

Unlocking the future of breast cancer biomarkers: A bibliometric perspective

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ABSTRACT

Background: Breast cancer remains one of the most prevalent malignancies affecting women worldwide. Biomarkers play a pivotal role in enhancing diagnostic, prognostic, and therapeutic strategies for personalized patient management. This study conducts a bibliometric analysis of breast cancer biomarker research from 1981 to 2025 to identify key research trends, thematic clusters, and emerging areas.

Methods: A total of 752 publications were retrieved from the Web of Science Core Collection using keywords related to breast cancer and biomarker types, including molecular, protein, serum, and genetic markers. Bibliometric tools such as R programming and Biblioshiny were employed to analyze publication trends, keyword co-occurrences, and thematic clusters.

Results: The study identified a 3.2% annual growth rate in publications, with China, the USA, and India as the leading contributors. Research articles constituted 86.9% of the publications. Thematic analysis highlighted "proteomics" and "angiogenesis" as emerging research areas, while extensively studied topics included "EGFR" and "cholesterol." The most central cluster encompassed "breast cancer, biomarkers, and metastasis," while motor themes included "prognosis, diagnosis, and colorectal cancer." Niche topics, such as "lncRNA and tumor," represented isolated but developed research areas.

Conclusions: Key challenges included a lack of standardized validation protocols and slow clinical integration of biomarkers. The evolving landscape of breast cancer biomarker research underscores the need for multi-omics approaches and AI-driven analytics to accelerate biomarker discovery and clinical translation. Addressing challenges in validation and adoption will be crucial for improving patient outcomes.

Keywords: bibliometric analysis, biomarkers, breast cancer, molecular diagnosis, precision medicine

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INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy among women worldwide and remains a leading cause of cancer-related mortality, despite advances in diagnostic and therapeutic interventions [1]. The complexity and heterogeneity of the disease pose significant challenges, driving extensive research into biomarkers—biological molecules that signal the presence, progression, or treatment response of a disease. These markers have transformed cancer care by enabling early detection, predicting prognosis, and guiding personalized treatment strategies [2].

The application of biomarkers such as HER2, estrogen receptor (ER), and progesterone receptor (PR) has revolutionized breast cancer management, leading to

targeted therapies like trastuzumab [3]. Despite these advancements, the ongoing search for novel biomarkers continues due to the complex nature of breast cancer, which limits the effectiveness of current markers. Researchers are now focusing on emerging candidates, including proteomic markers, non-coding RNAs, and metabolic indicators, to enhance diagnostic precision and therapeutic decision-making [4].

Bibliometric analysis offers a valuable tool for mapping research trends and identifying emerging themes in biomarker research. By analyzing publication patterns, thematic clusters, and keyword networks, bibliometric studies provide a comprehensive understanding of research development and future directions [5]. This analysis covers the period from 1981 to 2025, using tools like R programming and Biblioshiny to examine publication

trends, leading contributors, and thematic hotspots. Emerging technologies, including machine learning and AI, are facilitating complex pattern identification, accelerating biomarker discovery. While significant advancements have been made, challenges persist in validating and standardizing biomarkers for clinical use, often slowing their adoption in practice [1]. To address these limitations, researchers are increasingly adopting multi-omics approaches that integrate genomics, proteomics, and metabolomics to provide a comprehensive understanding of tumor biology. These methods hold great promise for identifying robust biomarkers that improve diagnostic accuracy and treatment outcomes [6].

Therefore, this bibliometric analysis underscores the evolving landscape of breast cancer biomarker research and highlights emerging areas for future investigation. Collaborative research, advanced analytical techniques, and efficient clinical integration of biomarkers will be essential to transforming breast cancer care and improving patient outcomes.

METHODS

Research design

Donthu et al.'s guide was employed in this bibliometric study [5]. The four recommended stages were followed when doing the analysis.

Step 1: Outlining the bibliometric goals and parameters of the study.

Step 2: Choosing the best bibliometric analysis.

Step 3: Gathering information for bibliometric evaluation.

Step 4: Conducting bibliometric analysis and documenting the results.

Universe of research

This research focuses on the bibliometric analysis of publications related to biomarkers in breast cancer, covering a wide time span from 1981 to 2025. The data comprise 752 scientific studies sourced from the Web of Science Core Collection, filtered based on English language and article type criteria. Key research areas include various biomarker types such as molecular, protein, serum, genetic, metabolic, diagnostic, prognostic, and predictive markers, all explored in the context of breast cancer and medical biochemistry. Ethics committee approval is not required.

Data collection

This study conducted a comprehensive bibliometric analysis of breast cancer biomarker research using the Web of Science Core Collection database, which is highly compatible with the Bibliometrix-Biblioshiny software and widely recognized for bibliometric studies. The

search was performed in January 2025, without restrictions on the publication timeframe, targeting research across all categories. The search strategy included a combination of key terms such as ["Breast cancer" OR "Breast tumor" OR "Breast carcinoma" OR "Malignant breast tumor" OR "Breast malignancy" AND "Marker" OR "Biomarker" OR "Biochemical Marker" OR "Biochemical indicator" OR "Molecular marker" OR "Protein Biomarkers" OR "Serum Biomarkers" OR "Genetic Biomarkers" OR "Metabolic Biomarkers" OR "Diagnostic Biomarkers" OR "Prognostic Biomarkers" OR "Predictive Biomarkers" OR "Serological marker" AND "Biochemistry" OR "Medical biochemistry"].

Only studies published in English were included, while publications in Italian (n=1) and Chinese (n=5) were excluded. One retracted publication was also removed from the dataset. Synonyms were standardized (e.g., "biomarker" and "biomarkers" unified as "biomarkers") to ensure consistency in the analysis. Data were downloaded in BibTeX format and imported into the Biblioshiny extension of the R programming environment for detailed examination.

During the analysis, only "author keywords" were used to ensure thematic accuracy. Basic bibliometric indicators were presented as counts, percentages, or proportional values. A word treemap was generated using the top 25 author keywords to visualize keyword frequency. Emerging research trends were assessed based on the most recent five-year period. For thematic analysis, the walktrap algorithm was employed, incorporating 100 author keywords. The minimum cluster frequency was set at 10, and the level count for each cluster ranged between one and three.

Ethical approval was deemed unnecessary for this research, as it involved secondary data collection from publicly accessible sources. The careful screening and refinement of data ensured the inclusion of high-quality studies, providing a robust foundation for bibliometric evaluation.

RESULTS

The bibliophily interface of the bibliometric tool, which is part of the open access R software (R 4.2.2. R Foundation), was utilized for data analysis. Calculations using statistics are the primary purpose of the R programming language. This well-developed programming language has capabilities that facilitate the visual presentation of data via graphs [7]. The R programming language was used to assess bibliometric analytic techniques in this study. Data analysis was conducted using the biblioshiny interface of the open access R program (R 4.2.2.) in the bibliometrix tool. For thorough scientific mapping investigations, the R package and the bibliometrix tool are recommended [8].

Basic information about the included publications is shown in Table 1. While the majority of the analyzed publications (86.9%) were research articles, the annual growth rate was determined as 3.2%. Among the studies examined, China (23.53%) stands out as the country with the highest number of publications. This is followed by the USA and India. The most frequently published journals include *Journal of Cellular Biochemistry* (16.22%) and *Clinical Biochemistry*.

The distribution of publications by year is shown in Figure 1. The number of articles in the distribution of years is in Table 2. The year with the highest number of publications was determined as 2018. This indicates that breast cancer research attracts more attention in certain periods.

When the treemap is examined, the prominent keywords other than the keywords of the research are “prognosis” (n=45, 6%), “apoptosis” (n=29, 4%) and “diagnosis, metastasis” (n=22, 3%). These words are followed by “emt, proliferation” (n=18, 2%), “colorectal cancer, gene expression, migration, prostate cancer, proteomics” (n=15, 2%) (Figure 2).

Trend topics show how themes related to a topic have been distributed throughout time. Five was determined to be the minimal word frequency in this investigation (Figure 3). The most frequently studied topics in the last five years are “proteomics” and “angiogenesis”, while the longest studied topics are “egfr” and “cholesterol”.

Thematic analysis was conducted using a rapid greedy algorithm using keywords (Figure 4). Five was found to be the minimal cluster frequency, and there was only one level for each cluster. The following ideas must be understood in order to interpret the analysis [5,9]. *Centrality*: The greater its strength, the more significant it is for the field of study. *Intensity*: The more cohesive and integrated the subject, the stronger it is. *Motor themes*: Regarded as sophisticated and essential issues for the study area. *Basic topics*: They highlight subjects that are still evolving within the research field. *Niche themes*: They demonstrate that there are distinct yet well-developed themes within the research field. *Developing or fading themes*: These are regarded as developing or fading themes in the subject of study.

According to the thematic map, “breast cancer, biomarkers, metastasis” among the basic themes is the cluster with the highest co-occurrence and the highest centrality. A significant portion of the nodes is located in the motor themes area. These are “prognosis, diagnosis, colorectal cancer” and “chemoprevention, oxidative stress, p53”. The “apoptosis, proliferation, migration” cluster is located on the centrality line. The keywords “lncrna, tumor” are niche themes that indicate a developed but isolated field of study. However, the topic “her2, triple-negative breast cancer” is among the newly emerging or disappearing themes of the field. Finally, the topic “angiogenesis” is on the density line.

Table 1: Basic publication information

General information	
Timespan	1981 to 2025
Sources (journals, books, etc.)	159
Documents	752
Annual growth rate	3.2%
Document average age	11.9
Average citations per doc	29.8
References	35,754
Author’s keywords (DE)	2,361
Authors	3,545
Authors of single-authored docs	32
International co-authorship	19.4 %
Co-authors per doc	5.6
Document type, n (%)	
Article	654 (86.9)
Review	80 (10.7)
Proceedings paper	14 (1.8)
Editorial material	4 (0.5)
Most relevant sources, n (%)	
Journal of Cellular Biochemistry	122 (16.2)
Journal of Steroid Biochemistry and Molecular Biology	71 (9.4)
Clinical Biochemistry	59 (7.8)
Cellular Physiology and Biochemistry	52 (6.9)
Molecular and Cellular Biochemistry	44 (5.8)
Corresponding author’s countries, n (%)	
China	177 (23.5)
USA	135 (17.9)
India	57 (7.5)
Canada	32 (4.2)
Iran	31 (4.1)

Table 2: Publication-year distribution table

Year	Articles	Year	Articles
2018	65	1997	10
2019	54	1994	9
2024	45	2001	8
2017	45	2002	7
2015	40	1998	6
2014	39	1996	6
2013	38	1990	6
2023	32	2000	5
2016	32	1999	5
2022	31	1995	5
2012	31	2025	4
2021	28	1991	4
2020	28	1992	3
2009	25	1988	2
2011	24	1987	2
2010	20	1989	1
2007	15	1984	1
2005	14	1983	1
2006	13	1982	1
2008	12	1981	1
1993	12	1986	0
2004	11	1985	0
2003	11	–	–

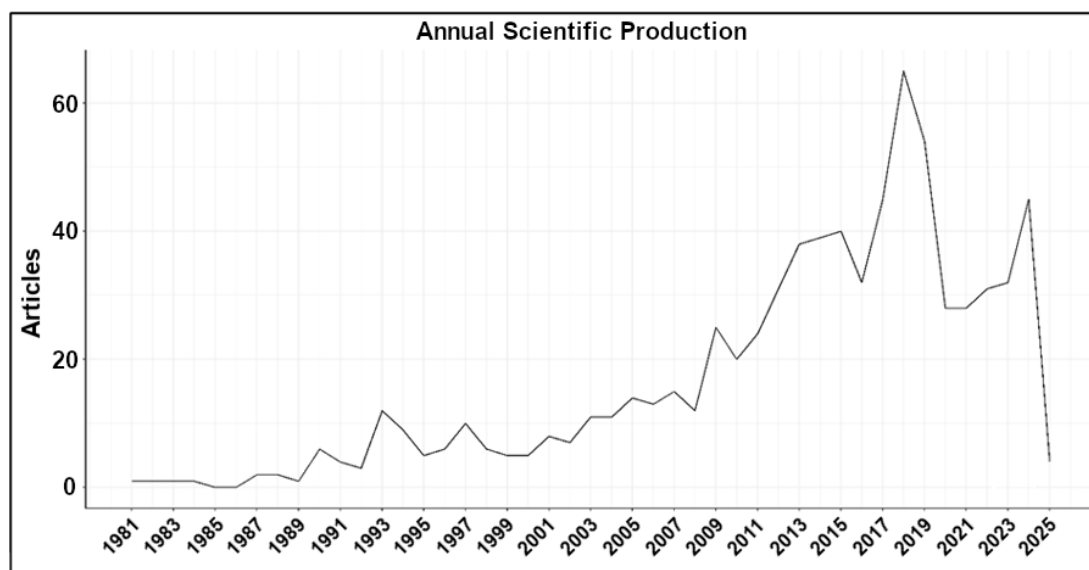


Figure 1. Annual distribution of publications between 1981 and 2025

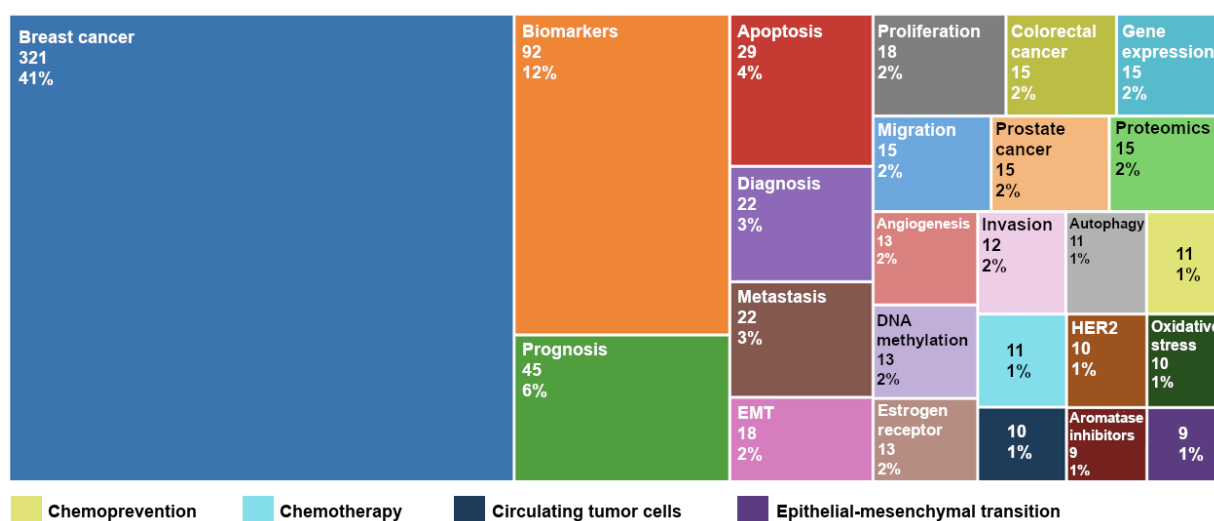


Figure 2. Treemap illustrating the distribution of prominent keywords in the analyzed studies

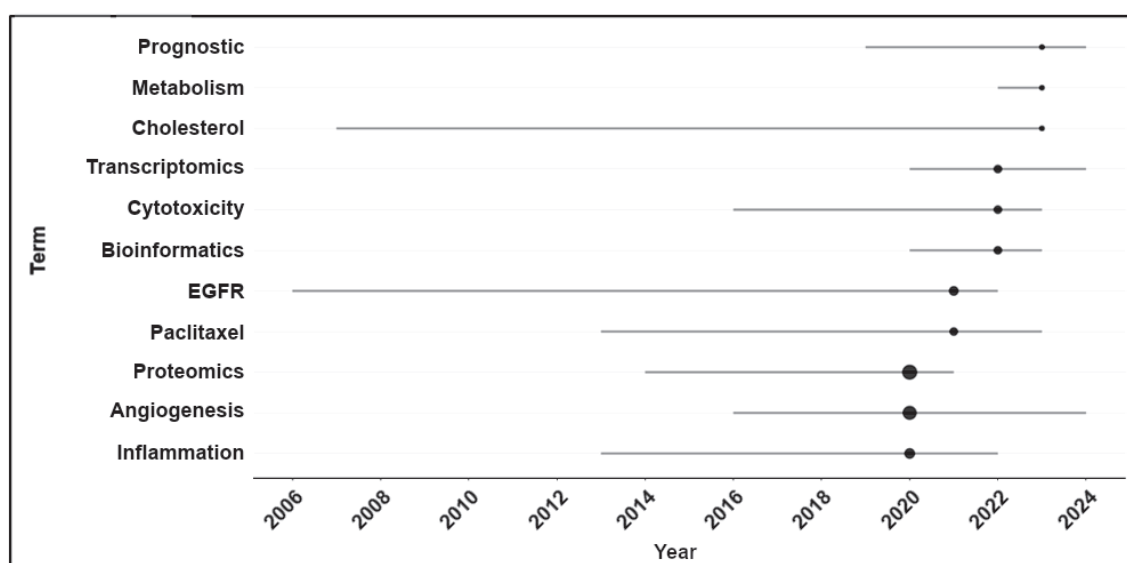


Figure 3. Temporal distribution of trending research topics

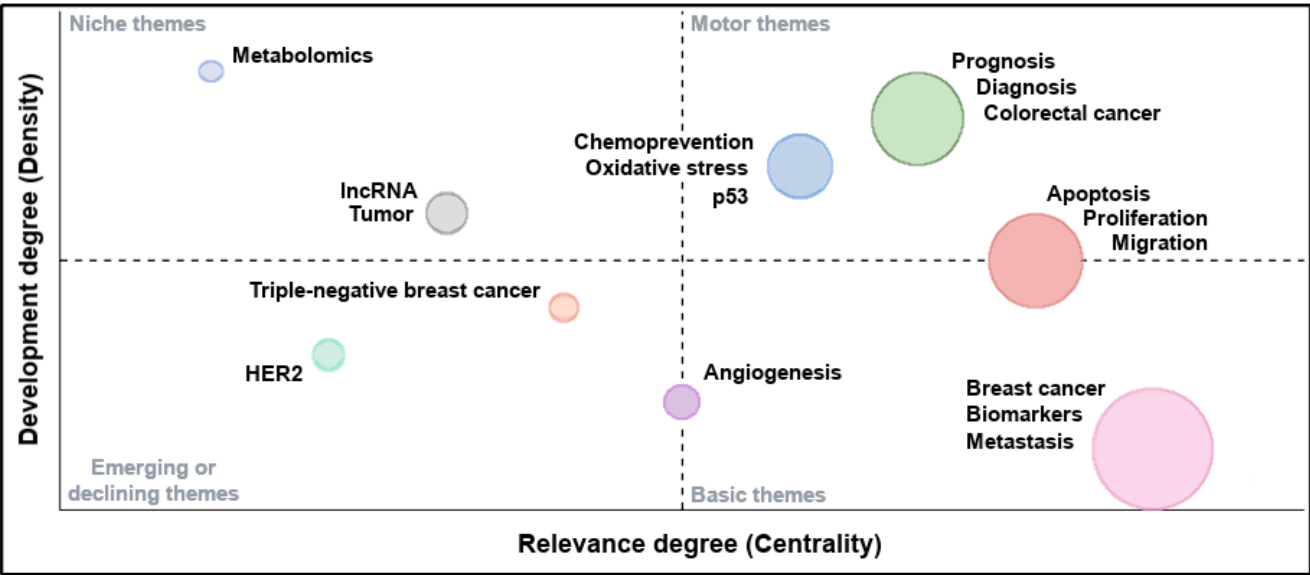


Figure 4. Thematic map showing major research themes and their relationships within the field

This analysis provides insights into the conceptual and intellectual framework of the field. A network cluster is represented by each node on the map, and words that are part of the cluster and have a higher formation network are represented by the node names. The amount of postings that contain the keyword and the location of the node, as determined by cluster centrality and density, determine the node sizes [9].

DISCUSSION

This bibliometric analysis provides comprehensive insights into the dynamic and evolving landscape of breast cancer biomarker research, highlighting key thematic advancements, geographic trends, emerging areas, and persistent challenges. The study reveals a steady 3.2% annual growth in publications, reflecting sustained interest in the field. Research articles dominate the literature (86.9%), emphasizing a strong focus on experimental studies to advance biomarker discovery. Geographically, China leads with 23.53% of publications, followed by the USA and India. China's leadership can be attributed to substantial government investment and international collaborations [10], while the USA continues to play a pioneering role in molecular diagnostics [11]. India's contributions, focusing on both fundamental and translational research, further underline the global commitment to this crucial area [12]. Additionally, the prominence of journals, such as *Journal of Cellular Biochemistry* (16.22%) and *Clinical Biochemistry*, highlights the interdisciplinary nature of breast cancer biomarker research, reflecting a strong focus on molecular and biochemical approaches to understanding tumor biology and advancing diagnostic and therapeutic strategies.

The increase in articles about breast cancer in 2018 may be attributed to several factors. Advances in high-throughput technologies such as next-generation sequencing (NGS) and proteomics likely fueled new biomarker discoveries, leading to heightened research interest. Additionally, the growing emphasis on precision medicine and

immunotherapy during this period prompted extensive studies on predictive and prognostic biomarkers [13].

The thematic map analysis provides valuable insights into the conceptual and intellectual framework of breast cancer biomarker research. According to the thematic map, proteomics and angiogenesis emerge as focal points. When the treemap is examined, the most prominent keywords beyond the research-specific ones are “prognosis” (n=45, 6%), “apoptosis” (n=29, 4%), and “diagnosis, metastasis” (n=22, 3%). These are followed by “emt, proliferation” (n=18, 2%) and “colorectal cancer, gene expression, migration, prostate cancer, proteomics” (n=15, 2%). Over the last five years, the most frequently studied topics are “proteomics” and “angiogenesis,” while the longest-studied topics are “EGFR” and “cholesterol.” Proteomics, in particular, has become a transformative research domain, offering dynamic insights into protein expression and post-translational modifications essential for understanding tumor behavior and treatment responses [14]. The placement of “angiogenesis” along the density line indicates sustained research interest, likely due to its critical role in tumor growth and therapeutic targeting. The sustained interest in angiogenesis aligns with its clinical importance, as biomarkers predicting angiogenic activity are crucial for assessing the efficacy of anti-angiogenic therapies [15]. Additionally, the growing focus on gut microbiota and tumor-infiltrating lymphocytes (TILs) signals a paradigm shift toward understanding the tumor microenvironment and immune dynamics, paving the way for innovative immunotherapeutic strategies [16].

The clusters identified on the map highlight key areas of focus and research dynamics. The cluster with the highest co-occurrence and centrality includes "breast cancer, biomarkers, metastasis," reflecting its foundational importance in the field. Notably, motor themes, which are highly developed and central to research progression, include clusters such as "prognosis, diagnosis, colorectal cancer" and "chemoprevention, oxidative stress, p53," indicating their continued relevance and influence on breast cancer studies. Interestingly, the "apoptosis, proliferation, migration" cluster sits along the centrality line, suggesting its established yet ongoing importance in understanding tumor biology. Niche themes, represented by keywords like "lncRNA" and "tumor," reveal areas of specialized but relatively isolated research, underscoring emerging avenues for exploration. The positioning of "HER2, triple-negative breast cancer" as an emerging or potentially declining theme highlights the evolving interest in subtype-specific research, possibly influenced by advancements in therapeutic strategies or shifts in research priorities.

Subtype-specific biomarker research has seen remarkable progress, particularly in HER2-positive and triple-negative breast cancer (TNBC). HER2-positive breast cancer has benefited from targeted therapies such as trastuzumab, although resistance remains a significant challenge. Biomarker research aimed at predicting therapeutic response is essential for overcoming this limitation. TNBC presents a more complex challenge due to its aggressive nature and lack of hormone receptor expression. Recent efforts to identify molecular signatures guiding personalized therapies underscore the importance of precision oncology in addressing the complexities of TNBC [17].

Prognostic and predictive biomarkers, integral subcategories of diagnostic biomarkers, play distinct but complementary roles in breast cancer management. Prognostic biomarkers provide information about the likely course and outcome of breast cancer, independent of treatment, and help identify patients requiring closer monitoring or more aggressive therapeutic approaches [3]. HER2 overexpression and lymph node involvement are examples of established prognostic markers. In contrast, predictive biomarkers, such as hormone receptor status (ER and PR) and HER2 expression, guide the selection of specific treatments, maximizing efficacy and minimizing side effects. As immunotherapies gain traction, biomarkers predicting immune response, including TILs, are increasingly crucial for optimizing treatment strategies [18].

Despite substantial advancements, several challenges persist in breast cancer biomarker research. One critical issue is the lack of standardized validation protocols,

which hinders the clinical translation of many promising biomarkers. Multi-center studies and robust validation frameworks are essential to ensure the reliability and utility of these discoveries. The inherent heterogeneity of breast cancer further complicates biomarker identification, necessitating a more nuanced and subtype-specific approach to biomarker discovery and validation [19]. Additionally, the slow and resource-intensive process of integrating validated biomarkers into clinical practice highlights the need for streamlined pathways to clinical adoption.

Emerging niche areas such as long non-coding RNAs (lncRNAs) and the tumor microenvironment are gaining traction. lncRNAs play significant roles in gene regulation and tumor progression, while the tumor microenvironment remains critical for understanding cancer Dynamics [20]. The integration of these markers into clinical workflows offers promising avenues for future research and therapeutic interventions.

Looking ahead, the future of breast cancer biomarker research lies in adopting multi-omics approaches, which integrate data from genomics, proteomics, transcriptomics, and metabolomics to provide a comprehensive understanding of tumor biology. These approaches will facilitate the discovery of robust biomarkers capable of improving diagnostic precision and therapeutic outcomes. The application of artificial intelligence (AI) and machine learning (ML) technologies is also expected to be pivotal in analyzing complex datasets, identifying patterns, and accelerating the pace of biomarker discovery [21]. Immune-related biomarkers, particularly those predicting response to immunotherapies, are likely to gain prominence as precision.

CONCLUSIONS

Only English-language articles were included in the analysis. Important research published in other languages may have been overlooked, potentially limiting the comprehensiveness of the findings. Although the study covers publications, the temporal analysis may still not capture the most recent cutting-edge research trends published post-data collection. The study provides a quantitative analysis of trends and themes but lacks qualitative insights into the scientific content, research methodologies, or clinical implications of the analyzed studies. This bibliometric analysis highlights the dynamic evolution of breast cancer biomarker research, showcasing significant advancements, emerging trends, and persistent challenges. The steady growth in publications reflects the research community's ongoing commitment to uncovering novel biomarkers that can enhance diagnostic precision and therapeutic strate-

gies. The thematic focus on proteomics, angiogenesis, and immune-related markers underscores the shift of the field toward comprehensive tumor biology insights and precision medicine approaches. While promising, the challenges of validation, standardization, and clinical integration remain key barriers to the widespread application of biomarkers. Addressing these limitations will require collaborative research efforts, multi-omics approaches, and the adoption of advanced analytical technologies such as AI and machine learning. By fostering innovation and streamlining clinical adoption, biomarker research can significantly contribute to improving breast cancer diagnosis, treatment, and patient outcomes.

ABBREVIATIONS

AI – artificial intelligence

BibTeX – tool/file format for referencing in LaTeX documents

EGFR – epidermal growth factor receptor

EMT – epithelial-mesenchymal transition

ER – estrogen receptor

HER2 – human epidermal growth factor receptor 2

lncRNA – long non-coding RNA

ML – machine learning

NGS – next-generation sequencing

PR – progesterone receptor

R (programming language) – R is a free software environment for statistical computing and graphics

TILs – tumor-infiltrating lymphocytes

TNBC – triple-negative breast cancer

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AUTHORS' CONTRIBUTION

GD: conceptualization, analysis, data visualization, writing.

CONFLICT OF INTEREST

None to declare.

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