Global Research Trends on C-Reactive Protein and Periodontitis: A Comprehensive Bibliometric Analysis

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ABSTRACT

Introduction: Periodontitis is a chronic inflammatory disease which leads to the progressive destruction of periodontal tissues and is linked to elevated CRP levels in researches. This bibliometric analysis focuses on research landscape indexed in PubMed from 2004 to 2024.

Methods: Articles were extracted from PubMed, and bibliometric data, including titles, authors, institutions, and keywords, were analysed using R programming and R Studio. The search strategy included terms related to periodontitis and CRP.

Results: A total of 231 documents were identified, reflecting significant contributions from the University of Pisa and the University of Catania. Key journals included the Journal of Clinical Periodontology and the Journal of Periodontology. Prominent authors were D'Aiuto F, Orlandi M, and Offenbacher S.

Conclusion: The study highlights the research on CRP and periodontitis, with notable contributions from leading researchers and institutions. It underscores the importance of CRP as a systemic inflammatory marker and its association with periodontitis.

Keywords: C-reactive protein; CRP; Periodontitis; Inflammation

1. INTRODUCTION

Periodontitis is a chronic inflammatory disease, primarily driven by dysbiosis in the dental biofilm, activating hyperimmune response of host. This results in progressive destruction of the supporting structures of the teeth [1]. Harmful bacteria and their byproducts not only damage the periodontium locally but also provoke systemic inflammation evident by increased level of various Interleukins (IL-1, IL-6, IL-17) [2-5].

One key marker of systemic inflammation in relation to periodontitis is CRP [6]. Literature has extensively highlighted elevated C-reactive protein (CRP) levels in various systemic diseases, but its association with chronic infections, such as periodontitis, is still an area of ongoing investigation [7-9].

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This bibliometric study aims to provide a comprehensive analysis of the research landscape surrounding CRP and periodontitis, identifying trends, key publications, and influential researchers in this field. The study will also highlight gaps in current research and propose directions for future studies for better understanding of the link between CRP levels and periodontitis.

2. MATERIAL AND METHODS

This bibliometric analysis employed the R programming language and R Studio software [10] to explore the research landscape concerning C-reactive protein (CRP) and periodontitis. The study focused on articles indexed in the PubMed Core Collection from the year 2004 to 2024.

Search Strategy: The search strategy utilized PubMed as the primary database [11], encompassing literature up to April 2024. The algorithm applied for PubMed searches was as follows:

((periodontitis OR periodontal health OR (periodontal diseases [MeSH])) AND (C-reactive protein OR (C-reactive protein [MeSH]) OR CRP OR Acute Phase Protein OR high sensitivity C-reactive protein OR hs-CRP).

Data extraction and analysis: The bibliometric analysis included extracting information such as title, author, institution, country, publication year, keywords, and citations. These details were imported into Microsoft Excel 2010 [12] (Redmond, Washington, USA). Citexs AI (Wuhan, China) was used for identifying related diseases. Visualization of countries, institutions, authors, journals, diseases, and keywords was carried out using R programming and R Studio software [13]. In the visualization, the size of nodes and the thickness of lines connecting nodes in R Studio indicated the volume of publications and the strength of connections.
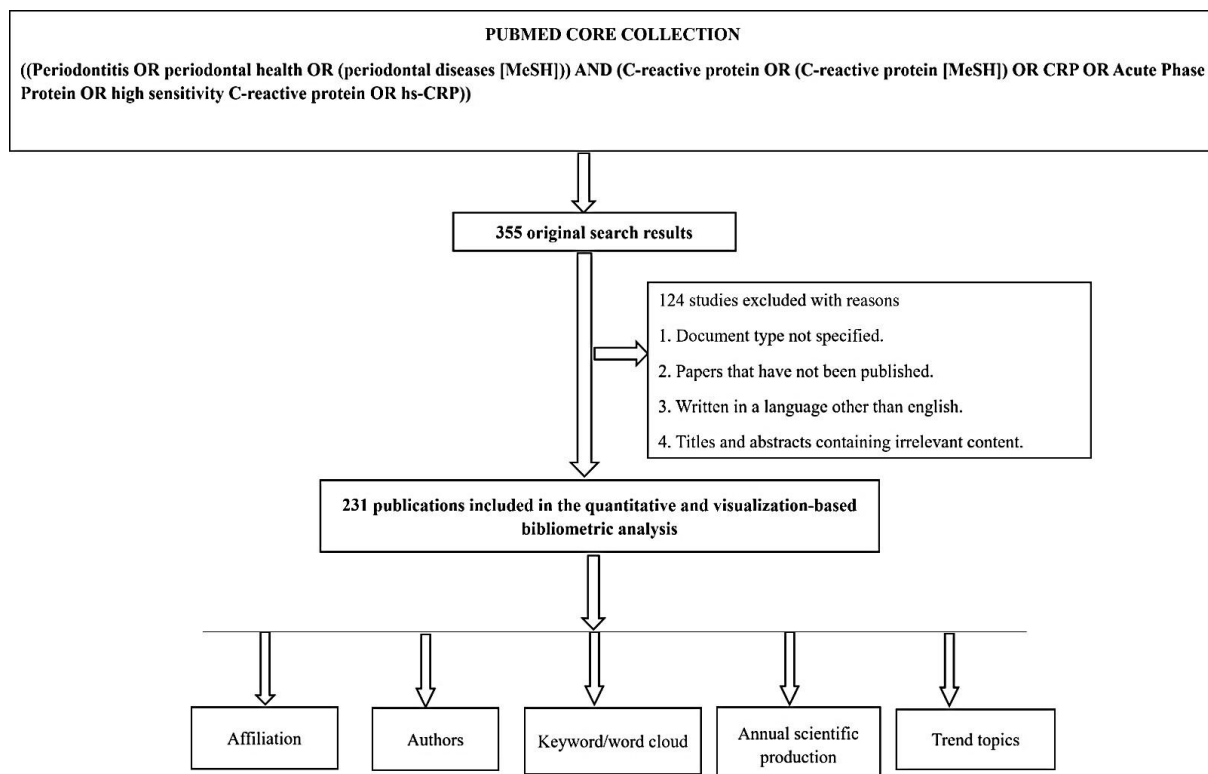

Figure 1: **Study Design for Bibliometric Analysis**

Data collection: Data extraction included information such as publication year, authors, affiliations, journals, citation counts, and keywords from retrieved articles.

3. DATA ANALYSIS

Publication Trends: Identification of publication trends over time to understand the evolution of research interest.

Descriptive analysis: Examine trends in publications over time, encompassing the distribution across different years and types of documents.

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Author analysis: Identify highly productive authors and collaboration networks within the field. Analyze author output and patterns of co-authorship.

Journal analysis: Assess the impact and influence of journals that publish research in sports dentistry. Evaluate journal metrics such as impact factor and citation count to gauge their significance.

Keyword analysis: Identify common keywords and themes across the literature. Analyze the frequency of keywords, networks of co-occurrence, and clusters of related themes.

Statistical Analysis: Descriptive statistics, network analysis, and visualization techniques were employed to interpret and present findings.

Visualization and Interpretation

- Employ bibliometric visualization methods such as co-authorship networks, keyword co-occurrence maps, and citation networks to illustrate connections and patterns within the data.

- Analysis of findings: Evaluate the outcomes of the bibliometric study in alignment with the specified research goals. Identify prominent trends, influential authors, emerging topics, and areas where research is lacking.

Ethical considerations: The study adhered to ethical guidelines for bibliometric analysis, ensuring proper attribution of intellectual contributions and adherence to copyright policies.

Limitations: Potential limitations include the scope and coverage of the PubMed database, language bias, and variations in indexing practices across journals.

4. RESULT

Table 1 and Figure 2- Shows That the bibliometric data spanning from 2004 to 2024, a total of 231 documents were identified across 126 sources. The field has shown an annual growth rate of 2.98%, reflecting steady expansion over the years. This research involved 1,116 authors, with 12 individuals contributing as single authors, highlighting a collaborative nature in the majority of publications. International co-authorship was observed in 15.15% of the documents, indicating a global perspective in research collaboration. On average, each document had 5.77 co-authors, underscoring extensive teamwork in scholarly outputs. A total of 944 unique author keywords were analysed, revealing diverse thematic focuses within the literature. The average age of documents was 9.16 years, suggesting ongoing relevance and longevity of research contributions. Notably, the average citation count per document was zero, indicating a need for increased visibility and impact of published works through enhanced citation practices and dissemination strategies. These findings provide insights into key trends, collaborative dynamics among authors, thematic emphases, and areas for potential growth and impact in the field of study.

Table -1 Main information

Description	Results
MAIN INFORMATION ABOUT DATA	
Timespan	2004:2024
Sources (Journals, Books, etc)	126
Documents	231
Annual Growth Rate %	2.98
Document Average Age	9.16
Average citations per doc	0
References	0
DOCUMENT CONTENTS	
Keywords Plus (ID)	944
Author's Keywords (DE)	944
AUTHORS	

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Authors	1116
Authors of single-authored docs	12
AUTHORS COLLABORATION	
Single-authored docs	14
Co-Authors per Doc	5.77
International co-authorships %	15.15
DOCUMENT TYPES	
case reports; journal article; research support, non-u.s. gov't; review	1
clinical trial	2
Clinical trial; comparative study; journal article; randomized controlled trial; research support, non-u.s. gov't	1
clinical trial; comparative study; journal article; research support, n.i.h., extramural	1
clinical trial; journal article	7
clinical trial; journal article; multicenter study	1
clinical trial; journal article; research support, n.i.h., extramural	2
clinical trial; journal article; research support, non- u.s. gov't	7
comparative study; controlled clinical trial; journal article	1
comparative study; journal article; meta-analysis; research support, non-u.s. gov't; review; systematic review	1
comparative study; journal article; multicenter study; randomized controlled trial; research support, non u.s. gov't	1
comparative study; journal article; randomized controlled trial	6
comparative study; journal article; randomized controlled trial; research support, n.i.h., extramural	1
comparative study; journal article; randomized controlled trial; research support, n.i.h., extramural; research support, non-u.s. gov't	1
comparative study; journal article; randomized controlled trial; research support, non-u.s. gov't	13
controlled clinical trial; journal article	2
controlled clinical trial; journal article; research support, non-u.s. gov't	3
Editorial; review	1
English abstract; journal article; randomized controlled trial	1
English abstract; journal article; review	3
journal article	3
journal article; meta-analysis	5
journal article; meta-analysis; research support, n.i.h., extramural; research support, non-u.s. gov't; review; systematic review	1
journal article; meta-analysis; research support, n.i.h., extramural; review; systematic review	1

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journal article; meta-analysis; research support, non-u.s.gov't; review; systematic review	3
journal article; meta-analysis; research support, non-u.s. gov't; systematic review	4
journal article; meta-analysis; review	1
journal article; meta-analysis; review; systematic review	2
journal article; meta-analysis; systematic review	6
journal article; multicenter study; randomized controlled trial; research support, n.i.h., extramural	4
journal article; multicenter study; randomized controlled trial; research support, non-u.s. gov't	2

Main Information

Plot | Table

Timespan 2004:2024	**Sources** 126	**Documents** 231	**Annual Growth Rate** 2.98 %
Authors 1116	**Authors of single-authored** 12	**International Co-Authorship** 15.15 %	**Co-Authors per Doc** 5.77
Author's Keywords (DE) 944	**References** 0	**Document Average Age** 9.16	**Average citations per doc** 0

Table 1 and Figure 2: Overview of Documents Retrieved from Major Databases

Figure 3 a: shows graphic illustration of "annual scientific production", a dynamic trend in scholarly article publication from 2004 to 2024. Over this period, there are noticeable fluctuations in yearly output, but the overall trajectory shows an upward trend in scientific production. The years from 2004 to 2005 marked a strong start with increased publication rates, followed by a decline in 2006-2007. Subsequent years, particularly from 2007 to 2010, witnessed a resurgence in publications, albeit with periodic declines in 2009-2010 and 2011-2012. From 2012 to 2015, there was a steady increase in output, interrupted by a downturn in 2015-2016. The trend resumed with growth from 2016 to 2018, although 2017-2018 saw a temporary dip. The years 2018-2020 showed renewed growth, though punctuated by a decline in 2019-2020. The period from 2020 to 2024 demonstrated overall growth, despite fluctuations, with a notable decline in 2021-2022 followed by an upward trend in 2022-2023 and a decline again in 2023-2024. This analysis underscores the evolving nature of scientific production in the field, reflecting varying periods of growth and consolidation across the years examined.
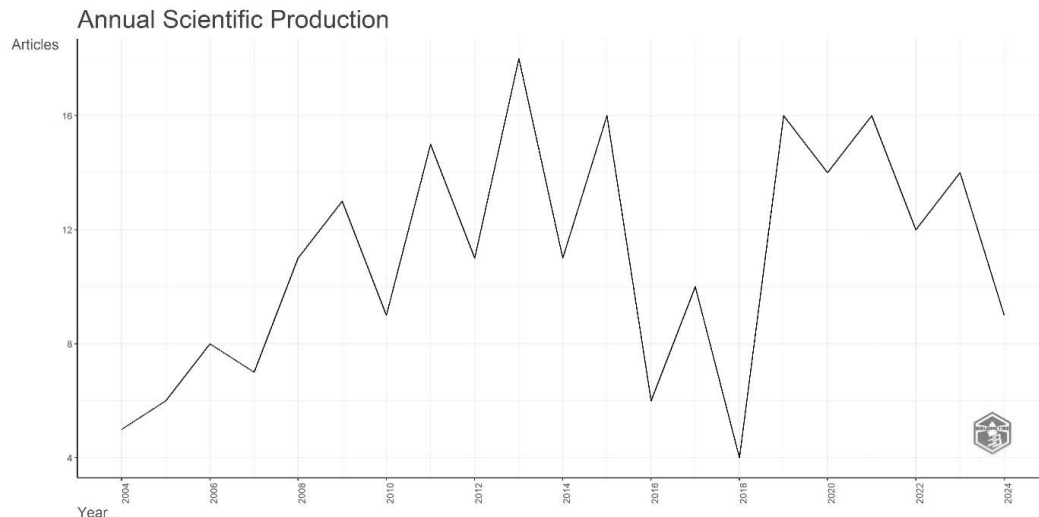
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Figure 3 a: Annual Scientific Production

Figure 3b: shows graphic representation of "most relevant affiliations" which provides a comprehensive view of the institutions with the highest representation among researchers in a specific field or topic. At the forefront is the University of Pisa, which leads with 29 affiliations, indicating a substantial concentration of researchers from this institution engaged in the subject matter. Following closely are the University of Catania and Southern Medical University, each with 19 and 18 affiliations respectively, underscoring their significant contributions to the field. The University Hospital of Pisa, alongside UCL Eastman Dental Institute, Federal University of Rio Grande do Sul, Federal University of Rio de Janeiro, Xi'an Jiaotong University, and the University of Hong Kong, also feature prominently with notable affiliations ranging from 16 to 12. This data highlights the collaborative efforts and institutional strengths in advancing research within the identified domain, reflecting a global participation and diversity among leading research institutions.
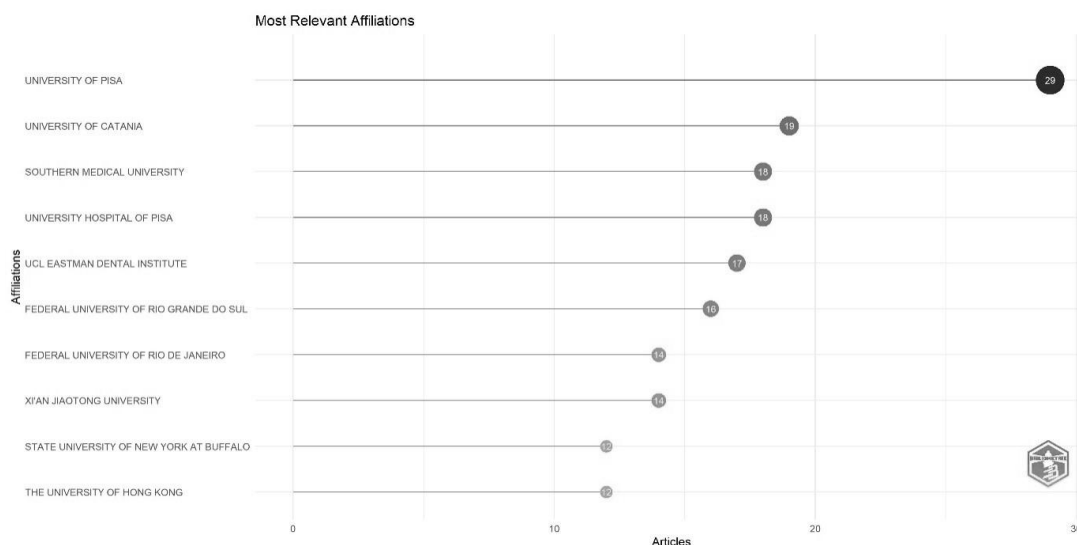

Figure 3b: Most Relevant Affiliations

Figure 3 c: shows graphic representation of the distribution of publication counts across prominent journals in the field of C reactive protein AND periodontitis provides a snapshot of key outlets for research dissemination. Leading the list are the Journal of Clinical Periodontology and the Journal of Periodontology, each with 26 publications, highlighting their central role as primary platforms for scholarly output in the discipline. BMC Oral Health follows with 6 publications, indicating its emerging importance in the field. Additionally, the Journal of Periodontal Research, Clinical Oral Investigations, Journal of Dental Research, Medicina Oral Patologia Oral Y Cirugia Bucal, Oral Diseases, PLOS ONE, and Trials each contribute 4 publications, demonstrating their significant contributions to advancing research and knowledge in periodontal and oral health sciences. This distribution underscores the diverse range of journals that researchers choose to publish in, reflecting varying scopes and audiences within the field while emphasizing the impact and influence of leading journals like the Journal of Clinical Periodontology and the Journal of Periodontology.
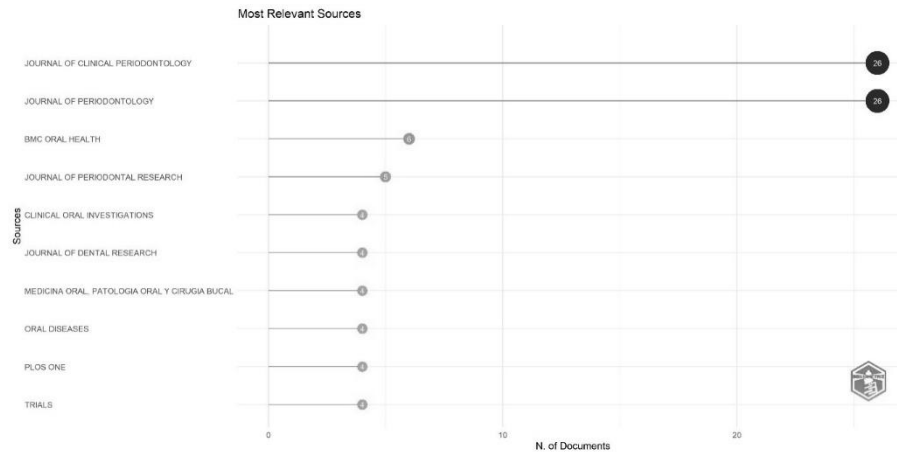
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Figure 3 c: Most Relevant Source

Figure 3 d: shows the list of authors and their respective publication counts that reveals a notable landscape of contributions in the field OF C-REACTIVE PROTEIN AND PERIODONTITIS. Leading this group is D'Aiuto F, with an impressive 13 publications, underscoring their pivotal role in advancing research. Following closely is Orlandi M, with eight publications, marking them as a significant contributor as well. Offenbacher S and Suvan J, each with seven publications, are prominent figures whose work likely intersects with clinical practices and innovative treatments. Graziani F, with six publications, maintains a robust presence, possibly focusing on specialized subtopics within the field. Additionally, Beck JD, Gennai S, Isola G, and Van Dyke TE, each with five publications, consistently contribute valuable insights, reflecting a steady research output. Golub LM, with four publications, although fewer, offers significant contributions that may be crucial for niche areas within the discipline. This distribution of publications underscores the importance of collaborative efforts and highlights emerging research trends. Analysing the specific themes and impact of these authors' work can provide deeper insights into current priorities, influential research areas, and potential future directions in the field.
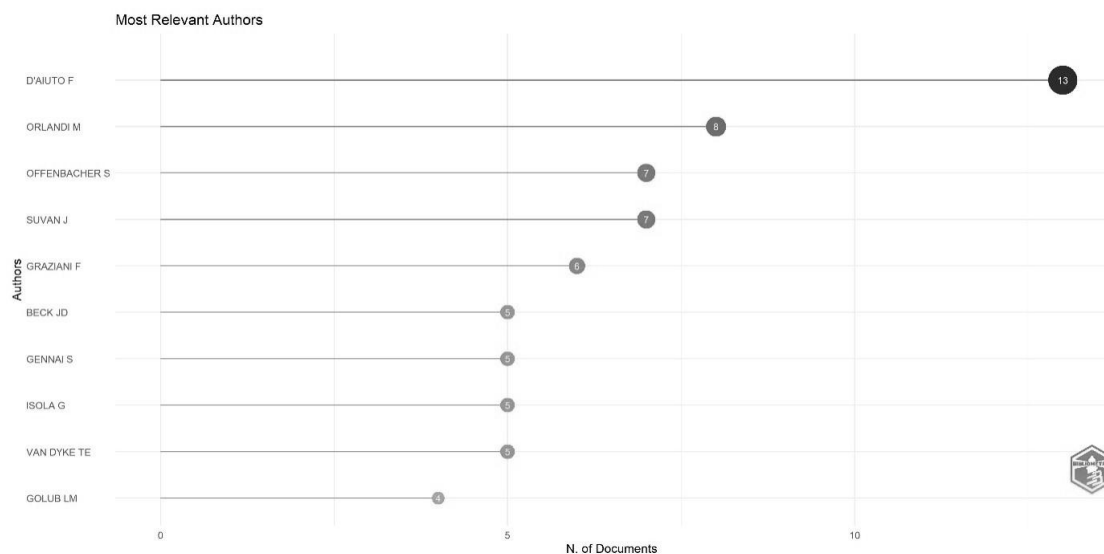

Figure 3d: Most relevant authors

Figure 4: shows a graphical visualization of a bibliometric analysis. This means it uses statistical methods to analyze academic publications. The specific field this analysis covers is ''C REACTIVE PROTEIN AND PERIODONTITIS.'' The x-axis of the graph shows the year, ranging from 2005 to 2023. The y-axis shows the term frequency, which represents the number of times a particular term appeared in the academic literature over this period. The lines on the graph represent different search terms. For example, the line labelled "interleukin-6" shows how often the term "interleukin-6" appeared in ''C REACTIVE PROTEIN AND PERIODONTITIS' 'research papers between 2005 and 2023. Overall, the graph shows a steady increase in research interest in ''C REACTIVE PROTEIN AND PERIODONTITIS'' over the time period covered by the analysis. This is because most of the lines trend upwards. Some of the terms that appear to have seen the most growth in research interest include: C-reactive protein, Biomarkers, Prognosis, Inflammation.
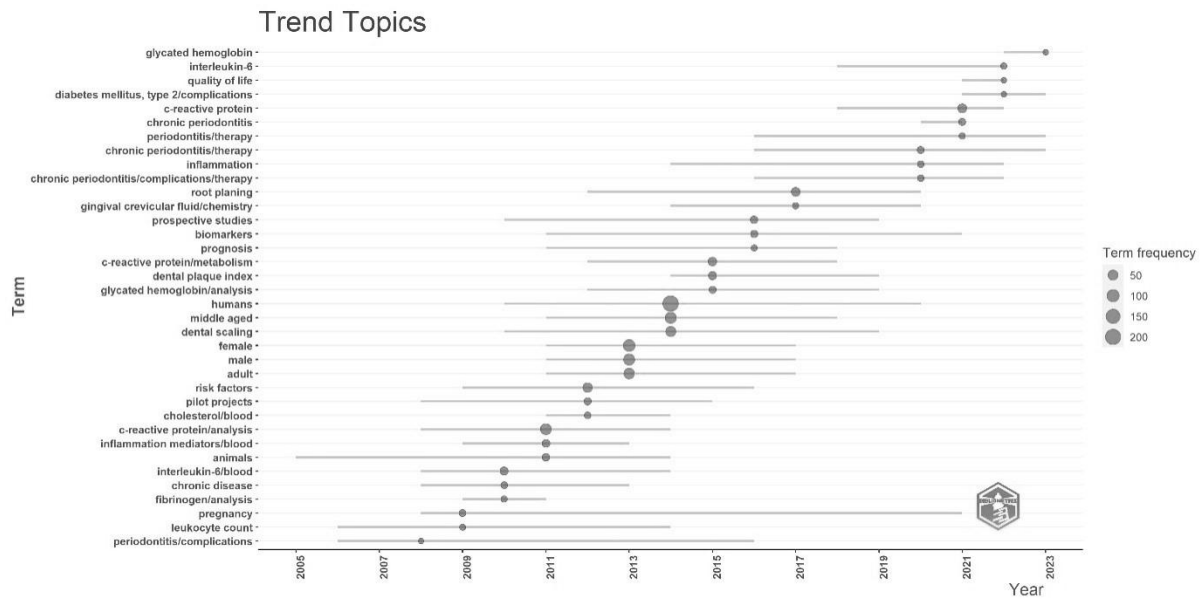
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Figure 4 – Most trend topics

These terms may represent areas of concentrated research effort within the field of C REACTIVE PROTEIN AND PERIODONTITIS.

- The most frequent term is "humans," which likely refers to the fact that most C "REACTIVE PROTEIN AND PERIODONTITIS "research focuses on humans.

- Other terms that appear frequently include "adult," "male," and "female," which suggests that a significant portion of "REACTIVE PROTEIN AND PERIODONTITIS' 'research is focused on adult populations.

It is important to note that this graph only shows the frequency with which terms appear in research papers. It does not necessarily reflect the quality or importance of the research. Research on periodontal disease is booming! A recent analysis of academic publications show a dramatic rise in research interest over the past two decades. This is particularly evident for terms like C-reactive protein, biomarkers, prognosis, and inflammation, suggesting these areas are hotbeds for current periodontal disease research. Interestingly, the analysis also shows a focus on adult human populations in periodontal disease research. While the most frequent term is simply "humans," terms like "adult," "male," and "female" appear often, highlighting this trend. It's important to remember that this analysis only shows how often terms appear, not the quality of the research itself. But overall, it paints a clear picture of a rapidly growing field with exciting new areas of investigation.

Figure 5: represents Tree map, which is a visual representation used to display hierarchical data using nested rectangles. Each branch of the hierarchy is represented by a rectangle, which is then tiled with smaller rectangles representing sub-branches. The size of each rectangle is proportional to a specific dimension, such as term frequency in this context.

1. Hierarchical Display: Tree maps show data in a structured manner, making it easy to understand the relationships and proportions among different elements.

2. Proportional Areas: The size of each rectangle corresponds to the frequency or magnitude of the represented term, providing a visual sense of scale.

3. Color Coding: Often, colors are used to distinguish between different categories or to highlight certain values, enhancing the map's interpretability.
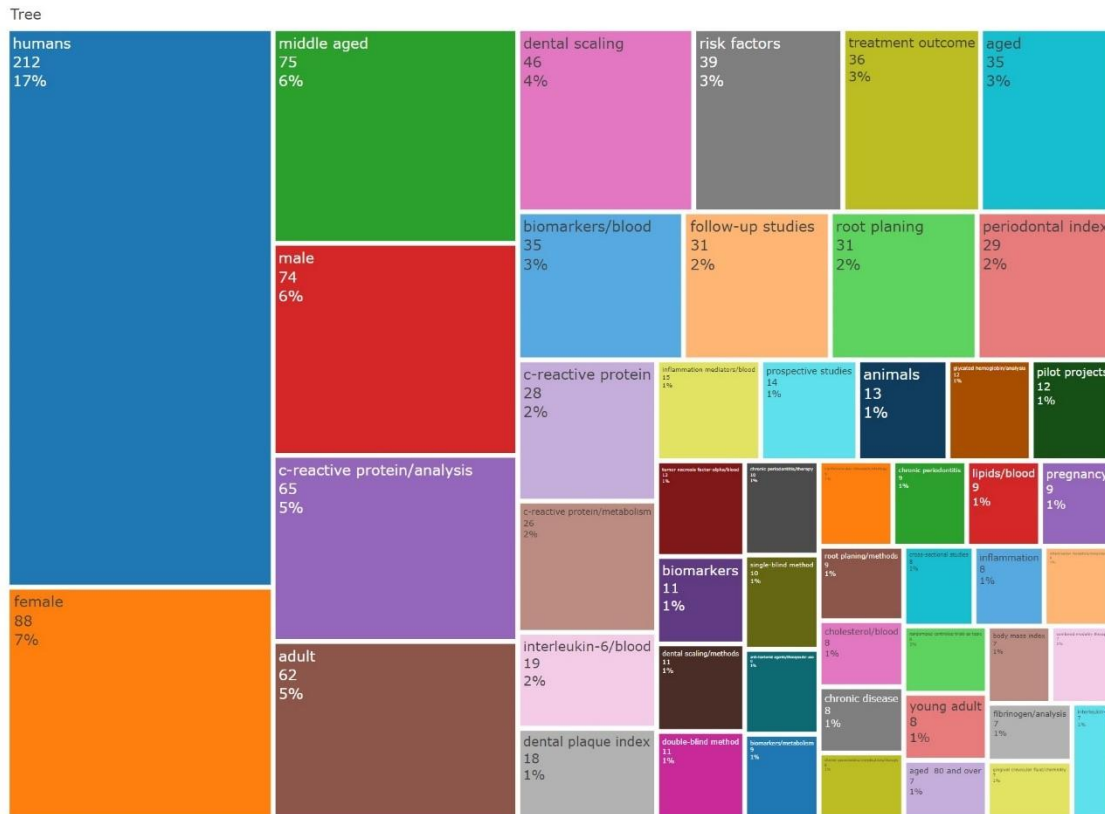
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Figure 5: Tree map

In this research, a tree map would effectively illustrate the relative importance of terms related to CRP and periodontitis. Larger rectangles for terms like "humans" and "female" indicate higher frequencies, while smaller ones for "IL-6" suggest its specific but crucial relevance in the inflammatory process associated with periodontitis. The term frequency data provided suggests that the research focuses on the relationship between C-reactive protein (CRP) and periodontitis, examining various factors and outcomes. Among the listed terms, "humans" appears most frequently, indicating the study population. "Female," "middle aged," "male," and "adult" highlight the demographic details, while "dental scaling" and "treatment outcome" point towards interventions and results related to periodontitis.

Most relevant term: interleukin-6 (IL-6)

Interleukin-6 (IL-6) is the most relevant term in the context of CRP and periodontitis. IL-6 is a cytokine involved in inflammation and the immune response, playing a crucial role in the body's reaction to infection and injury. It stimulates the production of CRP in the liver, thus linking it directly to CRP levels in the bloodstream. In periodontitis, an inflammatory disease affecting the tissues surrounding the teeth, IL-6 is significantly elevated, contributing to the disease's pathology. The increased IL-6 levels can lead to higher CRP levels, which is a marker for systemic inflammation. Therefore, monitoring IL-6 and CRP can provide insights into the severity and progression of periodontitis and the effectiveness of treatments like dental scaling.

The analysis of term frequency and the use of a tree map provide valuable insights into the study's focus areas, highlighting key demographic factors and the central role of inflammatory markers like IL-6 in understanding the relationship between CRP and periodontitis.

5. DISCUSSION

C-reactive protein (CRP) is an acute-phase protein produced by the liver in response to infection, inflammation, or tissue injury. Its levels rise as part of the body's natural immune response to chronic inflammatory conditions, including periodontitis [14]. When measured using high-sensitivity CRP (hs-CRP), even modestly elevated levels of CRP are associated with a heightened risk of various systemic diseases, including cardiovascular disease (CVD), diabetes, and rheumatoid arthritis [15].

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Studies indicate that periodontitis elevates CRP levels, suggesting that periodontal disease contributes to the overall inflammatory burden in affected individuals, for instance, Slade *et al.* (2003) reported a significant association between periodontitis and increased CRP levels, highlighting the potential role of periodontal disease as a risk factor for systemic conditions like CVD [16,17]. Furthermore, D'Aiuto *et al.* (2004) demonstrated that treatment of periodontitis leads to a reduction in CRP levels, indicating that periodontal therapy may help mitigate systemic inflammation [18,19].

This bibliometric analysis provides a comprehensive overview of the research trends and impacts associated with C-reactive protein (CRP) and periodontitis over the past two decades. The steady increase in publications, with an annual growth rate of 2.98%, underscores a growing interest in understanding the systemic implications of periodontitis and its association with CRP levels.

Research Trends: The data reveal a significant focus on CRP as a marker for systemic inflammation in periodontitis. The substantial representation of terms like "biomarkers" and "inflammation" highlights a concerted effort to elucidate the role of CRP in the inflammatory pathways associated with periodontal disease. The increasing frequency of these terms reflects a broadening scope of research, with a particular emphasis on the systemic impact of periodontitis beyond traditional dental considerations.

Institutional Contributions: Leading institutions, such as the University of Pisa and the University of Catania, have been pivotal in advancing this field. Their substantial number of affiliations and publications indicates a strong research output and influence. The prominence of journals like the Journal of Clinical Periodontology and the Journal of Periodontology further reinforces the central role of these platforms in disseminating key findings related to CRP and periodontitis.

Author Contributions: The analysis of authors reveals that influential researchers like D'Aiuto F, Orlandi M, and Offenbacher S have made notable contributions. Their extensive publication records and focus on CRP and periodontitis highlight their significant impact on advancing knowledge in this area. The collaborative nature of research, with numerous co-authors and international partnerships, emphasizes the interdisciplinary approach necessary to address the complexities of systemic inflammation and periodontal health.

Future Directions: Despite the progress, the study identifies gaps in the literature that warrant further exploration. Areas such as the precise mechanisms by which CRP influences periodontal disease progression and the potential for targeted therapies require additional research. Furthermore, enhancing the visibility and impact of published works through improved dissemination strategies could address the observed low citation counts and contribute to more robust clinical applications.

In summary, this analysis provides valuable insights into the evolving field of CRP and periodontitis research. By identifying key trends, influential contributors, and areas for future study, it lays a foundation for continued exploration and improvement in periodontal health management.

6. CONCLUSION

This bibliometric analysis of research on C-reactive protein (CRP) and periodontitis from 2004 to 2024 highlights the growing interest and evolving trends in understanding the systemic implications of periodontal disease. The steady annual growth rate of 2.98% in publications reflects an increasing focus on the role of CRP as a biomarker for systemic inflammation associated with periodontitis.

The study reveals significant contributions from leading institutions such as the University of Pisa and the University of Catania, with key journals like the Journal of Clinical Periodontology and the Journal of Periodontology serving as primary platforms for disseminating research. Prominent authors, including D'Aiuto F, Orlandi M, and Offenbacher S, have played pivotal roles in advancing knowledge in this field, indicating a collaborative and interdisciplinary approach to research.

Despite notable progress, the analysis identifies gaps that need further exploration, particularly in understanding the mechanisms through which CRP affects periodontal disease progression and exploring targeted therapeutic approaches. The low citation counts observed suggest a need for enhanced visibility and dissemination of research findings to maximize impact.

Overall, this study underscores the importance of CRP in the context of periodontitis and highlights the need for continued research to address existing gaps. By providing a comprehensive overview of research trends, key contributors, and emerging topics, this analysis lays the groundwork for future studies aimed at improving clinical practices and patient outcomes in periodontal health.

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