



A visual and bibliometric analysis of Parkinson's disease biomarker research

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Abstract

Aim: Biomarker research in Parkinson's lacks a systematic bibliometric review, despite a growing body of bibliometric studies. This study aimed to analyze publications on biomarkers that may play an important role in the diagnosis and treatment of Parkinson's disease.

Materials and Methods: In the study, bibliometric methods were used to analyze the related research in depth. Data were obtained from the Web of Science Core Collection database. Specific keywords consisting of MeSH terms were used as search criteria. The search was conducted in English and the type of publication was selected as article. Microsoft Excel, VOS viewer and the visualization and analytical capabilities of the Biblioshiny R package were used in the analysis, providing a versatile approach to achieve the study objectives.

Results: A total of 461 articles on Parkinson's disease biomarkers published between 2002 and 2023 in 170 journals met the criteria and were analyzed. Regarding publications and citations, the year 2022 stood out. Each document had an average of 6.28 co-authors. The main contributing countries were the United States, China and Italy, with a global co-authorship rate of 30.8%. Notable institutions included the University of Washington, Ruhr University Bochum and the Paracelsus Elena Clinic. "Journal of Neurochemistry," was the journal with the most publications. Through their total link strength, prominent terms such as "Parkinson's disease", "biomarker" and "alpha-synuclein" showed significant occurrences and thematic relevance.

Conclusion: The present study presents the inaugural bibliometric evaluation of biomarkers in Parkinson's disease. The gradual increase of papers since 2012 indicates persistent scholarly interest and foretells continued significance over the following ten years. Future research will be aided by the study's depiction of biomarker patterns, which provides insightful information. The term "Alpha-synuclein" stood out, highlighting its relevance in our research.



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Introduction

Parkinson's disease is a complicated, neurodegenerative condition characterized by dopamine impairments, motor and nonmotor deficits, and other symptoms [1]. James Parkinson first identified the disease's primary symptoms in 1817, when a description first appeared [2]. Parkinson's disease is primarily identified by its two hallmark motor symptoms, tremor and bradykinesia, caused by the degeneration of dopaminergic neurons in the basal ganglia's substantia nigra pars compacta. This condition, however, goes beyond the scope of motor dysfunction because it can

show various non-motor symptoms, including dysautonomia, cognitive impairment, and affective abnormalities, including despair and anxiety [3].

Parkinson's disease is the second most common neurodegenerative disorder [4]. Its prevalence has been shown to have significantly increased during the past three decades. The estimated incidence in developed countries is 0.3%. Rarely does it affect patients who are younger than 40 [4, 5]. Epidemiological studies have only rarely revealed associations. Rural living and pesticide exposure, notably paraquat, are currently risk factors [6]. The pathophysiology of the disease is influenced by environmental and genetic variables, and in 5% to 10% of instances, a single gene is the culprit [3]. The aging of the population is having a growing negative impact on productivity and medical

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resources. Two independent risk factors are male sex and getting older [3]. According to current hypotheses, oxidative stress, inflammation, aberrant protein handling, and mitochondrial dysfunction contribute to neuronal death in Parkinson's disease [7]. Depigmentation of the substantia nigra and locus coeruleus, along with neuronal death in the substantia nigra's pars compacta, is the pathological characteristic of Parkinson's disease. The processes of apoptosis and autophagy are both implicated [8].

Clinical findings adequately supported by testing are used to make the diagnosis. Except for genetic testing under certain conditions, which is only beneficial to a small percentage of patients, no procedure can be used to diagnose Parkinson's disease in vivo with 100% certainty [4]. Modern scientific research is heavily focused on investigating disease biomarkers, which can speed up and accurately diagnose patients, as well as the development of improved therapy modalities that address current medical needs [9].

However, it is essential to note that there is relatively little bibliometric research on Parkinson's disease. This lack of thorough bibliometric studies on Parkinson's disease draws attention to a topic that needs further scholarly focus. The landscape of Parkinson's disease biomarker research has not yet been systematically examined in published bibliometric studies on Parkinson's disease [10–12], which is noteworthy. This research gap reveals a region where thorough bibliometric analysis is inadequate, despite the increased emphasis on disease biomarkers for precise diagnosis and therapy. Such studies might offer insightful information about patterns, research directions, and gaps in Parkinson's disease biomarker research. Researchers could help progress the field's understanding by filling this knowledge gap, eventually improving Parkinson's disease diagnostic and treatment methods.

Materials and Methods

The current study used a bibliometric technique and a literature review to get a complete overview of the pertinent research. The investigation covered bibliometric factors like keywords, research collaboration patterns, and co-citation network analysis of references. It was necessary to extract data from the Web of Science Core Collection database to complete this undertaking, which allowed for a full examination of the progress of research on biomarkers related to Parkinson's disease. The following search techniques were used: topic = (Parkinson's disease OR Parkinson) and (Biomarker) and Biochemistry Molecular Biology or Chemistry (Research Areas). MeSH (<https://www.ncbi.nlm.nih.gov/mesh>) was used to find references to the terms such as "biomarkers" and "Parkinson's disease OR Parkinson." The language type was set to English, and the document type was an article. The deadline for the publication of articles was August 8, 2023. Following the data retrieval, documents were ultimately used to create a visual analysis. The sample size was not selected. Online articles searched in the Web of Science database were accessed according to the following inclusion criteria.

Inclusion criteria: The inclusion criteria were developed to make sure that the chosen studies matched the research's

goals and area of concentration. The following studies met the requirements and were analyzed.

- Type of Publication: published works in journals with peer review.
- Language: For inclusion, only studies written in English were taken into account.
- Date of Publication: Studies that were released up through the 8th of August, 2023, were included.
- Topic Pertinence: studies concentrating on Parkinson's disease biomarkers.
- Methodology: There were studies using a range of research techniques, such as experimental, observational, and clinical trials.

Statistical analysis

Bibliometric analysis and Web of Science-based literature analysis were used in the methodology of this study. Publications concerning biomarkers in Parkinson's disease were downloaded as complete records and cited as references in plain text files from the Web of Science database. The obtained data files were subsequently subjected to additional analysis to draw out pertinent data for the study. Microsoft Excel 2019, VOSviewer [13], and the Bibliometrix, Biblioshiny R package (version 4.1.2) were used to create graphs and bibliometric analyses (Biblioshiny is free and open-source software for bibliometric evaluation) [14]. VOSviewer was used because of its superior network and cluster research visualization features. Additionally, Biblioshiny was used for literature analysis because it is the best in its field. The study planned to be completed with a multifaceted approach using both methods together according to the objectives.

The VOSviewer application was also utilized to visualize the data. The visualization map's primary components were nodes and lines, and each node represented an examined element, such as an author, institution, publication, etc. Understanding the co-occurrence and co-citation interactions between nodes was made more accessible by links. The quantity and thickness of links between nodes revealed the strength of the association between nodes, and in general, the more nodes there were, the greater the frequency. A statistic called centrality gauges a node's significance inside a network. The centrality of the node increased as the shortest routes traveled through it. When a node's centrality was more than 0.1, it was frequently seen as a field's turning point [13].

Results

There was a total of 461 articles about biomarkers in Parkinson's disease that were indexed in the Web of Science database based on the study's selection criteria.

Main information

The first publications were issued in 2002. While some years had no publications, the year 2022 had the most (a total of 84). Surprisingly, 2022 also showed up as having

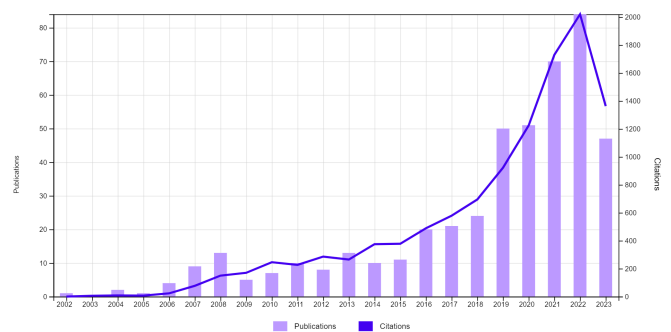
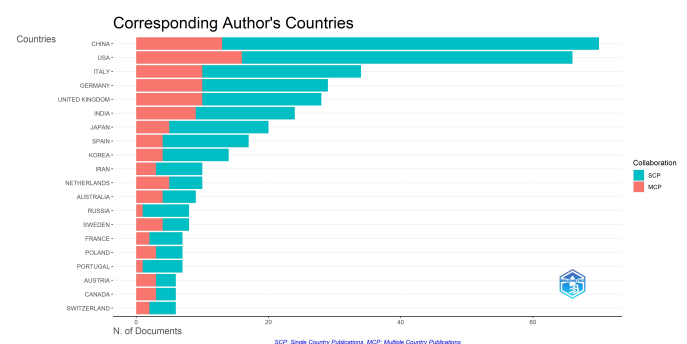
Table 1. Bibliographic coupling between top publishing countries.

Name of organization	Number of documents	Number of citations	Total link strength
The University of Washington	11	426	620
The Ruhr University Bochum	8	96	310
Paracelsus Elena Klinik	7	160	769
The University of Dundee	7	430	83
Karolinska Institute	6	170	826
Lund University	6	246	549
Sun Yat-sen University	6	17	151
Chang Gung University	5	60	384
Fudan University	5	73	80
Juntendo University	5	38	158
Newcastle University	5	205	325
Russian Academy University	5	40	32
University of Barcelona	5	57	96
University of Gothenburg	5	74	643
University of Malaysia	5	67	40
Perlis University of Oxford	5	65	193
Vrije University Amsterdam	5	61	403

• This data shows the analysis according to the corresponding author's organisation.

Table 2. Keyword analysis with VOSviewer.

Keyword	Number of occurrences	Total link strength
Parkinson's disease	170	256
Biomarker	93	178
Alpha-synuclein	61	126
Alzheimer's disease	40	93
Biomarkers	39	83
Neurodegeneration	29	73
Cerebrospinal fluid	21	56
Mass spectrometry	21	53
Neurodegenerative diseases	20	45
Proteomics	20	35
S disease	14	34
Brain	13	31
Dopamine	13	17
Neurodegenerative disease	13	27
Oxidative stress	13	23
Parkinson disease	12	28
Metabolomics	11	18
Amyotrophic lateral sclerosis	10	35
Dementia	10	21
Neuroinflammation	10	20

**Figure 1.** Web of Science database graph of the distribution of the number of citations and publications over the years.**Figure 2.** Corresponding Author's countries.

the most citations, with 2020 serving as the year of reference and receiving the most citations (Figure 1). The articles on Parkinson's disease biomarkers covered 2002-2023 and were taken from 170 journals. With an average document age of 4.58 years and roughly 24.34 average citations per document, these documents displayed a yearly growth rate of 20.81%. A total of 302 articles, or 72.59% of the total documents, were published from 2019 to 2023 among the articles that were published during that period. The total number of references was 28,465, and the document's contents included 1,734 keywords plus 1,324

author's keywords. The research showed collaborative efforts with 2,565 authors, 19 single-authored publications, and an average of 6.28 co-authors per document.

Countries/Regions

A total of 67 countries and regions were involved in the publication of biomarkers in Parkinson's disease, but only

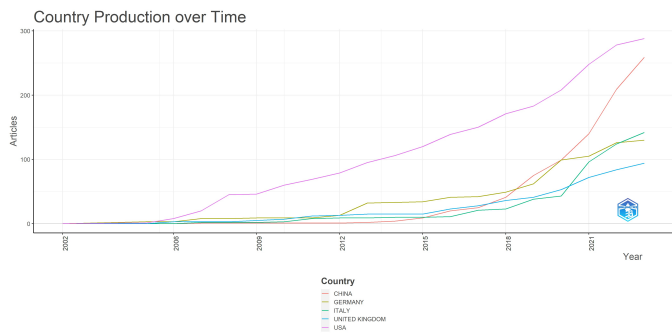


Figure 3. Top publishing countries' production over time.

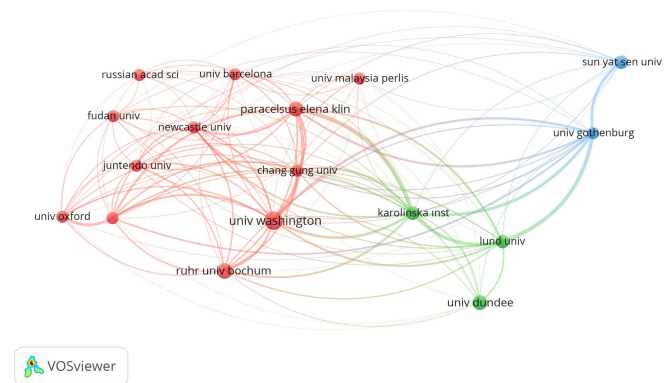


Figure 4. Bibliographic coupling between the countries.

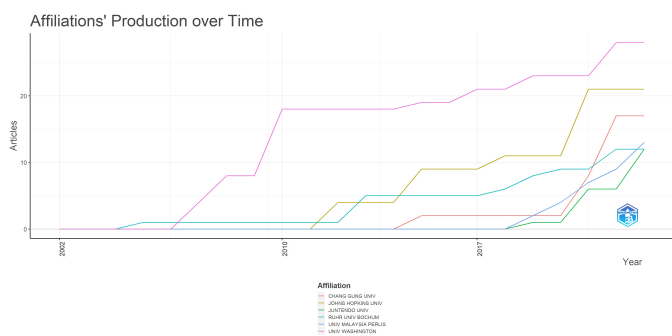


Figure 5. Affiliations' production over time.

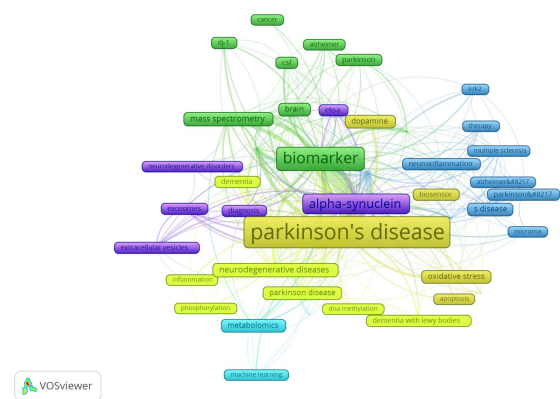


Figure 6. Keyword analysis.

15 countries and regions published more than 15 articles. The following countries had the most significant rates of publications in the area of biomarkers for Parkinson's disease: The United States of America (USA) (n = 90, 19.523%), People's Republic of China (n = 72, 15.618%), Italy (n = 42, 9.111%), England (n = 41, 8.894%), Germany (n = 41, 8.894%), India (n = 30, 6.508%), Japan (n = 28, 6.074%), Spain (n = 23, 4.989%), Sweden (n = 22, 4.772%), South Korea (n = 20, 4.338%), and the Netherlands (n = 19). The results of the biblioshiny tool indicated that some of the articles were produced in collaboration with different countries and regions and had a global co-authorship rate of 30.8%. Although the USA topped the list of countries with the highest number of publications, analysis by the Biblioshiny program showed that responsible authors from the People's Republic of China were the most Figure 2: blue bars represent publications from a single country publication (SCP), and red bars represent publications from multiple country publications (MCP). Figure 3 demonstrates that the US has had a high number of publications since 2006, whereas China has seen one since 2017. In 2020, a publishing trend also emerged in Italy.

Organizations

Analysis by VOS viewer revealed that 17 of the 461 documents published by 900 distinct organizations had at least five documents that met the standard. Several organizations stood out clearly regarding top citation publications and overall link strength. With 11 documents and 426 citations, the University of Washington significantly increased the link strength to 620. Another notable institution was Ruhr University Bochum, which had 8 documents, 96 citations, and a total link strength of 310. With 7 documents and 160 citations, Paracelsus Elena Klinik stood out as an essential contributor, displaying a significant total link strength of 769. Similarly, the 7 documents and 430 citations from the University of Dundee added up to a total link strength of 83. With 6 documents and 170 citations establishing its presence, Karolinska Institute had an impressive total link strength of 826. With 6 documents and 246 citations, Lund University followed suit, giving a total link strength of 549. In the end, Sun Yat-sen University came in third with a total link strength of 151, 6 documents, and 17 citations (Table 1). According to the data, the Karolinska Institute collaborated with other organizations more frequently. Figure 4 shows the bibliographic coupling between the organizations. Figure 5 shows the number of articles published by affiliated institutions over time. These data referred to the institutions of all authors and were produced with Biblioshiny. Accordingly, the number of publications from the University of Washington, which had the highest number, had increased over the years and continued to increase.

Citations

These publications were collectively cited 11,241 times, and when self-citations were excluded, the cumulative number dropped to 10,890 citations. On average, each publication was cited approximately 24.38 times. The dataset showed each article's total number of citations

across various publication years. Articles had a remarkably high mean of 283.25 citations in 2006, demonstrating significant scholarly attention. In contrast, the average number of citations was significantly lower in 2004 and 2002, at 88 and 69, respectively. The following two years, 2013 and 2014, kept their mean citation counts reasonably similar at 59.31 and 57.6, indicating a consistent level of intellectual activity. It was noteworthy that 2009 showed an average of 56.4 citations. These numbers shed light on the various academic influences and acclaim levels during this time.

Top journals with the most publications

The majority of publications were published in a few journals, primarily the "International Journal of Molecular Sciences" (54 articles), "Journal of Neurochemistry" (25 articles), "ACS Chemical Neuroscience" (17 articles), "Journal of Molecular Neuroscience" (13 articles), "Neurochemistry International" (10 articles), and "Sensors" (10 articles).

Keywords and trending topics

Out of the total pool of 1,329 author-assigned keywords, VOSviewer analysis revealed that a discernible subset of 48 keywords showed a frequency of occurrence amounting to at least five instances (as shown in Figure 6). Table 2 gives a thorough overview of the results of this keyword analysis. The tabulated data provides valuable insights into the dominant themes in the dataset by listing the dominant keywords—those that have appeared more than ten times—along with their cumulative link strengths.

The most frequently used keywords from the studied dataset were listed below, and each occurrence's number was indicated by the letter "n." Alpha-synuclein (n = 61), Parkinson's disease (n = 170), biomarker (n = 93), and Alzheimer's disease (n = 40) were the main terms with the highest frequency rates. Additionally, cerebrospinal fluid (n = 21), mass spectrometry (n = 21), neurodegeneration (n = 29), biomarkers (n = 39), and cerebrospinal fluid (n = 21) all hold important positions. Proteomics (n = 20), S disease (n = 14), neurodegenerative disease (n = 13), brain (n = 13), and dopamine (n = 13) were additional significant terms.

Discussion

The thorough examination of the field's research into Parkinson's disease biomarkers included 461 indexed articles taken from the Web of Science database. The study's time frame, from 2002 to 2023, revealed exciting trends in publishing. A peak year for article publications and citations, 2022, emerged, indicating greater attention and relevance. With a 20.81% average annual growth rate, the research landscape showed brisk growth. Notably, a sizable percentage of documents (72.59%) were published between 2019 and 2023, indicating a recent uptick in scholarly activity. The 2,565 authors worked together to produce an average of 6.28 co-authors per document, demonstrating the collaborative nature of this field of research.

Bibliometric tools are crucial for assessing the contribution of research papers to science. Bibliometric analysis that

uses a quantitative methodology presents, assesses, visualizes, links, and records research output on a particular topic. This approach makes it easier to map and visualize the scientific literature in a particular field in depth. Several bibliometric tools are available for data analysis [15–20]. The data analysis of the Web of Science database in this study was made possible using the VOSviewer and Biblioshiny tools, enhancing the thorough grasp and insights gained from the re-search environment.

Parkinson's biomarker research is an international endeavor, as evidenced by the participation of 67 countries and regions. Notably, the People's Republic of China, Italy, England, and Germany were significant contributors, each uniquely impacting the research landscape. Although the USA had the highest number of publications, the Biblioshiny analysis showed that authors from China significantly contributed, demonstrating a complex web of collaboration. The USA has maintained a consistent presence since 2006; China's surge started in 2017, and Italy showed a noticeable increase in 2020.

Geographical trends showed varying patterns of publication intensity.

Using VOSviewer, the landscape of research collaboration was examined, highlighting the prominence of organizations in terms of citation impact and link strength. Universities with significant influence included the University of Washington, Paracelsus Elena Klinik, and Ruhr University Bochum. Collaboration dynamics were explicit, with the Karolinska Institute exhibiting a propensity for more frequent collaboration. The study also examined citation patterns and discovered 11,241 citations, representing a significant scholarly activity. Notably, the average number of citations per publication was roughly 24.38, demonstrating the research's influence on academia.

Keywords in the literature express important concepts and subject topics. According to keyword co-occurrence analysis, it is feasible to understand the development and dispersion of several research hotspots in a given field [20, 21–23]. The study also looked at keyword trends and found that terms like alpha-synuclein, Parkinson's disease, biomarker, and Alzheimer's disease were frequently searched. Following VOSviewer analysis of the 1,329 author-assigned keywords, a subset of 48 keywords that appeared at least five times were identified, providing insights into recurrent themes. This thorough overview helps to clarify the rapidly changing field of Parkinson's disease biomarker research and its important implications for diagnostic and therapeutic approaches.

Lewy body inclusions, which are primarily made of alpha-synuclein, serve as another distinguishing feature of Parkinson's disease in addition to the selective neuronal loss in the substantia nigra pars compacta. Genetically and neuropathologically, this presynaptic protein is linked to Parkinson's disease [24, 25]. Our research revealed that aside from terms directly connected to the phrase "Parkinson's disease," the keyword "Alpha-synuclein" was the one that was used the most, and this demonstrates the importance of this keyword within the framework of our study. Other significant terms that are frequently used in the dataset were Alzheimer's disease (n = 40), Neurodegeneration (n = 29), mass spectrometry (n = 21), cerebrospinal

fluid (n = 21), biomarkers (n = 39), proteomics (n = 20), S disease (n = 14), neurodegenerative disease (n = 13), brain (n = 13), and dopamine (n = 13). Gaining a thorough understanding of the journals in our study with the highest publication frequency can provide researchers with invaluable advice on choosing the best publishing venues. As shown by the compilation of the study's preeminent journals for publication, notable journals, including "International Journal of Molecular Sciences", "Journal of Neurochemistry", and "ACS Chemical Neuroscience" significantly contributed to the substantial corpus of published articles.

Limitations

Although this is the first bibliometric analysis of biomarkers in Parkinson's disease, some drawbacks must be considered. Three primary limitations belong to this study. First, only the Web of Science core collection was chosen for the data analysis; additional databases, including PubMed, Dimensions, and Scopus, were left out. This study primarily focused on journals and gave less attention to other platforms for disseminating scientific knowledge (including books, working papers, and reports). As a result, some crucial studies, particularly recent ones, may need to be noticed. Second, the study's sample selection was influenced by several subjective factors. For instance, there can be some language bias because we only looked at papers in English. Future comparisons of articles written in other languages or nations may be possible. However, subjectivity might have impacted our search tactics, which is hard to eliminate in bibliometric studies. Third, our study concentrated on a bibliometric analysis designed to examine the organization of published information in Parkinson's disease biomarkers and biochemistry. The study's subject matter was not covered in full. This necessitates future literature reviews that are more organized.

Conclusion

The first bibliometric evaluation of biomarkers in Parkinson's disease is presented in this publication. Notably, since 2012, the number of articles has consistently increased, demonstrating continued scholarly interest. This field will continue to be prominent for the next ten years because of the substantial academic interest it continues to generate. The study's depiction of biomarker patterns and characteristics in Parkinson's disease provides insightful information that may be used as a practical bibliometric analysis to direct and motivate future research projects for experts in the area.

Conflict of interest

No conflict of interest was declared by the authors.

Ethical approval

The present study complied with the Helsinki Declaration, revised in 2013. Ethics committee approval was not required as no human or animal research existed.

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