2015, ATTR amyloidosis, cardiac amyloidosis-related diseases, familial amyloid neuropathies, polyneuropathy, hypertension were more frequent keywords regarding amyloidosis-related disorders. Drug safety, monoclonal antibody, carfilzomib, daratumumab, diflunisal, doxycycline, ixazomib, pomalidomide, patisiran, tafamidis were more common keywords of drug research. Moreover, clinical studies on transthyretin, prevalence, diagnostic imaging, positron emission tomography, transthoracic echocardiography, bone scintiscanning, complication, early diagnosis, risk factor, risk assessment, sensitivity & specificity, cohort analysis, prospective study, progression free survival, cardiovascular magnetic resonance, medical history, and quality of life were also more frequent keywords after 2015.

Discussion

This scientometric study attempted to analyze the bibliometric characteristics and research trends of all the papers on amyloidosis involving the oral cavity. The increasing annual number and citations of the papers on amyloidosis suggest that this disease has been attracted increasingly attention and investigation. Bibliometric characteristics including journals of publications, contributing authors, institutions and countries of origin, and keywords were identified in sequence (Table S2). These would aid

clinicians and researchers in choosing target journals, finding potential collaborators or partner institutions, as well as promoting mutual understanding and more reciprocal cooperation regarding amyloidosis research. Importantly, keywords frequency analysis can reflect the hotspots and concerned themes of research. As shown in Fig. 2B, there are actually the related disorders of amyloidosis involving the oral cavity in clinical practice. Oral involvement was reported to be associated with various types of amyloidosis including AL, ATTR, A β 2M and AA forms. Moreover, fatigue, dysphagia, dyspnea were the most reported symptoms.^{4–10} The prognosis was worse for systemic cases of cardiac and kidney amyloidosis, especially when associated with multiple myeloma.³

The strength of this scientometric study was to perform the chronological comparison (before 2015 versus after 2015) based on all the included papers. The more common keywords in different years can basically reflect research trends. Before 2015, Kidney amyloidosis and it related diseases and laryngeal diseases were more frequent. While ATTR amyloidosis, cardiac amyloidosis-it related diseases and polyneuropathy were more common after 2015. The trend of drug aspect, e.g. prednisone, colchicine, corticosteroid, doxorubicin, and vincristine before 2015 has changed to monoclonal antibody, daratumumab, tafamidis, proteasome inhibitor, carfilzomib, ixazomib, patisiran, pomalidomide, diflunisal, and doxycycline. Besides, the trend of clinical aspect has changed to complication, quality of life, risk factor, diagnostic imaging, prospective study, and early diagnosis after 2015. Herein, we highlight the awareness of early recognition and timely diagnosis and

improve the access to care for amyloidosis, since oral involvement frequently constitutes the first sign of this disease. Once the diagnosis of oral amyloidosis is identified by histopathologic biopsy, it is mandatory to carry out thorough medical investigations to further determine whether the amyloidosis is systemic or localized and accurately classify the subtype of systemic amyloidosis, which is fundamental to therapy and prognosis assessment.

In summary, this scientometric study on amyloidosis elucidated the current scenario and research trends in the field of this tumor. Finding the scientometrics would elucidate the comprehensive identification and recognition of the important research topics concerned, and help in improving in reciprocal collaboration and communication for investigations on this disease.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

This work was supported by National Construction Project of Clinical Key Specialized Department (No. [2013]544), and Excellent Research Physician Project of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jds.2024.12.010>.

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