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Bibliometric analysis of the scientific evolution of Parkinson's disease and its diagnosis through biochemical biomarkers

Alexander David Demera Chica[1]; Jhon Bryan Mina Ortiz[2]; Ronald Andreé Vitonera Rogel[3]; William Antonio Lino Villacreses[4]; Nereida Valero Cedeño[5]

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Abstract

Parkinson's disease (PD) is a leading cause of neurological disability worldwide, characterized by its chronic progression and lack of a cure. In this context, this study aimed to analyze the scientific evolution of PD and its diagnosis using biochemical biomarkers through a retrospective, descriptive bibliometric analysis with a quantitative approach, based on the 2020 PRISMA guidelines. This analysis evaluated 9,983 initial records in PubMed, of which 49 were included after screening. The results showed a sustained increase in publications, rising from 874 in 2015 to 1,390 in 2025, with China (n=9,643) and the United States (n=7,726) being the most represented. The network of co-occurrences reflected the integration of clinical, diagnostic, and therapeutic approaches, while the thematic map showed a shift towards more specialized lines of research. Furthermore, the clinical heterogeneity of PD was confirmed, and biomarkers with high sensitivity were identified, such as LRRK2 (Leucine-Rich Repeat Kinase 2) (95.4%) and plasma NfL (Neurofilament Light Chains in Plasma) (91.5%), as well as high specificity for beta-amyloid (91.1%) and ApoA1 (Apolipoprotein A-1) (91%). Cerebrospinal fluid biomarkers showed greater diagnostic accuracy. In conclusion, PD research has evolved toward an integrative approach that requires standardization and scientific collaboration.

Keywords: Bibliometrics; Parkinson's disease; clinical heterogeneity; cerebrospinal fluid; plasma NfL.

Análisis bibliométrico de la evolución científica de enfermedad de Parkinson y su diagnóstico mediante Biomarcadores Bioquímicos

Resumen

La enfermedad de Parkinson (EP) es una de las principales causas de discapacidad neurológica a nivel mundial, caracterizada por su progresión crónica y la ausencia de cura. En este contexto, el estudio tuvo como objetivo analizar la evolución científica de la EP y su diagnóstico mediante biomarcadores bioquímicos a través de un análisis bibliométrico retrospectivo de carácter descriptivo con enfoque cuantitativo, basado en la guía PRISMA 2020, que evaluó 9.983 registros iniciales en PubMed, de los cuales 49 fueron incluidos tras el cribado. Los resultados evidenciaron un crecimiento sostenido de publicaciones, pasando de 874 en 2015 a 1.390 en 2025, con predominio de China (n=9.643) y Estados Unidos (n=7.726). La red de coocurrencias reflejó la integración de enfoques clínicos, diagnósticos y terapéuticos, mientras que el mapa temático mostró una evolución hacia líneas más especializadas. Además, se confirmó la heterogeneidad clínica de EP y se identificaron biomarcadores con alta sensibilidad como LRRK2 (Quinasa 2 con Repeticiones Ricas en Leucina) (95.4%) y NfL plasmático (Cadenas Ligeras de Neurofilamentos en plasma) (91.5%), así como alta especificidad en beta-amiloide (91.1%) y ApoA1 (Apolipoproteína A-1) (91%). Los biomarcadores en líquido cefalorraquídeo evidenciaron mayor precisión diagnóstica. En conclusión, la investigación sobre EP ha evolucionado hacia un enfoque integrador que exige estandarización y colaboración científica.

Palabras clave: Bibliometría; Enfermedad de Parkinson; heterogeneidad clínica; líquido cefalorraquídeo; NfL plasmático.

Análise bibliométrica da evolução científica da doença de Parkinson e seu diagnóstico utilizando biomarcadores bioquímicos

Resumo

A doença de Parkinson (DP) é uma das principais causas de incapacidade neurológica em todo o mundo, caracterizada por sua progressão crônica e ausência de cura. Nesse contexto, este estudo teve como objetivo analisar a evolução científica da DP e seu diagnóstico utilizando biomarcadores bioquímicos por meio de uma análise bibliométrica retrospectiva e descritiva com abordagem quantitativa, baseada nas diretrizes PRISMA de 2020. Esta análise avaliou 9.983 registros iniciais no PubMed, dos quais 49 foram incluídos após a triagem. Os resultados mostraram um aumento sustentado nas publicações, passando de 874 em 2015 para 1.390 em 2025, com a China (n=9.643) e os Estados Unidos (n=7.726) sendo os países mais representados. A rede de coocorrências refletiu a integração de abordagens clínicas, diagnósticas e terapêuticas, enquanto o mapa temático mostrou uma mudança em direção a linhas de pesquisa mais especializadas. Além disso, confirmou-se a heterogeneidade clínica da DP e identificaram-se biomarcadores com alta sensibilidade, como LRRK2 (Leucine-Rich Repeat Kinase 2) (95,4%) e NfL plasmático (Neurofilament Light Chains in Plasma) (91,5%), bem como alta especificidade para beta-amiloide (91,1%) e ApoA1 (Apolipoproteína A-1) (91%). Os biomarcadores do líquido cefalorraquidiano demonstraram maior acurácia diagnóstica. Em conclusão, a pesquisa sobre DP evoluiu para uma abordagem integrativa que requer padronização e colaboração científica.

Palavras-chave: Bibliometria; Doença de Parkinson; heterogeneidade clínica; líquido cefalorraquidiano; NfL plasmático.

[1] Universidad Estatal del Sur de Manabí, Ecuador – Coordinator of the SICLAC Research Group. Member of the CEIC Research Group, Faculty of Medicine, Universidad del Zulia, Venezuela. Email: demera-alexander6230@unesum.edu.ec. ORCID: https://orcid.org/0009-0002-9204-3165

[2] Professor at Universidad Estatal del Sur de Manabí, Clinical Laboratory Program, Faculty of Health Sciences. Master's in Biotechnology. Master's in Biological Analysis and Laboratory Diagnosis. Jipijapa, Ecuador. Email: jhon.mina@unesum.edu.ec. ORCID: https://orcid.org/0000-0002-3455-2503

[3] Universidad Autónoma de Madrid, España. Universidad Técnica de Machala, Ecuador. Email: rvitonera1@utmachala.edu.ec. ORCID: https://orcid.org/0000-0002-5272-5551

[4] Professor at Universidad Estatal del Sur de Manabí, Clinical Laboratory Program, Faculty of Health Sciences. Master's in Clinical Laboratory Sciences. Master's in Clinical Laboratory with specialization in Microbiology. Master's in Biological Analysis and Laboratory Diagnosis. Master's in Quality Management. Email: william.lino@unesum.edu.ec. ORCID: https://orcid.org/0000-0001-5613-9958

[5] Professor at Universidad del Zulia, Faculty of Medicine, Clinical Research Institute "Dr. Américo Negrete". Doctor in Immunology. Maracaibo, Venezuela. Email: valero.nereida@gmail.com. ORCID: https://orcid.org/0000-0003-3496-8848

INTRODUCCIÓN

Parkinson's disease (PD) represents one of the leading causes of neurological disability worldwide, characterized by chronic progression and the absence of a definitive cure (1). According to recent estimates, by 2050 more than 25 million people will be living with PD, representing a 112% increase from 2025 (2). This rise is attributed primarily to population aging and global demographic growth (3,4).

The World Health Organization (WHO) (5) reported that in 2019, PD was responsible for 5.8 million disability-adjusted life years (DALYs) and caused 329,000 deaths—figures that have increased significantly since 2000. PD manifests with motor symptoms such as bradykinesia, muscular rigidity, resting tremor, and postural instability, as well as non-motor symptoms including cognitive impairment, sleep disorders, and autonomic dysfunction (6).

In the Americas, the United States records more than 90,000 new cases of PD annually, making it the second most prevalent neurological disorder, surpassing Alzheimer's disease (7). Advanced age, an aging population, and exposure to environmental factors such as pesticides and industrial solvents have been implicated in the rising incidence. Furthermore, men have been found to have a 1.5-fold greater risk of developing PD compared to women (8).

In Latin America, the prevalence and incidence of PD vary significantly across countries and regions. A meta-analysis by Kim et al. (9) estimated a prevalence of 472 per 100,000 inhabitants (95% CI: 271–820) and an incidence of 31 per 100,000 person-years (95% CI: 23–40) in 2023. These figures reflect not only differences in genetic and environmental factors, but also in access to healthcare services and the quality of epidemiological surveillance systems.

In Ecuador, a study by Franz et al. (10) analyzed 70 patients with early-onset PD, with a mean age of 42.6 years, and demonstrated the presence of pathogenic mutations in the PRKN and PINK1 genes—mainly PRKN deletions—highlighting a relevant genetic component in these cases. These findings underscore the need to complement diagnosis in ways that strengthen early detection of such degenerative diseases, optimize clinical stratification, and advance toward more precise and personalized care for PD patients in the Ecuadorian population.

On the other hand, a bibliometric analysis (BA) is an indispensable tool for exploring the structure and trends of scientific research, providing quantitative and qualitative information about the structure, impact, and dynamics of the scientific landscape. Moreover, in an era marked by remarkable growth in scientific output, conducting a bibliometric analysis is essential to evaluate the productivity, evolution, and distribution of studies focused on this type of disorder (11).

Given the growing global burden of PD, a comprehensive analysis of the scientific evolution of PD and the biochemical biomarkers implicated in this condition is warranted. Therefore, this study aims to analyze the scientific evolution of PD during the period 2015–2025 using a bibliometric approach that identifies research trends, geographic distribution, thematic networks, and main lines of study. It also seeks to characterize clinical types of the disease and evaluate the role of biochemical biomarkers in its diagnosis, with the goal of providing an integrated perspective that contributes to the strengthening of scientific knowledge and the improvement of diagnostic strategies.

METODOLOGÍA

Study design

A retrospective, descriptive bibliometric analysis with a quantitative approach was conducted on the scientific evolution of PD and its diagnosis through biochemical biomarkers, covering the period from 2015 to 2025. The organization and selection of documents followed the guidelines of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (12) guide, with the aim of ensuring a systematic, transparent, and reproducible process for identifying relevant original studies.

Scientific search strategy

The scientific literature was gathered from the PubMed database using controlled MeSH descriptors and free terms related to PD and its diagnosis through biochemical biomarkers. The following combination of keywords and Boolean operators was used:

("Parkinson Disease" OR "Parkinson's disease" OR "Idiopathic Parkinsonism" OR "neurodegenerativedisease")AND("Biomarkers" OR "Biochemical markers" OR "Molecular biomarkers" OR "Diagnostic biomarkers" OR "Blood biomarkers" OR "Cerebrospinal fluid biomarkers") AND ("Diagnosis" OR "Early diagnosis" OR "Differential diagnosis").

This strategy allowed the retrieval of studies with high scientific rigor, facilitating the identification of trends, emerging approaches, and relevant contributions to the development of bibliometric analysis.

Inclusion and exclusion criteria

Primary original studies and meta-analyses published within the defined period, in English, addressing PD and its diagnosis from a biochemical perspective were included. Narrative reviews, letters to the editor, conference proceedings, and other scientific event abstracts were excluded.

Bibliometric analysis

For the bibliometric analysis, the Bibliometrix software was used (direct link: https://www.bibliometrix.org/home/index.php/layout/biblioshiny), an R-based tool specifically designed for scientometric studies. This program allowed the importation, cleaning, analysis, and visualization of scientific information in a reproducible manner. Duplicate documents were identified through the DOI (Digital Object Identifier) and cross-referenced by similarity of authors, year, title, and journal.

The main bibliometric indicators assessed included the temporal evolution of scientific output, keyword analysis, co-occurrence networks, thematic maps, and the thematic evolution of the field. To identify conceptual clusters, the Walktrap algorithm was applied with a threshold ≥0.1, considering the frequency and relevance of terms associated with PD and biochemical biomarkers. Thematic maps were constructed based on centrality and density metrics, enabling the classification of topics into motor themes, basic themes, niche themes, and emerging or declining themes (13).

Data organization and extraction

The variables analyzed included year of publication, authors, country of origin, study type, diagnostic approach, types of biochemical biomarkers evaluated, key terms, and topics related to PD. For this purpose, a data matrix was created in Microsoft Excel 2019®, recording this information. This process was carried out by the responsible researchers, ensuring consistency, quality control, and traceability of the analyzed data.

Data analysis and synthesis

In the initial stage of the research process of this bibliometric analysis, a total of 9,983 articles were retrieved from the PubMed scientific database. Subsequently, after applying a rigorous screening and preliminary evaluation process, 2,524 were excluded due to duplication. During the screening phase, 7,410 studies were eliminated for not meeting the previously established eligibility criteria. As a final result, 49 investigations were selected that strictly met the methodological quality standards, systematically following the guidelines proposed by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guide (12) (Fig. 1).

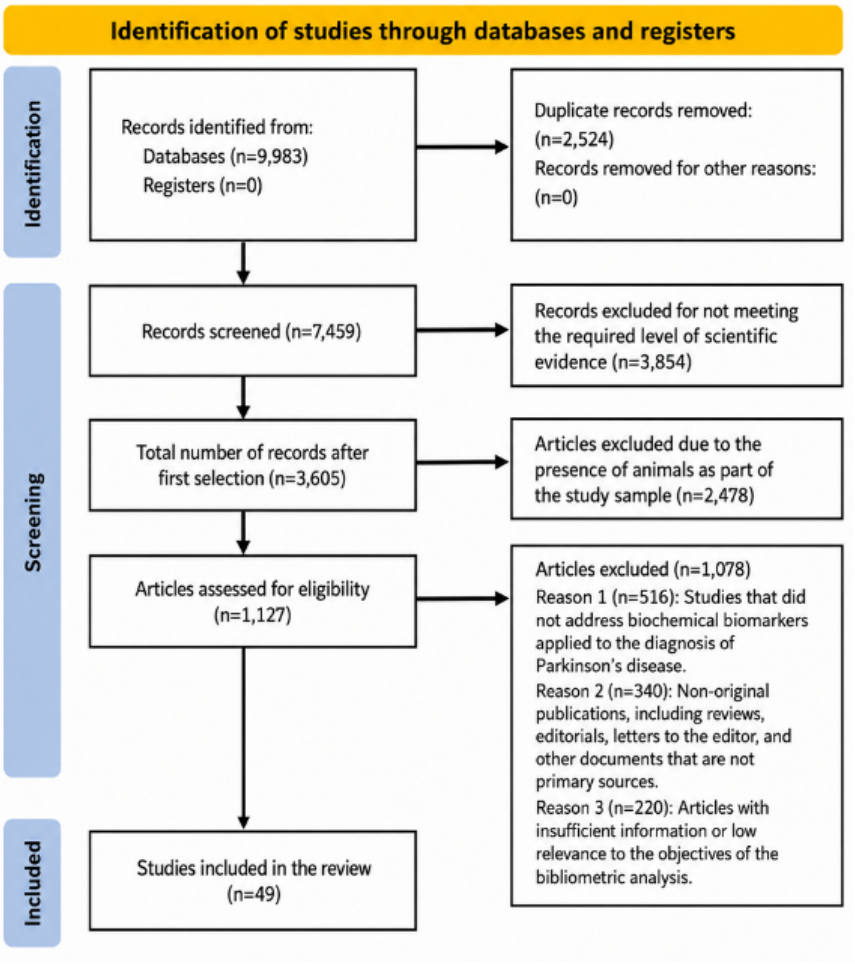

Figure 1. PRISMA study selection flowchart

Ethical considerations

The study was conducted in compliance with the ethical principles of scientific research, as it was based exclusively on the analysis of published literature. No human subjects or sensitive data were involved, ensuring transparency, academic integrity, and proper acknowledgment of the consulted sources. Likewise, bibliographic references were organized and cited in accordance with Vancouver guidelines, ensuring consistency, academic accuracy, and appropriate attribution of the scientific sources used in the study (14).

RESULTS AND DISCUSSION

Scientific productivity and sources on Parkinson's disease in PubMed (2015–2025)

Scientific productivity related to PD shows a growing and sustained dynamic over the evaluated period (Figure 2-A). In 2015, 874 publications were recorded, a figure that progressively increased to surpass 1,000 in 2017 (n=1,085). Although temporary declines were observed between 2018 (n=580) and 2023 (n=521), scientific output shows a notable resurgence in recent years, reaching 1,070 studies in 2024 and a maximum of 1,390 in 2025. This evolution underscores an increasingly consolidated scientific interest in deepening knowledge of the pathophysiological mechanisms, clinical manifestations, and diagnostic and therapeutic strategies of PD, confirming its relevance as a priority in contemporary neurological research.

Regarding the most consulted sources (Figure 2-B), Parkinsonism & Related Disorders stands out as the leading journal in the dissemination of scientific output on PD, with 3,907 publications, evidencing its central role in communicating clinical and experimental advances. It is followed by Movement Disorders (n=2,719), recognized for its high impact in the study of movement disorders. Likewise, the Journal of Parkinson's Disease contributes a significant volume of research (n=1,984), focused specifically on the clinical and therapeutic aspects of the disease. Neurology (n=1,513) and the International Journal of Molecular Sciences (n=851) complement the scientific output from clinical and molecular perspectives, respectively. Taken together, this distribution reflects the consolidation of specialized journals as fundamental pillars for the development and dissemination of knowledge on PD at the international level.

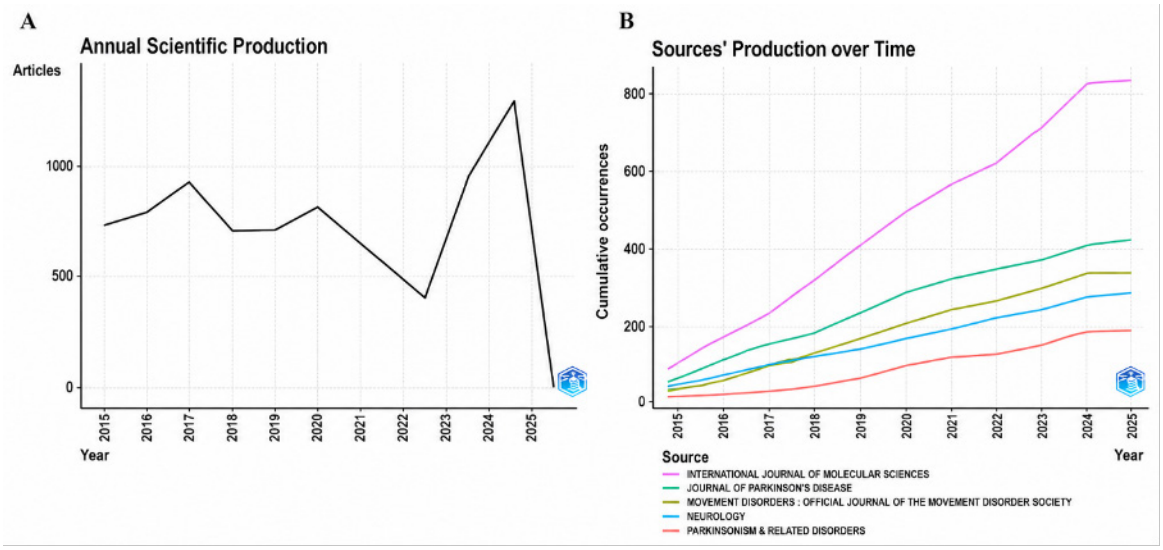

Figure 2. Annual scientific productivity (A) and main information sources on Parkinson's disease (B) in PubMed, 2015–2025

Geographic distribution of scientific output on Parkinson's disease (2015–2025)

The geographic distribution of scientific output on PD reveals a significant concentration in countries with highly consolidated neurological research systems (Fig. 3). China leads scientific production by a wide margin, with 9,643 publications, followed by the United States (n=7,726), reflecting the leadership of both nations in biomedical and neuroscientific research. At a second level are Italy (n=5,439) and Germany (n=2,989), countries with a strong tradition in the study of movement disorders, while Japan (n=2,254) and Canada (n=1,997) complete the group with the highest productivity.

This geographic pattern highlights the direct influence of investment in science, the availability of specialized centers, and the existence of robust academic networks in generating knowledge on PD. However, it also reveals inequality in scientific production at the global level, as regions with lower representation may face structural and funding limitations. In this context, it is essential to strengthen international cooperation and collaborative research strategies in order to broaden the comprehensive understanding of the disease and promote a more equitable approach to PD worldwide.

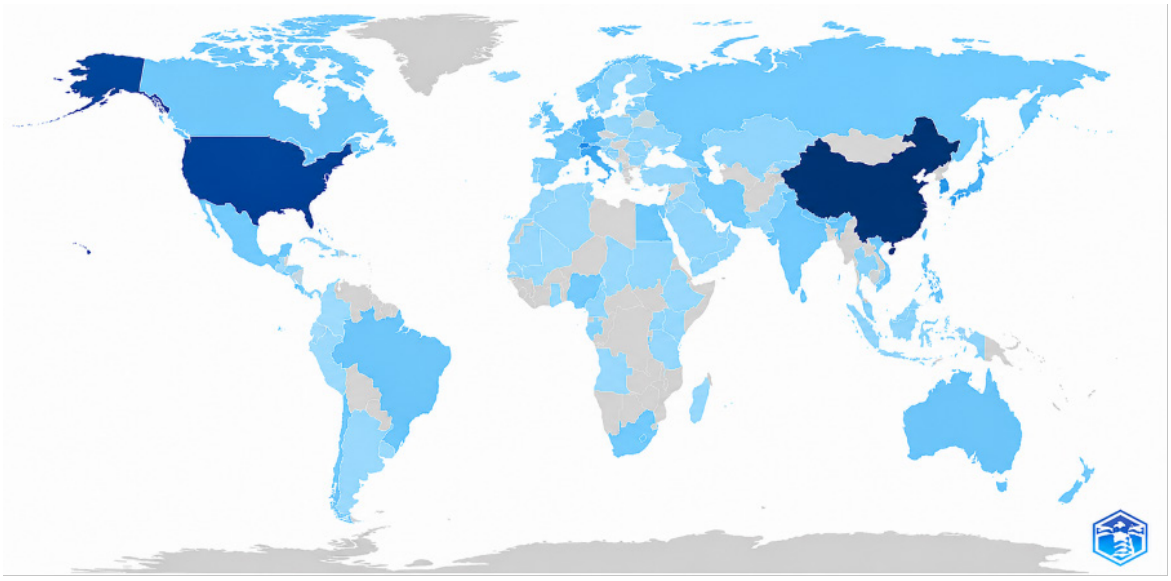

Figure 3. Geographic distribution of global scientific output on Parkinson's disease, 2015–2025

Co-occurrence network on Parkinson's disease (2015–2025)

The term co-occurrence network reveals a clearly organized conceptual structure comprising several interrelated clusters within PD research (Fig. 4). The central cluster (red) groups fundamental clinical concepts such as Parkinson's disease, disease progression, quality of life, risk factors, genetics, and therapeutic outcomes, reflecting a predominantly clinical-epidemiological approach centered on the patient.

The blue cluster is primarily associated with diagnostic and evaluation methods, highlighting terms such as brain imaging, positron emission tomography, and magnetic resonance imaging, evidencing the relevance of neuroimaging techniques in the characterization and follow-up of PD. The green cluster integrates demographic and phenotypic variables such as age, sex, and life stages, indicating an interest in understanding the clinical heterogeneity of the disease across the life course. Finally, the purple cluster is linked to the therapeutic approach, including antiparkinsonian agents and pharmacological strategies. This network demonstrates that PD research is structured around a solid clinical core, complemented by diagnostic, population-based, and therapeutic approaches. The interconnection between clusters suggests an evolution toward more comprehensive research, where understanding PD is not limited to motor symptoms but incorporates genetic, clinical, and quality-of-life dimensions, consolidating a multidimensional view of the disease.

Thematic map and thematic evolution of Parkinson's disease (2015–2025)

The thematic map organizes PD research according to its relevance and degree of development (Fig. 5). In the Motor Themes category, disease progression, brain pathology, and alpha-synuclein metabolism are positioned, indicating that these approaches constitute the most consolidated and active core of the field. Basic Themes include humans, elderly people, and diagnosis, along with diagnostic imaging, evidencing their transversal and fundamental role in clinical research. Niche Themes, such as prospective studies and cerebrospinal fluid analysis, reflect specialized lines with high scientific depth, although lower centrality. Emerging or Declining Themes, such as phenotype and magnetic resonance imaging, show areas with potential for future expansion. These results reveal a mature field that combines solid clinical foundations with specialized lines under development.

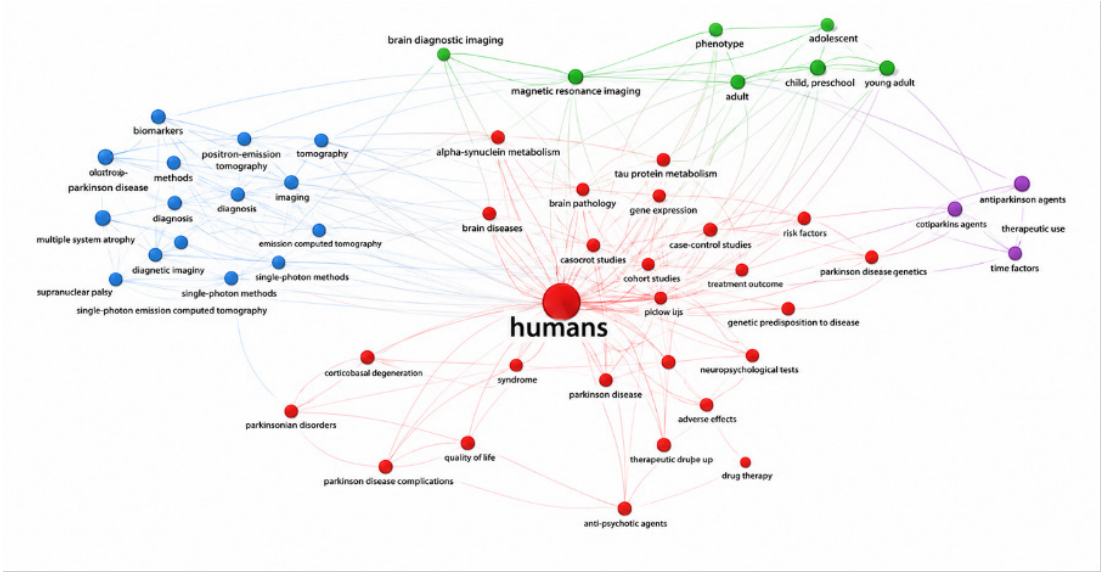

Figure 4. Co-occurrence network on Parkinson's disease, 2015–2025

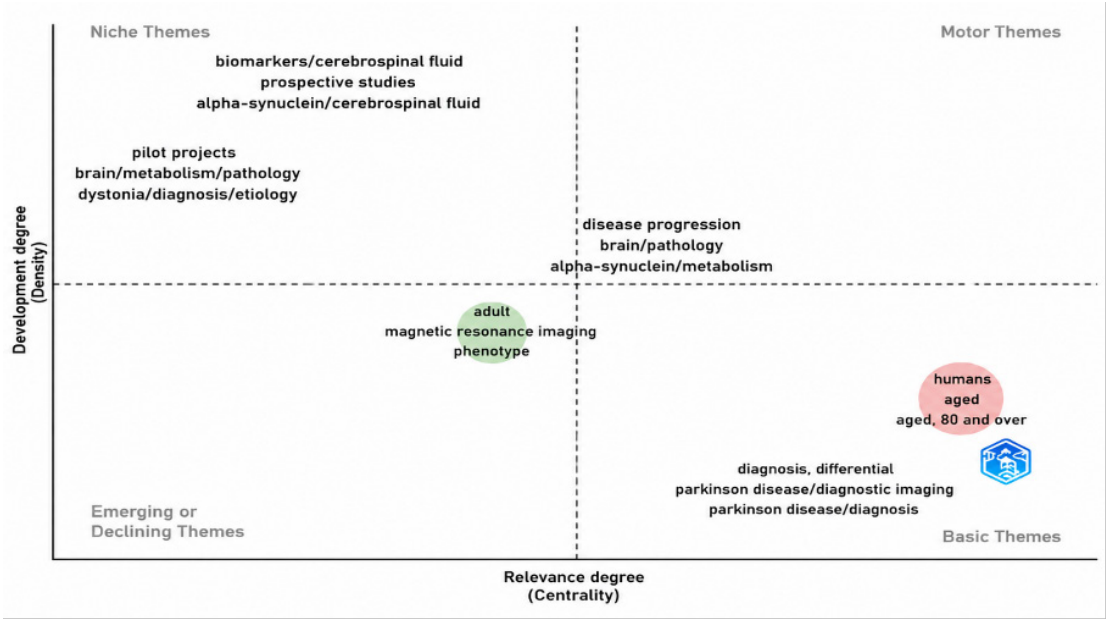

Figure 5. Thematic map on Parkinson's disease, 2015–2025.

The thematic evolution shows a progressive advancement of knowledge on PD (Fig. 6). In the initial stage (2015–2018), population-based and descriptive approaches predominate, focused on age, adults, and humans, along with cohort studies and general diagnosis. Between 2019 and 2020, a transition toward brain pathology, disease progression, and differential diagnosis is observed. During 2021–2023, these axes are consolidated and more specific diagnostic strategies are integrated. Finally, in 2024–2025, thematic diversification is evident, with greater analytical complexity and a comprehensive focus. Overall, this evolution reflects a shift from basic characterization toward a deeper, more clinical and structured understanding of PD.

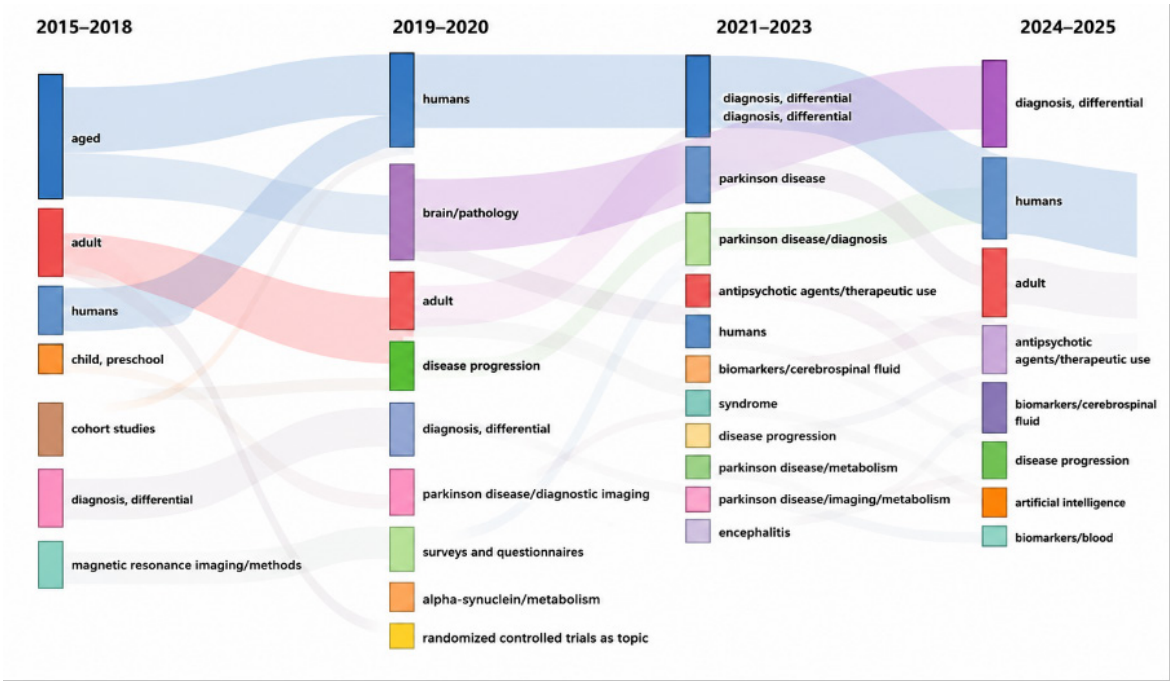

Figure 6. Thematic evolution of Parkinson's disease, 2015–2025.

Types and characteristics of Parkinson's disease and related disorders

With respect to the findings of this study, PD shows structured clinical heterogeneity encompassing predominant idiopathic forms, variants according to age of onset (juvenile, early, and late), as well as genetic presentations, and secondary and atypical forms. Idiopathic Parkinson's disease remains the most frequent, while early-onset and juvenile forms are associated with a greater genetic component and a more prolonged disease course. Late-onset disease, by contrast, presents a faster course with greater functional and cognitive deterioration. Similarly, atypical and secondary parkinsonisms reflect differentiated etiological mechanisms—neurodegenerative, vascular, pharmacological, and toxic—that condition specific clinical manifestations and complicate the diagnostic approach, as shown in Table 1.

However, Fereshtehnejad et al. (15) revealed that PD is not a uniform entity, but rather a heterogeneous disorder with multiple clinical subtypes and different prognoses, having identified subgroups of PD combining motor and non-motor symptoms, categorizing patients with worse cognitive and motor progression versus more benign subgroups.

Furthermore, Campbell et al. (16) consider that psychiatric, cognitive, and motor symptoms have demonstrated significant separation of subtypes with distinct prognostic implications. Similarly, Pan et al. (17) highlight patterns of brain progression and neurodegeneration that distinguish subtypes with lesser or greater atrophy and clinical deterioration.

On the other hand, Cheng et al. (18) emphasize that classification by clinical subtypes improves understanding of disease progression and promotes a more individualized therapeutic approach. They also note that the growing identification of cognitive and neuropsychiatric manifestations supports a comprehensive view of PD as a multisystem disorder, reinforcing the need for early diagnosis and differentiated clinical approaches.

Table 1. Types and characteristics of Parkinson's disease and related disorders (parkinsonisms)

Authors, Year, Country	Study Type	N	Type of Parkinson's	Characteristics
Idiopathic Parkinson's Disease				
Luan et al. (19), 2015, China	Observational	401	Idiopathic Parkinson's	The most common type (affects 85% of patients). Called 'idiopathic' because its exact cause is still unknown. Usually appears after age 60.
Karunanayaka et al. (20), 2016, USA	Observational	56	Juvenile Parkinson's	Manifests before age 21 and usually has a strong genetic component.
Schlossmacher et al. (21), 2017, Canada	Documentary	3	Early-onset Parkinson's	Appears between ages 21 and 45. Has a slow progression but a higher risk of motor complications associated with prolonged pharmacological therapies.
Jellinger (22), 2018, Austria	Retrospective	345	Late-onset Parkinson's	Standard diagnosis after age 45–60. Progresses rapidly, with greater cognitive and functional impairment.
Trinh et al. (23), 2019, Germany	Observational	7	Familial or Genetic Parkinson's	Represents 10%–15% of diagnoses. Confirmed when the patient has two or more first-degree relatives with the disease or a specific genetic mutation is identified. Unlike the idiopathic form, this is due to mutations in specific genes such as LRRK2, PRKN, SNCA, PINK1, or GBA.
Atypical Parkinsonisms				
Shahnawaz et al. (24), 2020, USA	Experimental	151	Multiple System Atrophy (MSA)	Affects the autonomic nervous system (control of blood pressure, bladder, etc.).
Lolekha et al. (25), 2021, Thailand	Retrospective	136	Progressive Supranuclear Palsy (PSP)	Characterized by early balance problems and difficulty moving the eyes vertically.
Sandor et al. (26), 2022, UK & USA	Longitudinal, multicenter	842	Corticobasal Degeneration (CBD)	Usually affects one side of the body more and may present with 'alien hand syndrome'.
Secondary Parkinsonisms				
Sampedro et al. (27), 2023, Spain	Retrospective	44	Drug-induced	Caused by certain drugs (such as some antipsychotics) that block dopamine.
Zedde et al. (28), 2024, Italy	Documentary	8,301	Vascular	Result of small cerebral infarcts affecting the movement-related areas.
Lorenzo et al. (29), 2025, USA	Observational, multicenter	335	Toxic	Due to exposure to substances such as manganese or carbon monoxide.

Abbreviations: N: Sample size; LRRK2: Leucine-Rich Repeat Kinase 2; PRKN: Parkin RBR E3 ubiquitin-protein ligase; SNCA: Synuclein alpha; PINK1: PTEN-induced kinase 1; GBA: Glucocerebrosidase beta.

Biochemical biomarkers in the diagnosis of Parkinson's disease

According to the findings in Table 2, biochemical biomarkers in Parkinson's disease show diagnostic variability depending on their nature and sample type. Leucine-Rich Repeat Kinase 2 (LRRK2) and plasma Neurofilament Light Chain (NfL) stand out for their high sensitivity (>90%), suggesting their usefulness for early detection, while beta-amyloid peptide, Fatty Acid-Binding Protein 3 (FABP3), and Apolipoprotein A1 (ApoA1) show high specificity (>89%), favoring diagnostic confirmation. In contrast, NfL presents low sensitivity in certain studies, limiting its value as an initial test. Overall, cerebrospinal fluid (CSF) biomarkers exhibit a better diagnostic balance than serum biomarkers, reflecting greater proximity to central neurodegenerative processes.

Table 2. Biochemical biomarkers used in the diagnosis of Parkinson's disease

Authors, Year, Country	Study Type	N/PD	Mean Age (SD)	Sample Type	Biochemical Biomarkers	Sn	Sp
Ishii et al. (38), 2015, Japan	Cross-sectional	103/53	64.3 ± 9.8	CSF, Plasma	Alpha-synuclein	87.0%	63.2%
Caviness et al. (39), 2016, USA	Experimental	54/44	81.1 ± 6.8	Brain tissue (cortex)	Beta-amyloid peptide	84.0%	91.1%
Chiasserini et al. (40), 2017, Italy	Multicenter	208/54	66.0 ± 8.9	CSF	Heart-type fatty acid binding protein (FABP3)	86.4%	89.0%
Arora et al. (41), 2018, Canada	Experimental	89/7	72.3 ± 13.1	CSF, Serum, Brain tissue	Leucine-Rich Repeat Kinase 2 (LRRK2)	95.4%	89.6%
Lin et al. (42), 2019, China	Prospective	178/116	68.5 ± 11.2	Plasma	Neurofilament Light Chain (NfL)	53.2%	90.5%
Rotunno et al. (43), 2020, USA	Longitudinal cohort	196/81	63.2 ± 8.8	CSF	Proteomic profile	78%	84%
Milanowski et al. (44), 2021, Czech Republic, Germany, Poland, Ukraine	Experimental, multicenter	541/4	55.3 ± 8.6	CSF	DJ-1 protein	88.2%	89.1%
Batzu et al. (45), 2022, UK	Experimental	94/59	63.80 ± 11.24	Plasma	Neurofilament Light Chain (NfL)	91.5%	90.0%
Koros et al. (46), 2023, Greece	Longitudinal	421/195	61.63 ± 9.69	Serum	Uric acid	81.3%	87.2%
Paslawski & Svenningsson (47), 2023, Sweden	Observational	180/78	67.80 ± 6.44	Serum	Apolipoprotein A1 (ApoA1)	75.0%	91.0%
Nikitina et al. (48), 2024, Russia	Observational	71/27	65.22 ± 56.70	Serum	Brain-Derived Neurotrophic Factor (BDNF)	71.7%	75.0%
Li et al. (49), 2025, China	Observational	282/58	59.81 ± 7.93	Plasma	Glial Fibrillary Acidic Protein (GFAP)	75.6%	85.1%

Abbreviations: N: Sample size; PD: Parkinson's disease; SD: Standard deviation; Sn: Sensitivity; Sp: Specificity; CSF: Cerebrospinal fluid.

The results are consistent with certain scientific evidence. Katayama et al. (30) reported an NfL sensitivity close to 55% and a specificity of 88–91%, values similar to those observed (53.2% and 90.5%), confirming its utility as a marker of progression rather than early diagnosis. Similarly, Zimmermann et al. (31) described CSF proteomic profiles with approximately 75–80% sensitivity and 80–85% specificity, consistent with the data obtained (78% and 84%).

Likewise, Han et al. (32) documented that biomarker combinations can achieve sensitivities above 90% and specificities close to 95%, surpassing individual performance. However, Arya et al. (33) reveal that the identification of proteins such as misfolded α-synuclein or pTau217 in blood enables large-scale, cost-effective diagnosis, while also strengthening prodromal detection with the capacity to predict the disease up to 20 years before motor symptoms appear, as reinforced by Navarrete et al. (34).

Added to this is what was reported by Gualerzi et al. (35), who highlighted the use of exosomes or extracellular vesicles to study the propagation of pathologies directly from the central nervous system to the periphery. Mention must also be made of emerging areas such as the gut-brain axis as investigated by Oliver and Hu (36), which has allowed analysis of how the microbiome and intestinal inflammation influence disease development. Finally, immunological

mechanisms are explored in depth, specifically the role of neuroinflammation with markers such as Glial Fibrillary Acidic Protein (GFAP) as an indicator of progression and severity (37).

CONCLUSIONS

The scientific evolution of PD between 2015 and 2025 shows sustained growth in productivity, supported by high-impact specialized journals and a marked geographic concentration in countries with greater scientific development. This dynamism is organized into co-occurrence networks that integrate clinical, diagnostic, and therapeutic dimensions, reflecting a solid research structure. Furthermore, the thematic map and thematic evolution showed a transition from descriptive approaches toward more complex lines focused on pathophysiology, progression, and diagnosis, consolidating a field in constant scientific maturation.

In addition, PD is confirmed as a clinically heterogeneous entity, characterized by multiple subtypes that differ in onset, progression, and motor and non-motor manifestations. From slow-evolving forms, such as the tremor-dominant or early-onset phenotype, to more aggressive variants such as the rigid-akinetic or rapidly progressing form, phenotypic diversity conditions prognosis and therapeutic response. This variability underscores the importance of precise clinical classification, aimed at optimizing patient stratification and promoting a more individualized approach.

In bibliometrics, NfL is the biomarker generating the largest volume of publications alongside GFAP, as they are considered the benchmark markers of neurodegeneration and axonal damage. The triad is focused on synuclein (specific to the pathology), GFAP (glial inflammation), and NfL (neuronal death). However, the current bibliometric trend highlights amplification and technical precision techniques such as the Seed Amplification Assay (SAA) for synuclein in blood, which allow detection of misfolded proteins in minimal quantities, marking the beginning of an era of high-precision molecular diagnosis.

Author contributions

Demera Chica Alexander David: study conception, methodological design, data analysis, and manuscript writing; Jhon Bryan Mina Ortiz: data collection, bibliographic database cleaning, and writing support; Ronald Andreé Vitonera Rogel: bibliometric analysis, interpretation of results, and critical review of content; William Antonio Lino Villacreses: information organization, table preparation, and manuscript review; Nereida Valero Cedeño: study development, critical review, and final content validation.

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