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A Bibliometric Analysis of Stem Cell Research in Infertility: Insights and Trends

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What's known on the subject? and What does the study add?

Infertility affects millions worldwide, and stem cell therapies have emerged as a promising alternative to traditional treatments. Despite increasing research, there has been a limited number of comprehensive bibliometric analyses regarding global trends, key contributors, and influential studies. This study analyzes 1,710 articles (1982-2024) using bibliometric mapping, identifying key authors, institutions, and research trends. The findings highlight the dominance of the United States and China in publications, the rising focus on spermatogonial stem cells, and the need for global collaboration to enhance research diversity and impact.

Abstract

Objective: This study aims to examine, using bibliometric mapping methods in the Web of Science database, the development of research articles related to infertility, which has become a significant global issue, and an innovative treatment method, stem cells, between 1982 and 2024.

Materials and Methods: Initially, 1,710 articles were retrieved using the keywords "stem cell" and "infertility". The data were analyzed using the Biblioshiny web interface in Bibliometrix, an open-source R package. The analyses were conducted under several categories: Basic data information, annual scientific production, country and institutional analysis, co-authorship and influential authors, most-cited articles, Bradford's law analysis, and Sankey diagrams.

Results: According to the findings, the United States ranks first among the countries with the most publications, while the Chinese Academy of Sciences stands out as the leading institution researching stem cell applications in infertility treatment. The journals publishing the most on the topic were identified as *Human Reproduction* and *Biology of Reproduction*. Keyword analyses revealed that recent research trends focus on spermatogonial stem cells, reproductive biology, and germline cells.

Conclusion: This study demonstrated the potential of stem cell therapies in infertility treatment and the dynamics of the scientific literature in this field. Consequently, the increasing number and diversity of studies on stem cells and infertility indicate that scientists in the field are highlighting and exploring this topic more extensively.

Keywords: Bibliometric analysis, biblioshiny, infertility, stem cell, Web of Science

Introduction

Infertility is a major health issue affecting millions of couples worldwide, limiting or preventing biological conception. The World Health Organization defines infertility as the failure to achieve pregnancy after one year or more of regular, unprotected intercourse (1,2). Globally, 10-15% of couples experience infertility, which imposes psychological, social, and economic burdens (3,4). Infertility may result from genetic, hormonal, or environmental factors, as well as age-related reproductive decline, structural anomalies, and infections (5). Alongside conventional methods and assisted reproductive technologies, innovative strategies like stem cell therapies are gaining attention (6). Induced pluripotent

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stem cells, with their self-renewal and differentiation potential, offer therapeutic promise in restoring fertility (7).

Stem cells are undifferentiated cells present in embryonic, fetal, and adult stages, capable of self-renewal, long-term proliferation, clonality, and differentiation based on the body's needs (8,9). Their versatile differentiation potential, ability to promote angiogenesis, immunomodulatory effects, and paracrine signaling make them promising candidates for infertility treatment (10). Therefore, stem cell research offers new therapeutic possibilities and hope for reproductive restoration, with growing evidence supporting the efficacy and safety of stem cells. In recent years, interest in stem cell therapies has surged, as reflected by the increasing number of publications. However, bibliometric analyses on this specific topic remain scarce. These analyses are valuable for assessing research trends, impact, and knowledge flow in a given field (11,12). The Web of Science (WoS) Core Collection is among the most widely used citation databases for these analyses, offering data on publication trends, authors, journals, institutions, countries, languages, and funding (13,14). Additionally, the Bibliometrix R package enables in-depth visual and quantitative analysis of collaboration networks, themes, and influential literature (15,16).

In this context, evaluating the role of stem cell therapies in infertility is essential to understand the scientific development in this field. This study aims to explore the evolution and impact of research on stem cell-based infertility treatment between 1982 and 2023, using bibliometric tools to reveal trends and key contributions.

Materials and Methods

This bibliometric study was based on data retrieved from the WoS Core Collection, a widely recognized citation database in academic research. The search was conducted on August 15, 2024, using the query TS = ("stem cell" AND "infertility"), targeting titles, abstracts, author keywords, and keywords plus. The search was limited to original research articles published in English between 1982 and 2024. Non-article documents (e.g., reviews, editorials, conference abstracts) were excluded, and data were downloaded in plain text format compatible with bibliometric tools.

The WoS Core Collection was chosen for its high-quality indexing, rich metadata, and compatibility with Bibliometrix and Biblioshiny used in this study. Although databases like Scopus and PubMed offer valuable data, WoS ensures consistency, reproducibility, and data integrity. Analyses included:

- **Descriptive metrics** (publication trends, citation averages)
- **Citation and productivity mapping** (top authors, articles, core journals via Bradford's Law)
- **Network analyses** (co-authorship, institutional and country collaborations)
- **Keyword co-occurrence and trend analysis** (bubble plots, Sankey diagrams)
- **Geographical and citation network visualizations** (global output maps, cluster-based citation networks)

Since the study used publicly available data from published literature, no ethical approval was required.

Results

Bibliometric Overview of the Study Period

The period covered by our study ranges from 1982 to 2024. The analyzed dataset comprises 1,710 articles from 580 distinct scientific sources (excluding books and reviews). The annual growth rate of academic publications in our field is 11.37%. The average time elapsed since the publication of the examined articles is 7.21 years, with 30.59 citations per document on average. Additionally, the total number of references obtained from the data is 57,394 (Table 1).

In our study, when analyzing the developmental trend of publications over the years, it is observed that the publication

Table 1. Details of publications between 1982 and 2024 using the keywords "infertility" and "stem cells"

Description	Main information about data	Results
Timespan		1982:2024
Sources (journals)		580
Documents		1710
Annual growth rate (%)		11.37
Document average age		7.21
Average citations per document		30.59
References		57394
	Document contents	
Keywords plus (Id)		4010
Author's keywords (De)		3172
	Authors	
Authors		8849
Authors of single-authored documents		52
	Authors collaboration	
Single-authored documents		55
Co-authors per document		7.39
International co-authorships (%)		23.33
	Document types	
Article		1710

rate, which began in 1982, remained relatively limited until the 1990s. However, in the following years, research in this field gained momentum. The number of publications reached an exceptionally high level in the 2000s and peaked at 174 in 2022 (Figure 1).

Average Citations by Year

Figure 2 shows the average citation counts of articles between 1982 and 2023. Citations generally followed a fluctuating trend, with a significant increase in 1997, surpassing 15. A decline was observed in the 2000s, followed by stabilization. An increase was observed in 2019, but a decrease was observed in 2023. The peak in the late 1990s mainly indicates that studies published during this period were heavily cited.

Sankey-based Visualization of Citation and Keyword Networks

Upon examining the Sankey diagram related to our study, it is clear that in the first column, which lists the analyzed studies cited by authors in the literature, Kanatsu-Shinohara, 2003 ranks first, followed by other studies. In the middle column, the names of researchers actively contributing to this field are displayed, positioning them at the center of the scientific network. At the top of this column is the researcher "Orwig KE". The third column shows which key topics or keywords are associated with the cited studies, with "spermatogonial stem cells" ranking first (Figure 3).

Journal-based Analysis of the Literature

Our literature searches show that the journal *Human Reproduction* (63) has the highest number of publications using stem cell and infertility keywords. This journal is followed by *Biology of Reproduction* (54) and *Fertility and Sterility* (48). The other journals listed are shown in Figure 4.

Identification of Core Resources with Bradford Distribution

The data were also analyzed using Bradford's law to show journal distribution. In Figure 5, the horizontal axis shows the logarithmic journal ranking, and the vertical axis shows the number of articles. The shaded gray area marks the core sources with the highest publication counts. Key journals include

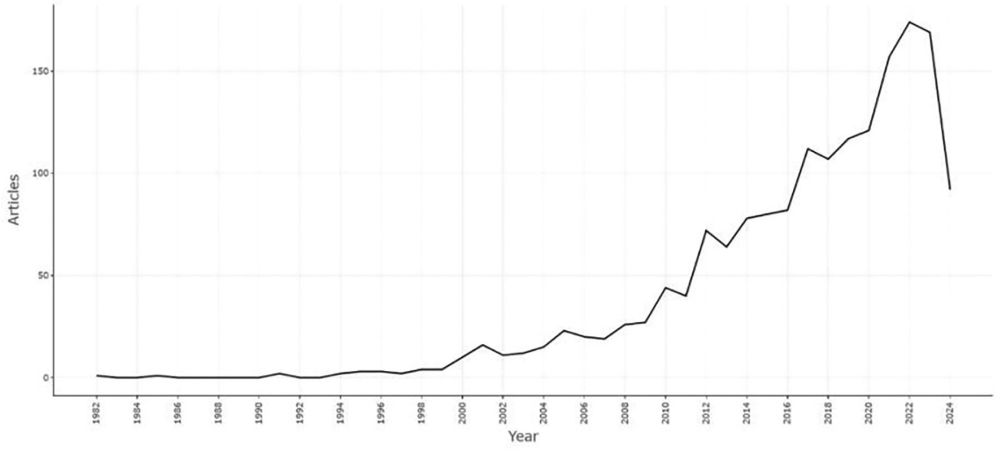

Figure 1. The numerical distribution of publications in the literature between 1982 and 2024

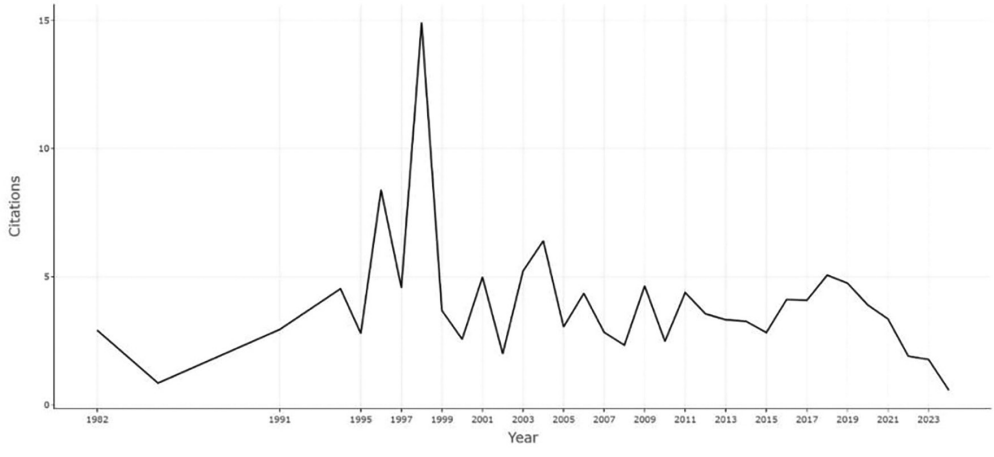

Figure 2. The distribution of the average citation counts of articles published between 1982 and 2024 by year

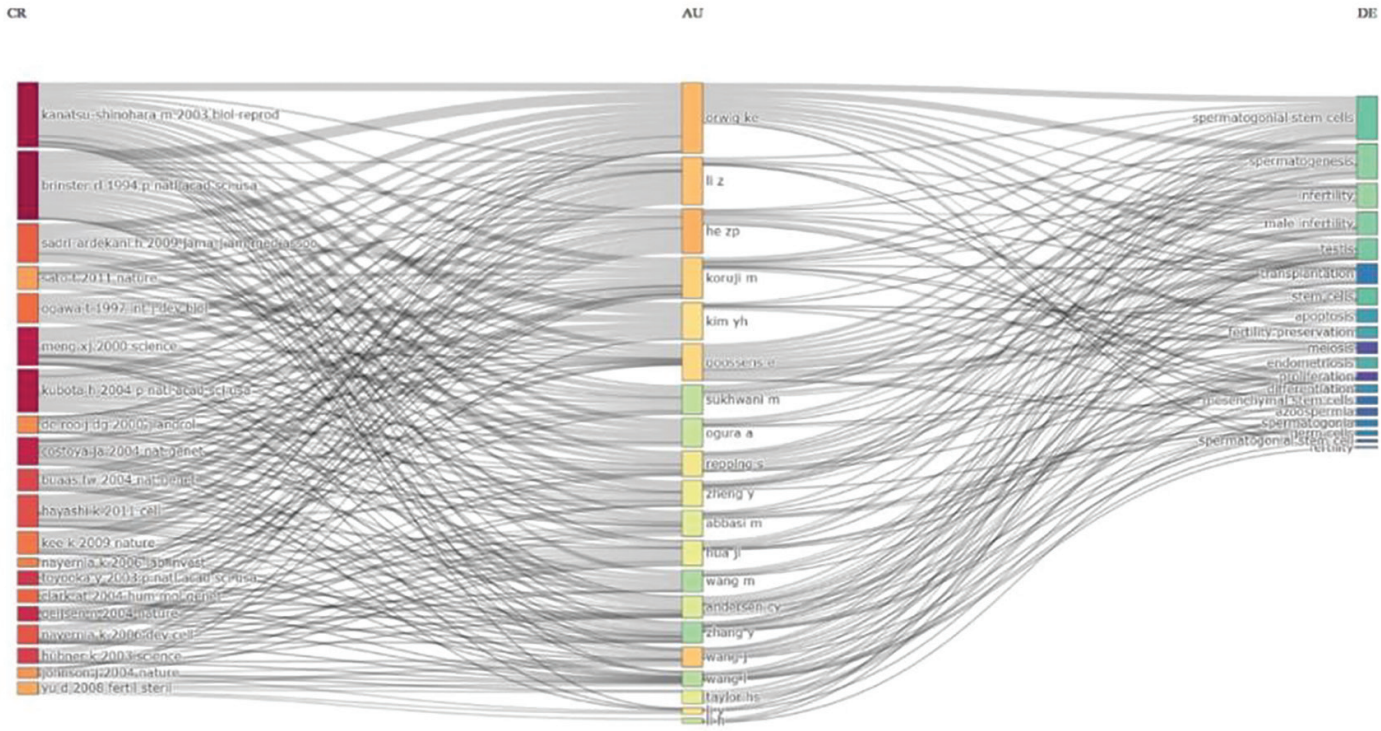

Figure 3. Three-field Sankey diagram (left column → keywords plus, middle column → authors, and right column → keywords of cited works)

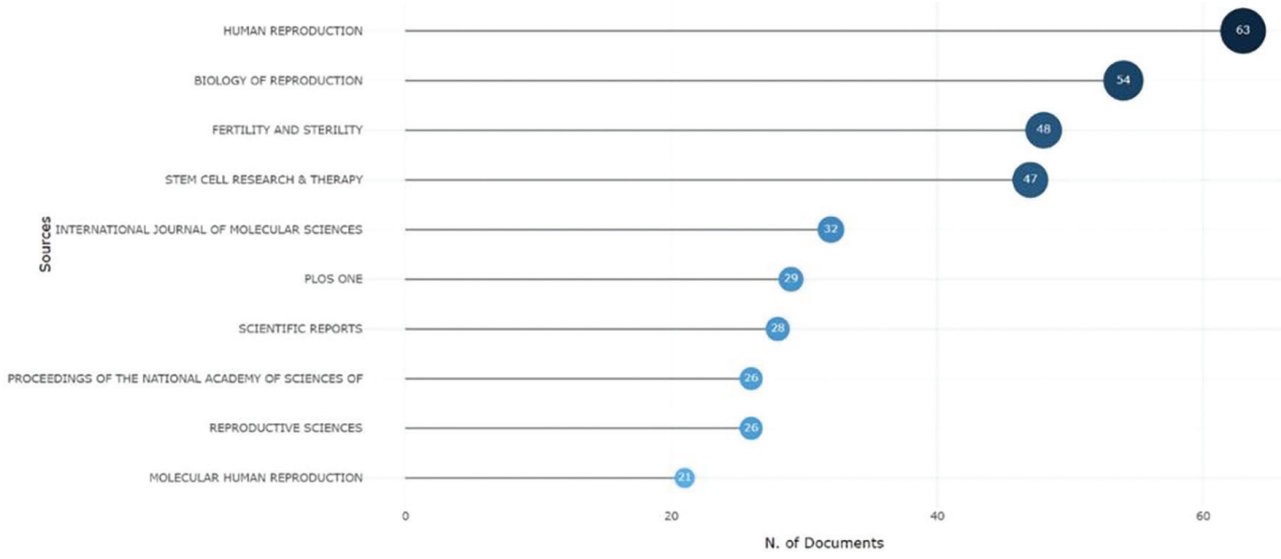

Figure 4. The top 10 journals with the highest number of publications from the literature search using the keywords stem cells and infertility

Human Reproduction, *Biology of Reproduction*, and *Fertility and Sterility*, with others listed in the figure.

Most Productive Authors in the Field

When examining the top 10 active authors with the most publications on stem cells and infertility, our research found that the researcher HE ZP (29) ranks first. They are followed by "Orwig KE" (27) and "LI Z" (22). The other active authors are shown in Figure 6.

Institutional Analysis of Research Productivity

In our study, results were evaluated not only individually for research on stem cells and infertility but also from an institutional perspective. This analysis is vital for understanding the academic activity levels and research productivity of institutions in this field. As shown in Figure 7, the Chinese Academy of Sciences and the University of California System had the highest number of publications, with 118 and 112 papers, respectively. The Tehran

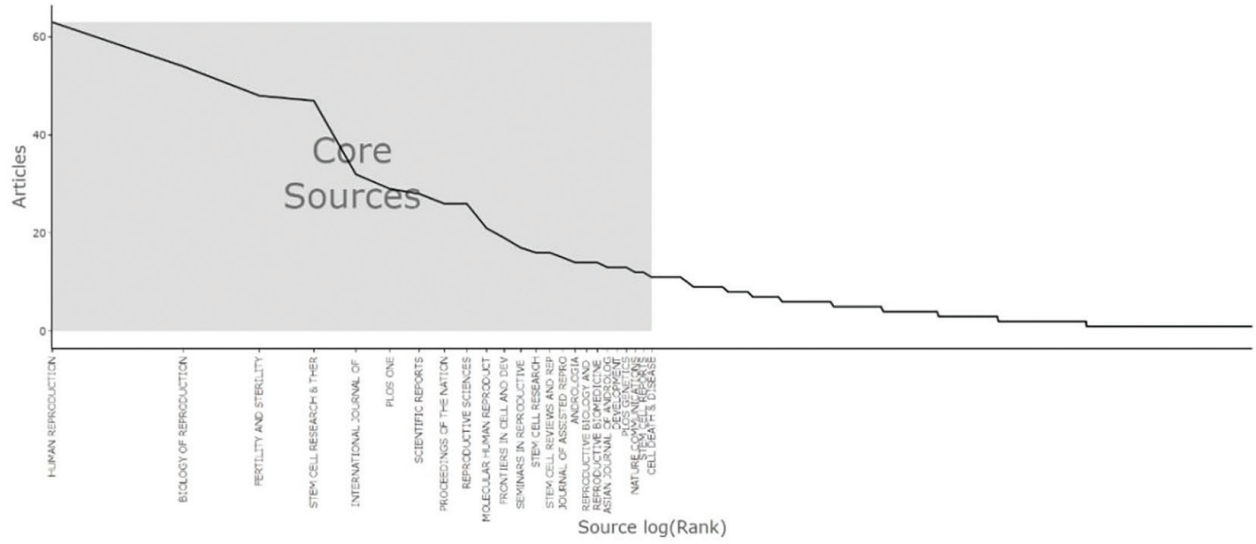

Figure 5. Core journals and article distribution in the literature according to Bradford's law

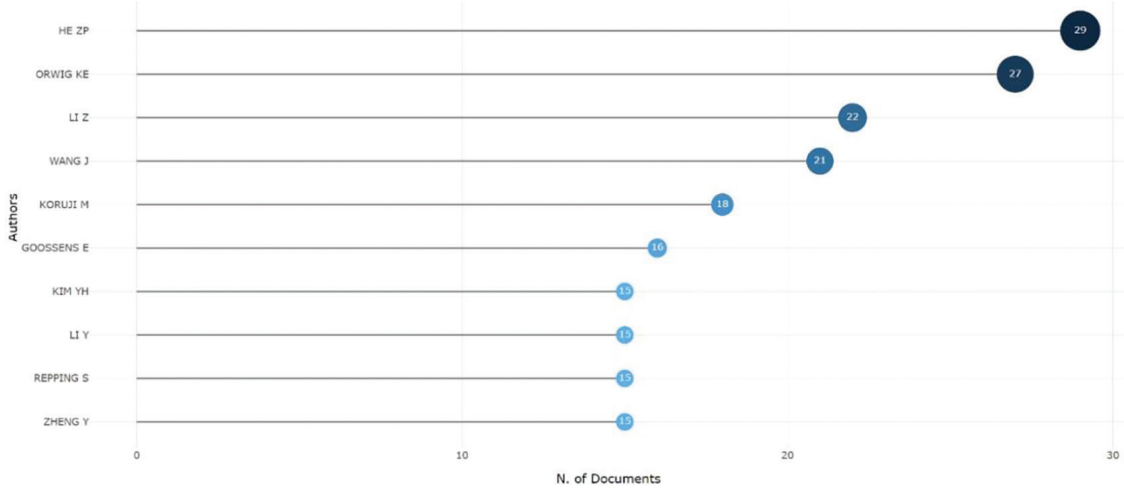

Figure 6. Top 10 authors by publications

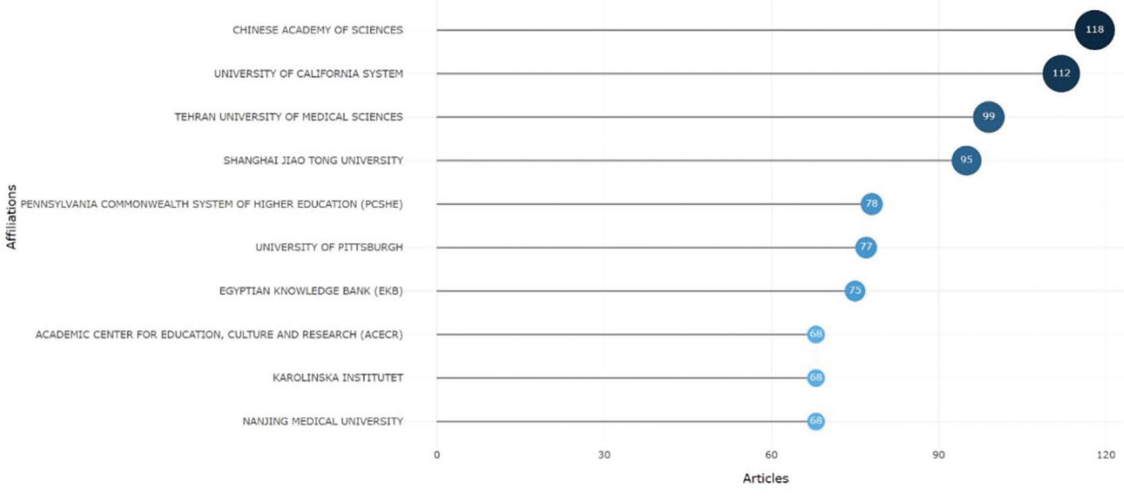

Figure 7. Top 10 publishing institutions in the field

University of Medical Sciences followed with 99 publications, ranking third. Other active institutions include Shanghai Jiao Tong University, the Pennsylvania Commonwealth System of Higher Education, and the University of Pittsburgh.

Publication Distribution by Country and International Cooperation Analysis

Figure 8 presents the distribution of corresponding authors' countries, comparing single country publications (SCP, turquoise) and multiple country publications (MCP, red). China and the United States lead in total output, with China favoring SCPs and the United States showing a higher MCP ratio. Iran ranks third mostly for its contribution of SCPs. Other countries follow in sequence, as shown in Figure 8.

Global Distribution of Scientific Research Output

Figure 9 shows a world map of global scientific production, where color intensity indicates output levels-dark blue for the highest, followed by blue, light blue, and grey. The United States and China, marked in dark blue, lead in scientific research and publications. Iran appears in shades of blue, reflecting moderate output. Countries with lower productivity are shown in lighter tones.

Term Usage Trends by Years

Figure 10 shows the frequency of specific terms in scientific research over time. The horizontal axis represents years, and the vertical axis lists popular terms. Between 2009 and 2011, terms such as "germ cell apoptosis", "human testicular tissue", and "embryo" were more common, while between 2015 and 2021, focus shifted, to "stromal cells", "expression", and "proliferation".

Citation Network Visualization and Scientific Impact Analysis

Figure 11 illustrates citation relationships and scientific impact among publications. Each node represents a study, with connecting lines indicating citation relationships. Node colors indicate different research clusters, grouping studies by topic. Larger, bold-labeled nodes such as "Brinster and Zimmermann (20) 1994" represent highly cited, influential works. Numerous lines from a node-for example, "Brinster and Zimmermann (20) 1994"-highlight that this study has been widely referenced cited.

Geographical Distribution of Scientific Cooperation Networks between Countries

Figure 12 presents a bibliometric map of global scientific collaboration. Lines represent country-to-country collaborations, with thickness indicating their strength. The United States, China, Germany, and the United Kingdom show the most extensive networks, highlighting their central role in global research.

Discussion

Infertility is a significant global health issue, affecting millions and arising from diverse genetic, hormonal, and environmental factors (17). Recently, stem cell-based therapies have emerged as promising alternatives to conventional treatments. With their self-renewal and differentiation abilities, stem cells offer potential for regenerating reproductive tissues (18). This

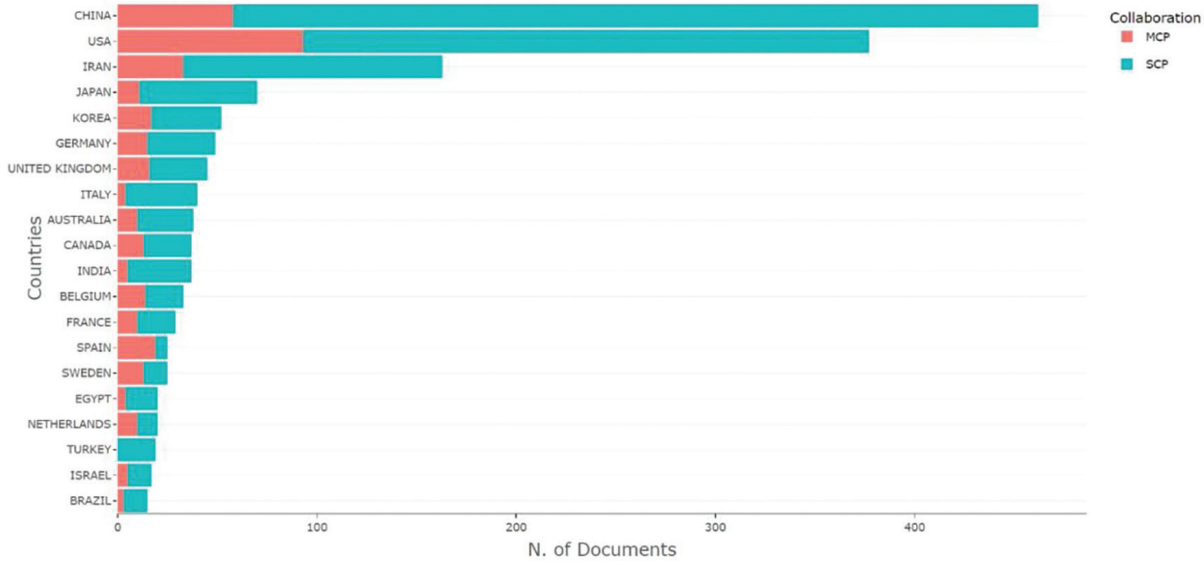

Figure 8. National (SCP) and international (MCP) distribution of scientific publications made by countries

SCP: Single country publications, MCP: Multiple country publications

therapeutic potential has increased scientific interest in the field. Bibliometric analyses offer key insights into research trends in stem cell-based infertility treatments, identifying influential studies, emerging topics, and research gaps to guide future work.

This study examines the role of stem cell therapies in infertility treatment through bibliometric analysis. Results show a notable rise in related research, thus highlighting its growing potential in reproductive medicine. Stem cell studies have gained broad national and international attention, with increased collaboration accelerating scientific progress in this field.

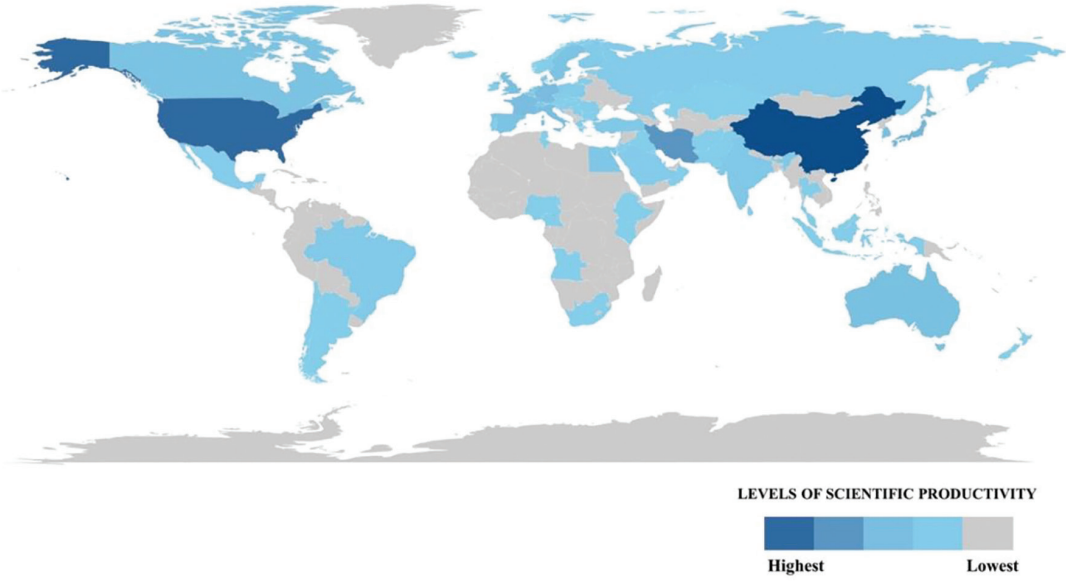

Figure 9. A color-coded world map showing the amount of scientific production of countries

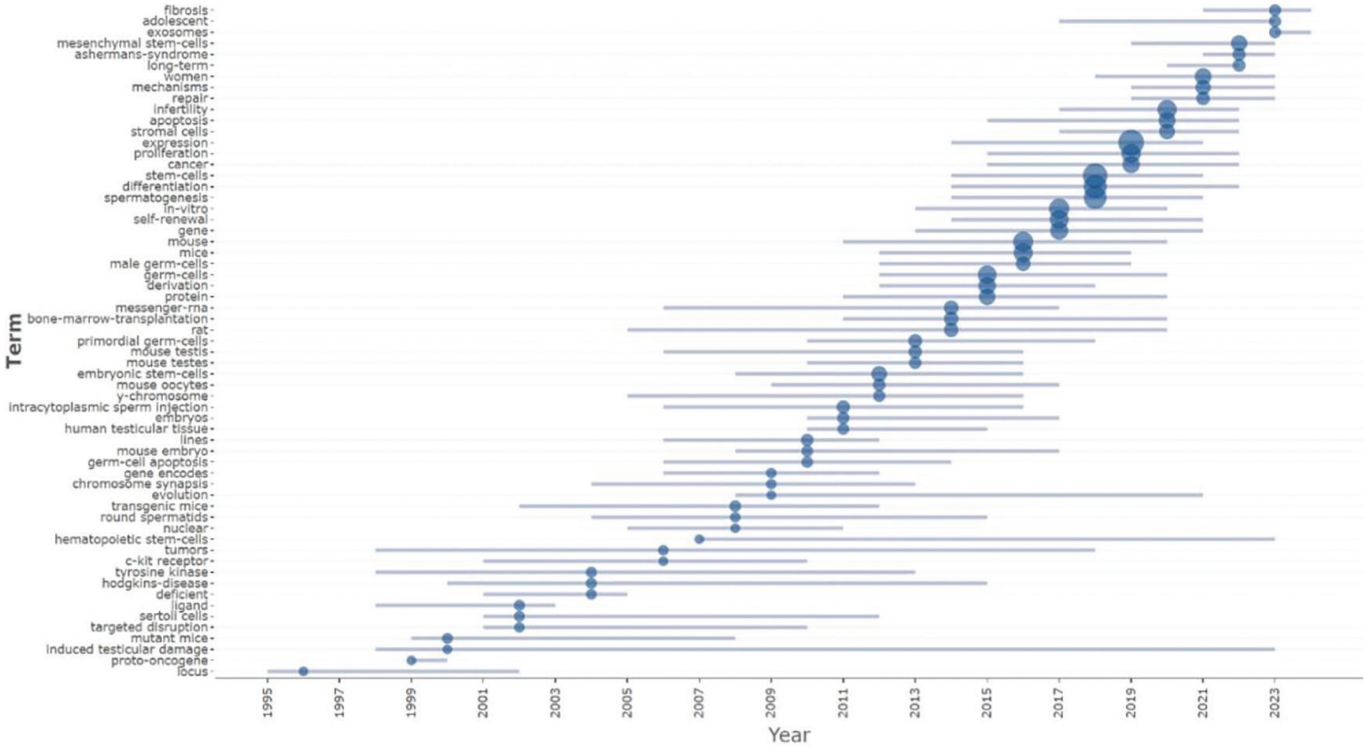

Figure 10. Popular topics and keywords in infertility and stem cell research from 1982 to 2024. The lines indicate the emergence of keywords, while the size of the bubbles represents the frequency of their usage over the years

The distribution of publications over the years shows that stem cell research, which began in 1982, remained limited until the 1990s. A marked increase followed, likely reflecting the growing recognition of stem cell therapy as a promising approach for infertility treatment. The sharp rise in the 2000s suggests a peak in scientific interest in this field (Figure 1).

The analysis of citation counts shows notable fluctuations over the years. A significant increase occurred in 1997, indicating heightened attention from the scientific community. However, this was followed by a period of stabilization, and a decline has been noted in more recent years (Figure 2). This decrease is likely due to the limited time these newer studies have had to gain academic visibility. In biomedical research, it often takes time for new findings to accumulate citations. Moreover, open-access policies and shifts in publishing practices have likely influenced citation dynamics. While open access increases article availability, it may also alter citation patterns. Changes in research priorities have also played a role. For instance, the transition from classical stem cell therapies

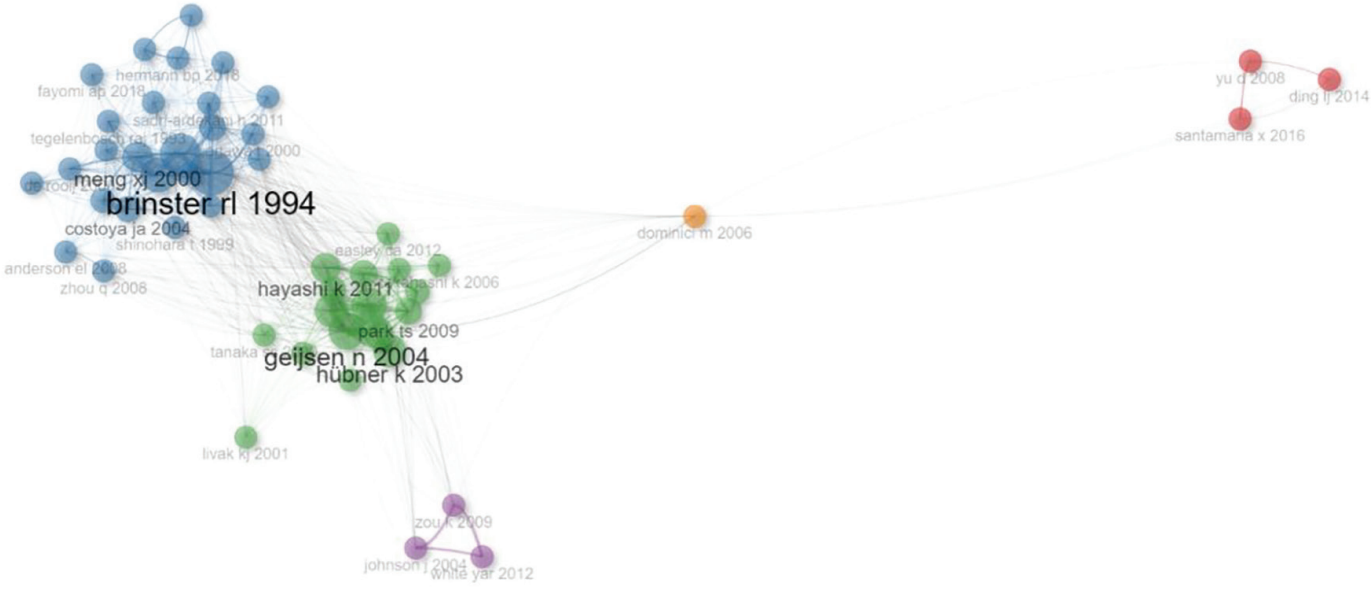

Figure 11. A network visualization depicting citation relationships and scientific impact among academic publications

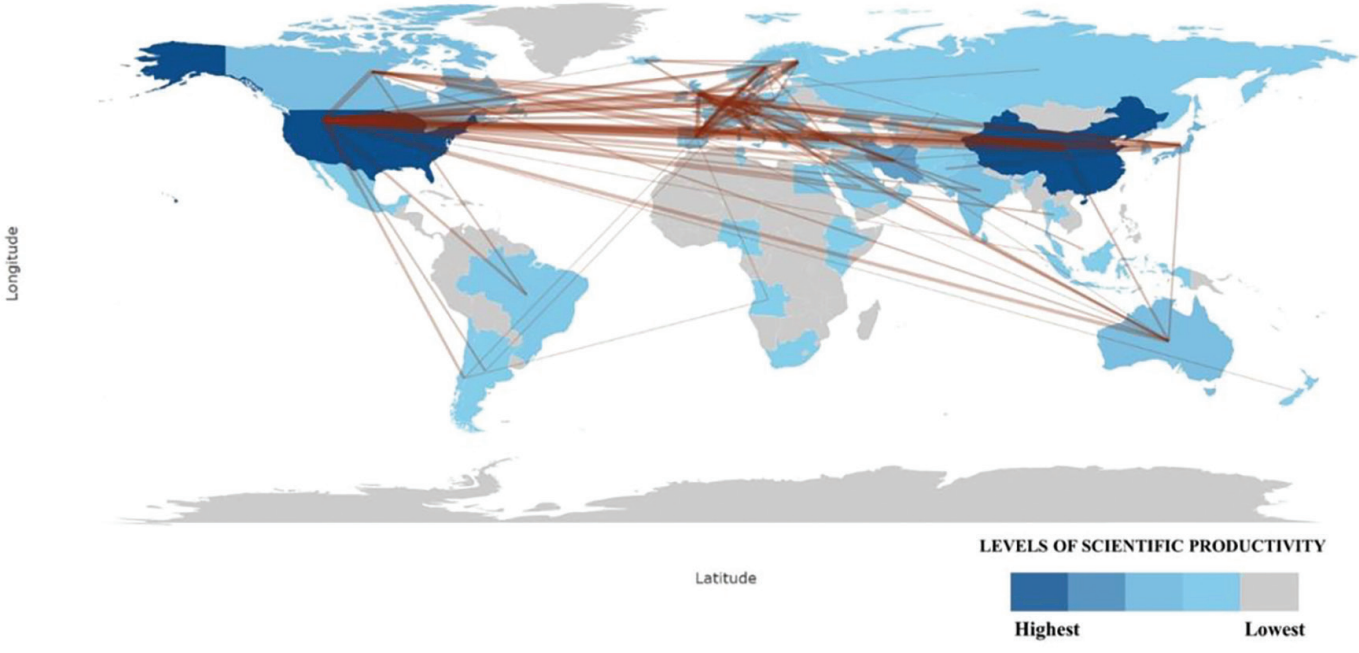

Figure 12. Global collaboration networks among authors

to newer biotechnological approaches may have reduced interest in certain areas, contributing to the observed decline. These trends underscore the need for deeper evaluation of the academic impact of recent studies (19). Citation network analyses further reveal that some works have become foundational in the field. Notably, Brinster and Zimmermann's (20) 1994 study is frequently cited in research on stem cells and infertility (Figure 11) (20). Brinster and Zimmermann's (20) 1994 study introduced one of the first experimental findings on spermatogonial stem cell transplantation, offering a pioneering approach in the fields of stem cell biology and infertility treatment. By providing key insights into the functional integration of germ cells during spermatogenesis, the study has become a foundational reference both conceptually and methodologically. As an early and influential contribution to the field, the study continues to receive frequent citations.

The Sankey diagram analysis visually illustrates the active researchers, key topics, and foundational elements of the literature on stem cells and infertility. This method reveals how the research network is structured and highlights influential studies and authors in the field (21). It enables researchers to map existing knowledge, position their work within this framework, and plan future studies accordingly. Among the frequently associated terms, spermatogonial stem cells (SSCs) stand out. The analysis also shows that Orwig KE holds a central position in this research area (Figure 3). The rising interest in SSCs reflects a growing focus on regenerative strategies for male infertility. SSCs are particularly promising for restoring spermatogenesis in prepubertal cancer survivors and patients with non-obstructive azoospermia. Recent advances in cell isolation, *in vitro* expansion, and transplantation techniques have strengthened the foundation for personalized fertility treatments. Nonetheless, several challenges remain, including safety concerns, ethical issues, and regulatory limitations. Future research should aim to bridge the gap between experimental data and clinical application, with attention to both efficacy and long-term safety.

Bradford's law is used to examine how scientific publications on a specific topic are concentrated around a core group of sources. It also identifies journals that publish fewer articles, offering insights into the distribution and relevance of sources within the field (22). This analysis helps determine the most cited and influential core journals in the literature. According to this principle, research on stem cells and infertility is clustered in specific journals. The "Core Sources" section of the figure, shown in grey, highlights these key journals. Notably, *Human Reproduction*, *Biology of Reproduction*, and *Fertility and Sterility* appear as the most prolific and influential sources (Figure 4). Their high publication volume reflects both the academic importance and the focused interest in this area.

An analysis of international collaboration networks shows that the United States and China lead in scientific output and are highly involved in global partnerships. In contrast, countries like Iran appear to focus more on national-level research, with limited international engagement (Figures 8 and 9). This highlights both the importance of global scientific collaboration and the unequal distribution of research activity. The concentration of output in the United States and China may limit the generalizability of findings. Studies conducted in specific geographic, genetic, or socioeconomic contexts may not fully reflect broader population needs. This imbalance also points to a lack of diverse perspectives and may constrain innovation in stem cell therapies for infertility. Promoting equity in research funding and fostering collaboration with underrepresented regions are essential for a more inclusive understanding of the field. Additionally, the global map of scientific output reveals disparities in research productivity and the dominant influence of certain countries (Figure 9). For bibliometric studies, such visualizations help explore geographic patterns and the underlying factors, including differences in funding, education systems, and economic development.

Bibliometric analyses tracking term frequency over time reveal shifts in research trends and highlight topics that gain prominence during specific periods. These analyses examine how the use of key terms evolves, offering insight into changing focus areas within the field. In recent years, terms such as stromal cells, expression, and proliferation have appeared more frequently, suggesting increased interest in these topics (Figure 10). Such data can inform future studies by identifying emerging areas that warrant further investigation.

Citation networks illustrate the relationships, connections, and scientific impact among academic publications (Figure 11). These maps help identify pioneering studies, track the evolution of specific research areas, and reveal links between different disciplines. They also point to influential works and highlight areas needing further exploration, offering opportunities for new research and collaboration. Similarly, the global collaboration map shows that international partnerships in this field are widespread and not limited by geographic proximity, emphasizing the global nature of scientific research (Figure 12).

In recent years, although there has been a noticeable increase in studies focusing on SSCs and stromal cells, further research is needed to translate experimental approaches into clinical applications. In particular, there is a significant lack of long-term follow-up studies that evaluate the safety, efficacy, and ethical dimensions of stem cell-based infertility treatments. Additionally, the geographic imbalance in research productivity highlights the need for studies with broader inclusivity and regional diversity. Future research is also encouraged to explore the integration of stem cell-based approaches with gene editing

technologies and assisted reproductive platforms. Addressing these gaps and achieving comprehensive progress in the field will require interdisciplinary and multicenter studies conducted through global collaborations.

Study Limitations

This study has several limitations that should be acknowledged. First, it is limited to English-language publications indexed in the WoS database. This may introduce a language and indexing bias, potentially excluding relevant research published in other languages or included in different academic databases, thus underrepresenting the diversity of global perspectives and findings. Additionally, while the analysis relied solely on published literature, excluding grey literature and unpublished data, the latter may contain valuable insights and contribute to a more comprehensive understanding of the field.

Another inherent limitation of bibliometric analysis is its inability to assess the methodological rigor or clinical applicability of the included studies. While this study successfully identifies influential authors, research trends, and key publication outlets, it does not evaluate the scientific quality, experimental validity, or translational relevance of the cited works. Therefore, the results should be interpreted as a macro-level overview of the research landscape, rather than a critical appraisal of individual studies.

Moreover, the notable concentration of scientific output in a few countries, particularly the United States and China, highlights an imbalance in global research contributions. This geographic concentration may limit the generalizability of findings and underscores the need for more inclusive international collaboration and support for underrepresented regions. Addressing these limitations in future research through systematic reviews, meta-analyses, and broader database coverage will strengthen the transparency, inclusivity, and analytical depth of bibliometric studies in this domain.

Conclusion

This study highlights the potential of stem cell therapies in infertility treatment and provides a bibliometric analysis of the scientific literature. While the United States and China dominate research output, this geographic concentration underscores the need for greater inclusivity and contributions from underrepresented regions to achieve a globally relevant understanding of stem cell therapies.

Key themes like spermatogonial and stromal stem cells highlight a focus on therapeutic applications. However, gaps remain in addressing diverse populations and generating long-term safety data, limiting the generalizability of results. Limited input from underrepresented regions also restricts innovation diversity.

Tackling these issues requires balanced funding, inclusive policies, and global collaboration. Supporting studies with neutral or negative results and prioritizing underrepresented regions can reduce publication bias and promote more equitable progress in stem cell therapies for infertility.

Ethics

Ethics Committee Approval: Not necessary.

Informed Consent: Not necessary.

Footnotes

Authorship Contributions

Concept: O.A.A., Ç.G., F.A., Design: O.A.A., Ç.G., Data Collection or Processing: Ç.G., Analysis or Interpretation: O.A.A., Ç.G., F.A., Literature Search: O.A.A., Ç.G., F.A., Writing: O.A.A., Ç.G., F.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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