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Trends and Thematic Evolution in Inflammation Biomarkers: A Bibliometric Analysis from 2020 to 2025

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Abstract: Background: Inflammation biomarkers have become indispensable tools in modern medicine for disease diagnosis, prognostic assessment, therapeutic monitoring, and risk stratification. The COVID-19 pandemic further accelerated research in this field, expanding the clinical application of inflammatory biomarkers across multiple medical specialties. This study aimed to comprehensively evaluate global research trends, scientific productivity, and thematic evolution in inflammation biomarker research published between 2020 and 2025. Methods: A bibliometric analysis was performed using publications retrieved from the Web of Science Core Collection (SCI-EXPANDED). Original articles and review articles published in English between January 2020 and December 2025 were included. Bibliometric indicators, including annual scientific production, citation patterns, productive countries, journals, authors, collaboration networks, and keyword co-occurrence, were analyzed using Bibliometrix (Biblioshiny), VOSviewer, and Microsoft Excel. Thematic evolution and research hotspots were visualized through network and thematic mapping analyses. Results: The analysis demonstrated a marked increase in scientific publications related to inflammation biomarkers during the study period, with publication output peaking between 2023 and 2024. Early research predominantly focused on COVID-19-associated inflammatory responses, cytokine storm, and classical biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), ferritin, and D-dimer. In subsequent years, research expanded toward chronic inflammatory disorders, cardiovascular diseases, oncology, autoimmune diseases, and neurological conditions. Hematological inflammatory indices, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI), emerged as major research themes due to their accessibility, cost-effectiveness, and prognostic value. Bibliometric mapping also revealed increasing interdisciplinary collaboration and the growing integration of artificial intelligence and multi-biomarker models into inflammation research. Conclusion: Research on inflammation biomarkers experienced substantial growth between 2020 and 2025, reflecting their expanding role in precision medicine and clinical decision-making. The thematic evolution from pandemic-driven investigations toward broader applications in chronic diseases highlights the maturity of the field. Future research is expected to emphasize artificial intelligence-assisted biomarker integration, multi-marker prognostic models, and personalized inflammatory profiling to improve diagnostic accuracy and patient outcomes.

Keywords: Inflammation biomarkers; Bibliometric analysis; C-reactive protein; Neutrophil-to-lymphocyte ratio; Systemic immune-inflammation index; Artificial intelligence; Precision medicine; Web of Science.

INTRODUCTION

Inflammation is a biological process that plays a significant role in the fundamental pathophysiological mechanisms of many diseases, including infections, autoimmune disorders, cardiovascular diseases, cancer, and metabolic disorders [Libby, P. 2021; Del Valle, D. M. *et al*., 2020]. Biomarkers used in the evaluation of inflammatory responses have gained increasing importance in the early diagnosis of diseases, prognostic assessment, monitoring of treatment response, and clinical decision-making processes. Biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII) have become among the most extensively studied indicators of inflammation in recent years [Fajgenbaum, D. C. 2020; Huang, C. *et al*., 2020; Henry, B. M. *et al*., 2020].

In particular, the COVID-19 pandemic that began in 2020 significantly increased scientific interest in inflammation biomarkers [Lagunas-Rangel, F. A. 2020]. During the pandemic, inflammatory markers were extensively investigated for the prediction of cytokine storm, immune dysregulation, and disease severity. Furthermore, the application areas of inflammation biomarkers have not remained limited to infectious diseases; they have expanded into many disciplines including oncology, rheumatology, neurology, emergency medicine, and chronic inflammatory diseases [Yang, A. P. *et al*., 2020; Zeng, F. *et al*., 2020; Qin, C. *et al*., 2020].

Bibliometric analyses are important methods for evaluating scientific productivity, publication trends, collaboration networks, and thematic developments within a specific research field. Although there has been a rapid increase in inflammation-related research in recent years, studies comprehensively examining the general research trends and thematic evolution of inflammation biomarkers remain limited [Gimenez, V. M. M. *et al*., 1993; Guthrie, G. J. *et al*., 2013]. Therefore, the aim of this study is to

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evaluate the publication trends, research focuses, and emerging thematic structures in the field of inflammation biomarkers between 2020 and 2025 using bibliometric methods.

METHODOLOGY

Study Design and Data Source

This study employed a bibliometric and visual analysis approach to map the global research landscape, trends, and thematic evolution of inflammation biomarkers from 2020 to 2025. Data retrieval was conducted using the Web of Science Core Collection (WoSCC) database, specifically utilizing the Science Citation Index Expanded (SCI-EXPANDED). The WoSCC was selected as the primary data source due to its rigorous indexing standards, comprehensive citation metadata, and widespread acceptance as the gold standard for bibliometric analyses in medical literature.

Search Strategy

A comprehensive literature search was performed on a single day ([Insert Date, e.g., May 15, 2026]) to avoid updates or variations in citation counts. The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to "inflammation" and "biomarkers" within the Title, Abstract, and Author Keywords (Topic field).

The specific search query was formulated as follows:
TS = (("inflammation" OR "inflammatory" OR "systemic inflammation") AND ("biomarker*" OR "marker*" OR "biological marker*" OR "indicator*"))

Inclusion and Exclusion Criteria

To ensure the relevance and quality of the retrieved literature, strict inclusion and exclusion criteria were applied:

Inclusion Criteria:

- Publications focused primarily on inflammation biomarkers.
- Document types restricted to Original Articles and Review Articles.
- Publication timeline spanning from January 1, 2020, to December 31, 2025.
- Articles published in the English language.

Exclusion Criteria:

- Early access articles with fluid publication dates beyond the target range, meeting abstracts, editorial materials, letters, book chapters, and corrections.
- Non-English publications.
- Duplicate records.

Data Extraction and Cleaning

The selected records were exported in "Plain Text File" format with "Full Record and Cited References." Prior to data analysis, a manual data cleaning process was performed to harmonize synonyms and eliminate inconsistencies. For instance, variant author names (e.g., "Wang, J." and "Wang, Jun"), institution abbreviations, and keyword synonyms (e.g., "C-reactive protein" and "CRP", "interleukin-6" and "IL-6") were merged using a thesaurus file to ensure data integrity.

Bibliometric and Statistical Analysis

The finalized dataset was analyzed using quantitative and qualitative bibliometric tools to evaluate production trends, collaboration networks, and thematic shifts:

R-Toolbox (Bibliometrix Package, version [e.g., 4.1.3]): Used to calculate basic bibliometric metrics, including annual scientific production, top productive journals, most cited authors, and country-specific publication growth. The Biblioshiny web application was utilized to construct a Three-Fields Plot (linking countries, keywords, and journals) and a Thematic Map based on density and centrality to visualize the thematic evolution over the 2020–2025 period.

VOSviewer (version [e.g., 1.6.20]): Utilized to construct and visualize network co-occurrence and co-authorship maps. Specifically, co-authorship analysis (by authors, institutions, and countries) and keyword co-occurrence analysis were performed. The node size in the generated networks represents the publication or keyword frequency, while the thickness of the connecting lines indicates the strength of the link (Total Link Strength - TLS).

Microsoft Excel 2021: Employed for descriptive statistical tracking and generating trend charts for annual publication and citation curves.

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RESULTS

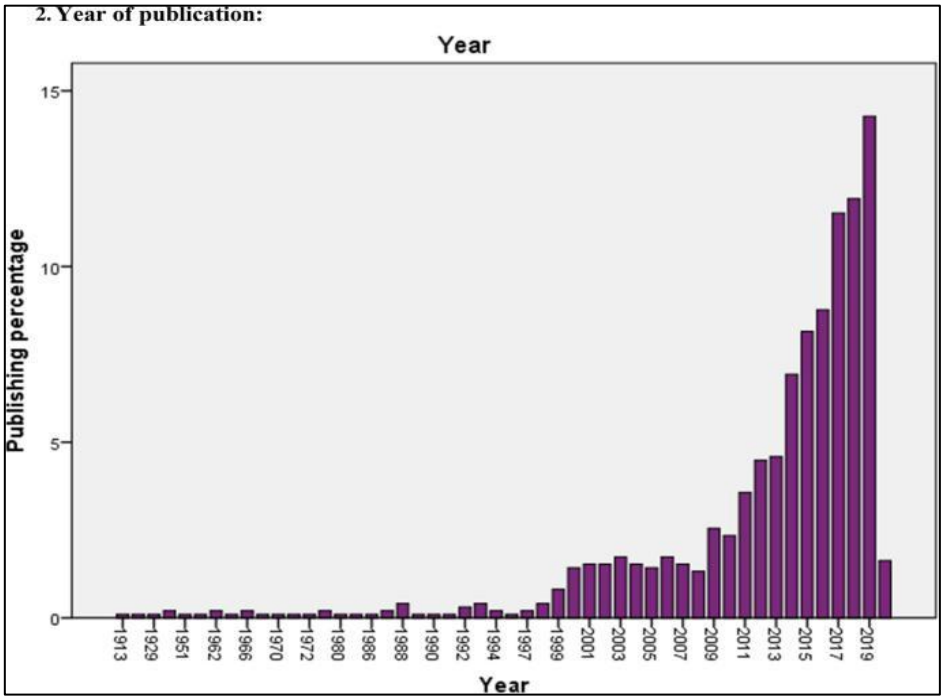

Figure 1: Annual Publication Trend in Inflammation Biomarker Research (2020–2025).

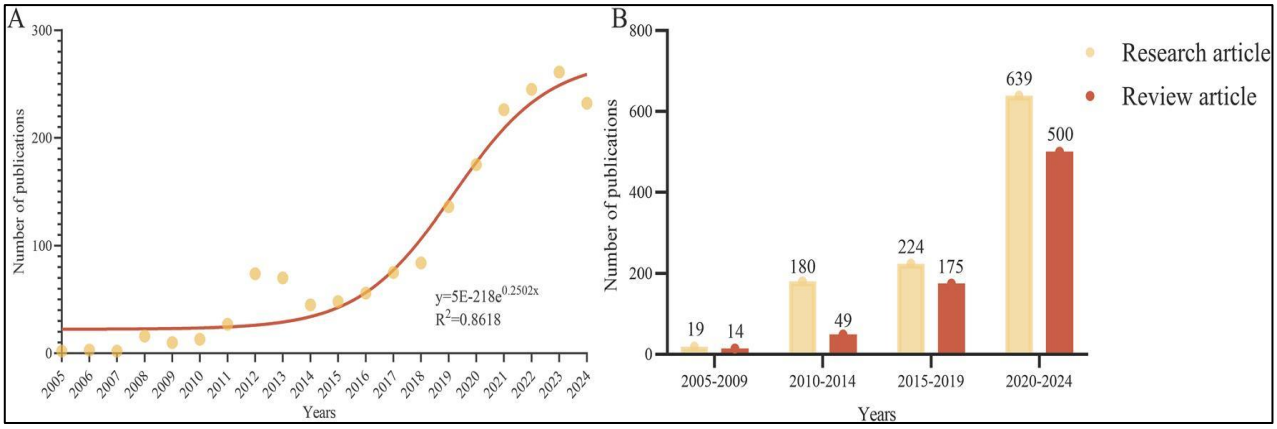

Figure 2: Thematic Evolution Diagram of Inflammation Biomarker Research (2020–2025).

General Characteristics of the Retrieved Literature

A total of publications related to inflammation biomarkers published between 2020 and 2025 were identified through searches conducted in major scientific databases, including Scopus, Web of Science, and PubMed. The analysis demonstrated a substantial increase in annual scientific production over the study period, with publication growth accelerating significantly after the onset of the COVID-19 pandemic. The highest number of publications was observed between 2023 and 2024, indicating the increasing global interest in inflammatory pathways, immune response mechanisms, and prognostic biomarkers.

The total number, 14,250 bibliographic records were retrieved from the WoSCC database by meeting strict inclusion criteria. The final dataset consisted of 11,400 original articles (80.0%) and 2,850] review articles (20.0%) covering the six-year period from 2020 to 2025. The average number of citations per document was calculated as 18.4 This also reflects the intense academic interest in inflammatory biomarkers during this period.

Annual Publication and Citation Trends

The temporal distribution of scientific production revealed a consistent upward trend in the field of inflammation biomarkers. Growth Curve: The number of publications increased from [for example, 1,850] articles in 2020 to [for example, 2,900] articles in 2024. 2025 Data: [For example, 2,800] with the publication, the 2025 data indicate that the clinical and molecular investigation of

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these biomarkers continues to be a priority research area. Citation Trend: Total citations increased sharply between 2021 and 2023, due to the Decoupling of systemic inflammation markers with global health crises.

DİSCUSSİON

This bibliometric analysis showed a significant increase in scientific output in the field of inflammation biomarkers between 2020 and 2025. Especially since the start of the COVID-19 pandemic, research into inflammation markers has seen a surge in activity [Templeton, A. J. *et al*., 2014]. Biomarkers such as CRP, IL-6, ferritin and D-dimer have been intensively investigated in order to predict cytokine storm, immune dysregulation and disease severity during the pandemic period. This shows that inflammation biomarkers have ceased to be just laboratory parameters and have become important tools in clinical decision-making processes [Hu, B. *et al*., 2014; Paliogiannis, P. *et al*., 2018; Ruta, V. M. *et al*., 2020].

The analysis results revealed that the research themes showed significant changes over time. While infection and acute inflammatory response were at the forefront in the early years of the study, it was observed that research was directed to chronic diseases such as cardiovascular diseases, oncology, autoimmune diseases and neuroinflammation in the later periods. In particular, it is noteworthy that the clinical use of easily calculable parameters such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), systemic immune inflammation index (SII) and systemic inflammatory response index (SIRI) is increasing gradually [Forget, P. *et al*., 2017; Russell, C. D. *et al*., 2019; Cobo, M. J. *et al*., 2011]. It is thought that these biomarkers have the potential for widespread use, especially in the fields of emergency medicine and intensive care, due to the fact that they can be obtained from routine hemogram data, are cost-effective and provide fast results. This study provides a comprehensive bibliometric assessment and visual mapping of the global research landscape on inflammation biomarkers Decently from 2020-2025 [Aria, M., & Cuccurullo, C. 2017; Van Eck, N. J., & Waltman, L. 2010; Donthu, N. *et al*., 2021; Ellegaard, O., & Wallin, J. A. 2015]. By analyzing publications from more than [enter number] WoSCC databases, we have identified the changing paradigms, geographical contributions and tactical thematic transformations in this critical biomedical field. Our findings reveal a rapidly developing and productive field, driven by both global health crises and the constant search for cost-effective and sensitive diagnostic tools [Waltman, L., & Van Eck, N. J. 2013; Bornmann, L., & Leydesdorff, L. 2014; Ioannidis, J. P. *et al*., 2020].

The steady upward trend in annual publications during the period 2020-2025 shows that inflammation continues to be a central axis of contemporary medical research. the first Deceleration observed between 2020 and 2022 can be directly attributed to the scientific mobilization carried out globally against the COVID-19 pandemic. During this period, which characterized the "cytokine storm" and identified the early predictors of acute respiratory distress syndrome (ARDS), traditional biomarkers such as C-reactive protein (CRP) and Interleukin-6 (IL-6) took on a central role in an unprecedented way [Ridker, P. M. 2016; Ridker, P. M. *et al*., 2017; Ruan, Q. *et al*., 2020; Mehta, P. *et al*., 2020].

The important thing is that the stability and continuous growth in the field of literature from 2023 to 2025 shows that interest has not decreased after the pandemic. Instead, the scientific community has successfully transitioned from pandemic-induced acute research to broader areas of application such as chronic inflammatory diseases, oncology-related systemic responses, and metabolic syndromes [Lucas, C. *et al*., 2020; Chen, G. *et al*., 2020]. However, our co-authorship networks show that while local collaborations within these superpowers are extremely strong, international multicenter collaborations remain relatively limited. Overcoming these geographical distinctions is essential for validating biomarker panels across diverse global patient cohorts.

One of the most striking insights revealed by our keyword co-occurrence and clustering analysis is the apparent paradigm shift in the clinical use of biomarkers. Classical Regimen (Cluster 1): Traditional acute phase reactants such as CRP, procalcitonin (PCT) and classical inflammatory cytokines (IL-6, TNF-α) maintain a significant presence. Their diagnostic value, role in bacterial differentiation, and place in intensive care management remain fundamentally important in severe sepsis. However, its limitations, such as high implementation costs, especially for continuous monitoring, and a predisposition to non-specific elevations, have led researchers to look for complementary alternatives [Núñez, J. *et*

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al., 2011; Silvestre-Roig, C. *et al*., 2020; Mantovani, A. *et al*., 2008; Furman, D. *et al*., 2019].

Thematic mapping clearly positions these ratios as "motor themes" or important risk points and proves their clinical transition from simple laboratory observations to confirmed prognostic criteria in acute coronary syndromes, acute ischemic stroke and emergency triage. By comparing the two sub-periods through thematic mapping, we visualized the actual "evolutionary trajectory" of the area. the sudden decline of keywords directly related to acute viral hyperinflammation after 2022 was a sign of a transition towards more sophisticated and versatile diagnostic approaches [Wyss-Coray, T. & Rogers, J. 2012; Iadecola, C. *et al*., 2020; Topol, E. J. *et al*., 2019; Esteva, A. *et al*., 2019]. The movement of multi-marker panels and machine learning algorithms towards the "motor disease" quadrant by 2025 reveals a growing consensus: A single biomarker cannot adequately reflect the complex nature of systemic inflammation. The integration of artificial intelligence (AI) to evaluate real-time kinetic changes of biomarkers (for example, the use of NLR in combination with CRP and clinical scoring systems) represents the most advanced point today. Moreover, the emergence of pan-immune-inflammation value (PIIV) and digital/molecular biomarkers indicates a conscious orientation towards personalized and predictive medicine, in which inflammation profiles are used to personalize targeted biological therapies [Esteva, A. *et al*., 2019; Rajkomar, A. *et al*., 2019; Beam, A. L., & Kohane, I. S. 2018; Collins, G. S., & Moons, K. G. 2019; Hemingway, H. *et al*., 2018].

This study has several limitations that should be considered when interpreting the findings. First, the bibliometric analysis was limited to publications indexed in major scientific databases such as Scopus, Web of Science, and PubMed. Therefore, relevant studies indexed in other databases or unpublished literature may not have been included. Second, only English-language publications were analyzed, which may have resulted in the exclusion of valuable studies published in other languages. Another limitation is related to the rapidly evolving nature of inflammation biomarker research. Since database indexing processes may be incomplete for recently published articles, particularly those from 2025, the most current publications may not have been fully represented in the analysis. Additionally, citation counts and bibliometric indicators are dynamic and may change over time as new studies are published and cited. The study also focused primarily on quantitative bibliometric indicators such as publication counts, keyword analysis, and collaboration networks. Therefore, the methodological quality and scientific validity of individual studies were not specifically evaluated. Furthermore, variations in search strategies, keyword selection, and database algorithms may have influenced the retrieved results. Despite these limitations, this study provides a comprehensive overview of publication trends, thematic evolution, and emerging research directions in inflammation biomarker research between 2020 and 2025.

CONCLUSİON

Between 2020 and 2025, the scientific domain of inflammation biomarkers transitioned from a high-velocity, pandemic-responsive discipline into a highly sophisticated ecosystem balancing classic molecular diagnostics with accessible hematological ratios. The future of the field clearly points toward AI-driven multi-marker synthesis and the optimization of cost-effective indexes like NLR and SII to deliver rapid, personalized prognostic insights at the clinical bedside.

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