Uncovering a Decade of Research Trends in Glucocorticoid-Induced Osteoporosis: A Bibliometric and Visualization Analysis (2014-2023)

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Abstract:

Glucocorticoid-induced osteoporosis (GIOP) is a common consequence of prolonged glucocorticoid therapy. GIOP is characterized by a significant decrease in bone mineral density, leading to an increased risk of fractures and associated morbidity. As a complex medical condition, it has been the subject of extensive research over the years. To gain insight into the evolving landscape of research on GIOP, a bibliometric analysis can provide a comprehensive overview. This study aims to shed light on the importance of GIOP as a critical research area, drawing attention to the need for further investigation, the identification of knowledge gaps, and the promotion of interdisciplinary collaboration in the ongoing battle against GIOP. Every piece of information was gathered from the SCOPUS. All original research articles regarding GIOP from 2014-2023 were retrieved. VOSviewer was used to analyze the distribution of countries, institutions, journals, authors, and keywords. We are identifying patterns throughout the domain by creating maps of co-occurrence keywords and finding high-volume keywords. From 2014 to 2023, there were 494 pertinent articles published, with the highest annual publication count recorded in 2021. China emerged as the leading country in this field, contributing 198 publications, while Guangdong Medical University led as the top institution with 14 publications. "Bone" stood out as the journal with the most studies and cited journal. Fu Q., Hofbauer L C., Liang D. and Ren H. are the most prolific author in this field with each contributing 7 articles. The cooccurrence classification of glucocorticoid-induced osteoporosis field development map yields 9 clusters. Osteoporosis, glucocorticoid, and glucocorticoid-induced osteoporosis dominate the network. The findings of this bibliometric study offer valuable insights into the state of GIOP research over the last decade. This information enables researchers to promptly identify the current focal points and emerging trends within this field.

1 INTRODUCTION

Glucocorticoids, both natural hormones and synthetic drugs, primarily interact with the glucocorticoid receptor, exerting anti-proliferative, anti-inflammatory, vasoconstrictive effects, and immunosuppressive. They find extensive use in

treating acute and chronic inflammatory conditions, lymphoproliferative diseases, mitigating chemotherapy or radiotherapy side effects, and preventing organ transplant rejection. Additionally, they are employed as chronic replacement therapy for individuals with adrenal insufficiency (Laurent et al., 2022). Approximately 1% of adults, especially older individuals, use glucocorticoids chronically. Based

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on observational studies, oral glucocorticoid use is about 3% in older man and post-menopausal women (Fadet et al., 2015).

However, chronic exposure to glucocorticoids elevates the risk of adverse effects, including bone loss leading to osteoporosis and an increased susceptibility to fractures. Drug-induced secondary osteoporosis occurs most commonly due to glucocorticoid-induced osteoporosis (GIOP). There is rapid bone loss in the early phase followed by a slower but continuous decline on initiation of glucocorticoid therapy. In glucocorticoid-induced osteoporosis (GIOP), there is a notably increased risk of vertebral fractures, with those using high doses facing a fivefold higher risk. Moreover, the risk of hip fractures rises by 130%, and non-vertebral fractures exhibit a 65% increase (Balasubramanian et al., 2018).

The economic burden of GIOP is not well-defined but is believed to be substantial. Fracture risk escalates early in glucocorticoid therapy. Frequently, these adverse effects manifest before a notable decline in bone mineral density (BMD) becomes evident (Laurent et al., 2022). Discontinuation of glucocorticoids may lead to a partial recovery of BMD and a reduction in fracture risk after about a year. Fractures in glucocorticoid-induced osteoporosis (GIOP) often happen at BMD levels higher than those observed in postmenopausal osteoporosis. Studies suggest that both the current daily dose and high cumulative doses are risk factors for fractures. Long-term glucocorticoid users may experience fracture prevalences of 30-50% (Weinstein, 2011). The severity and risk of fractures in osteoporosis associated with endogenous Cushing syndrome are correlated with the duration and intensity of hypercortisolism (Belaya et al., 2015).

The underlying mechanisms of glucocorticoidinduced osteoporosis (GIOP) are intricate, involving direct effects on bone cells (such as osteocytes, osteoclasts, and osteoblasts) and indirect effects through the gonadotropic axes and suppression of the somatotropic. Moreover, there is a reduction in the absorption of calcium in the intestines, and the development of glucocorticoid-induced myopathy and cataracts, increasing the susceptibility to falls (Weinstein, 2011). Glucocorticoids contribute to the promotion of osteoclastogenesis and prolong the lifespan of osteoclasts. They additionally hinder osteoblastogenesis, induce adipogenesis, and initiate apoptosis in osteoblasts and osteocytes. These impacts are, to some extent, controlled by the inhibition of Wnt agonists and the increased expression of Wnt signaling inhibitors, such as Dkk1 and sclerostin (Schepper et al., 2020). This not only

results in diminished bone mass but may also impact the unmineralized bone matrix, potentially elucidating their effects beyond bone mineral density (BMD) (Vestergaard, 2020). Recent preclinical studies have also suggested that an excess of glucocorticoids disrupts the intestinal microbiota and the natural circadian rhythm of glucocorticoids, further contributing to the adverse effects on bone health (Schilperoort et al., 2021)

exploration of glucocorticoid-induced osteoporosis (GIOP) has a rich history spanning nearly 90 years, dating back to the initial recognition of the harmful impacts of glucocorticoids (GC) on bone (Lukert and Raisz, 1990). Throughout the years, numerous clinical and fundamental investigating glucocorticoid-induced osteoporosis (GIOP) have been carried out. However, despite the extensive research, solely one bibliometric analysis concentrating on GIOP has been previously documented. This study utilized the Web of Science Core Collection (WoSCC) as the primary literature source, employed CiteSpace for data analysis, and concentrated on the period from 2012 to 2022 (Jiang et al., 2022).

Bibliometrics, a statistical and mathematical tool, is utilized to gain insights into the trends, current status, and future directions of a particular research field by quantitatively assessing factors such as the geographical distributions and number of papers. (Gasparyan et al., 2018). Additionally, bibliometric analysis can offer valuable references for government policy formulation, guiding funding decisions, and recognizing scientific researchers contributions (Qiu et al., 2018). Because of these benefits, bibliometric analysis has been extensively utilized in diverse medical research areas, encompassing osteoporosis, male osteoporosis, postmenopausal osteoporosis, and beyond. (Qiu et al., 2018; Gao et al., 2020; Wu et al., 2021).

Given the recent developments in GIOP research, there is a pressing need for a continuous bibliometric analysis in this field. The present study seeks to underscore the significance of GIOP as a crucial research area, emphasize the necessity for further exploration, pinpoint knowledge gaps, and foster interdisciplinary collaboration in the ongoing efforts against GIOP. To achieve these objectives, the authors utilized Scopus as the literature source and employed VOSviewer as the analytical software.

2 MATERIALS AND METHODS

2.1 Data Collection

The Scopus database was utilized for the identification of publications subjected to analysis. The search query involved the keywords: TITLE-ABS-KEY (glucocorticoid-induced osteoporosis) AND PUBYEAR > 2013 AND PUBYEAR < 2024 AND (LIMIT-TO (PUBSTAGE, AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (SRCTYPE, "j")) AND (LIMIT-TO (EXACTKEYWORD, "Article")). The data considered for examination spans the timeframe from 2014 to 2023 based on updates corresponding to timestamps. Additionally, the outcomes of the search were not only preserved as Scopus documents for bibliometric scrutiny but were also stored in Excel documents, ensuring that the titles of the documents contained pertinent keywords. This supplementary step was implemented to facilitate manual searches when deemed necessary.

2.2 Research Tools

Data pertaining to eligible documents, meeting the specified criteria, encompassed details such as journal, language, author, title, abstract, keywords, publication years, affiliation, citation count, and document type. This information was exported in CSV format, with the data capture date set at November 25, 2023. VOSviewer (version 1.6.20) was employed for the analysis of Co-occurrence. Two standardized weight attributes, identified as "Total Link Strength Attribute" and "Link Attribute", were applied throughout the analysis (Stephan, Veugelers, Wang, 2017).

3 RESULTS

3.1 Research Developments in the Glucocorticoid-Induced Osteoporosis

A total of 494 publications were identified after eliminating duplicate entries. The surge in scientific publications within the glucocorticoid-induced osteoporosis field reflects a global uptick in the number of researchers, as depicted in Figure 1. Between 2014 until 2023, there was a discernible escalation in glucocorticoid-induced osteoporosis

research, with the pinnacle occurring in 2021. Noteworthy spikes were observed in 2018 and 2021, marking respective increases of 21.27 percent and 15 percent compared to the preceding year.

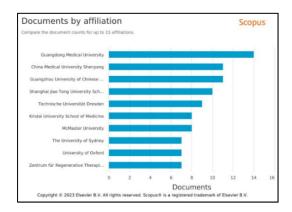


Figure 1: Trend research of GIOP in the worldwide for 10 years

3.2 The Most Profilic Authors

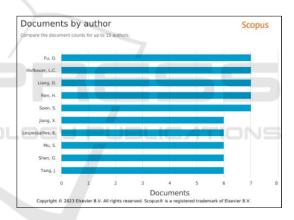


Figure 2: Top Ten Contributing Authors in the area GIOP research worldwide

Fu Q., Hofbauer LC., Liang D. and Ren H., emerge as the most prolific authors in this domain, each contributing to seven articles. They are followed by Tang, J., Lespessailles, E., Jiang, X., Shen, G., and Mu, S., each having contributed to six papers.

3.3 The Most Profilic Affiliations

Guangdong Medical University stands out as the top contributor in this field, having authored fourteen articles. Following closely are China Medical University Shenyang and Guangzhou University of Chinese, each with eleven articles to their credit. Subsequent contributors include Shanghai Jiao Tong University, Technische Universitat Dresden, Kindai University School of Medicine, McMaster University, The University of Sydney, University of Oxford, and Zentrum fur Regenerative Therapies.

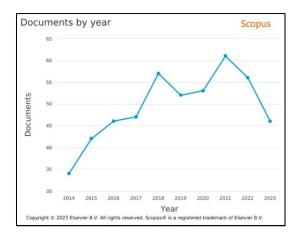


Figure 3: Top Ten Affiliations in the area of GIOP research worldwide

3.4 Top Ten Countries

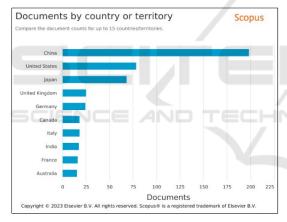


Figure 4: Top Ten Countries in the area of GIOP research worldwide

China emerges as the primary contributor in this domain, having authored 198 articles. The United States and Japan follow in second and third place, with 78 and 68 articles, respectively.

3.5 Top Ten Sponsors

The primary contributor in this area is the National Natural Science Foundation of China, with 97 documents indexed in Scopus. Following in second place is the National Institutes of Health, with 24 documents.

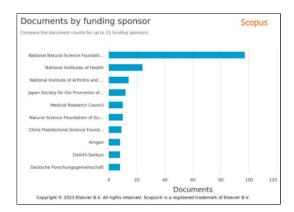


Figure 5: Top Ten Funding Sponsors in the area of GIOP research worldwide

3.6 Subject Area

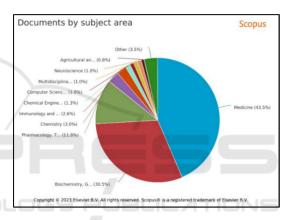


Figure 6: The most subject area of GIOP.

The predominant field of study in glucocorticoid-induced osteoporosis research within Scopus journals is medicine, constituting 43.5%. Subsequently, there is Biochemistry, Genetics, and Molecular Biology, constituting 30.5%, along with Pharmaceutics, Toxicology, and Pharmacology, holding a share of 11.8%.

3.7 Top Source by Year

From 2014 to 2023, Bone held the leading position, publishing 26 articles, followed by Osteoporosis International and Journal of Bone and Mineral Metabolism with 19 and 16 articles respectively. During 2014-2023, the number of articles accepted from each source fluctuated. The largest increases were recorded by Bone sources in 2014-2015 and 2019-2020.

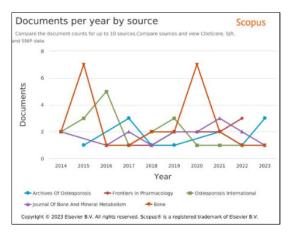


Figure 7: Top Source by year in the area of GIOP research worldwide

3.8 Topic Area Visualization Using Vosviewer

The depiction of keywords associated with research themes on glucocorticoid-induced osteoporosis was automatically represented as circles in Vosviewer. The size of each circle corresponds to the significance of an item or keyword, expanding in size with increased frequency. Varying colors were assigned to circles within clusters (van Eck and Waltman, 2014).

The outcome was derived through the utilization of Vosviewer, which employed the frequency of author keywords based on bibliographic data. A minimum occurrence threshold of 4 was set, resulting in a pool of 1033 keywords, of which only 65 met the specified condition. After conducting the analysis, nine separate clusters were recognized to depict trends within the research sector of glucocorticoid-induced osteoporosis, each characterized by a distinct color.

The gathered keywords were categorized into these nine clusters, and as anticipated, "osteoporosis" stood out prominently. Figure 8 in the network visualization illustrates the interconnections among the examined issue areas, delineating the relationships between the clusters. Each cluster encompasses numerous keywords that exhibit substantial coherence within the map's structure.

In each cluster, distinct frequent instances of keywords illustrate the predominant research subjects investigated in prior studies. The top three clusters are marked by the most recurring keywords, with Cluster 1 highlighting the terms "osteoporosis" (187) and "glucocorticoids" (65) as the most prevalent. In the second cluster, "glucocorticoid-induced osteoporosis" (112) holds dominance.

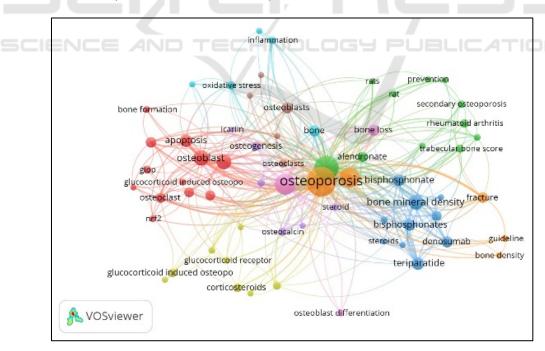


Figure 8: Network Visualization of GIOP field publication co-occurrence map using Vosviewer.

4 DISCUSSIONS

From our current study, 494 publications on Glucocorticoid-induces Osteoporosis indexed in the Scopus database were analyzed. As the most frequently occurring keyword, "Osteoporosis" has a strong relationship with "Glucocorticoid" and "Glucocorticoid-induced Osteoporosis". The analysis highlighted two key focal points: the pathomechanism and treatment of Glucocorticoid-induced Osteoporosis (GIOP).

Extensive research has been conducted on the effects of glucocorticoids in triggering osteoporosis, and Vosviewer analysis results show a total of 76 articles with "Glucocorticoid" as the main keyword. In addition, Glucocorticoid is interconnected with other research topics, with a total of 146 total link strength, making it an important research trend, especially regarding its relationship with osteoporosis, especially secondary osteoporosis. Notably, the keyword "Glucocorticoid" ranks third in frequency after "osteoporosis" and "Glucocorticoid-induced osteoporosis".

The use of glucocorticoids has seen an increase in various countries over the past two decades. However, this rise is coupled with inappropriate usage (Luo et al., 2022). In France, the prescribing rate of oral glucocorticoids exceeded 17%, but a substantial portion of these prescriptions was deemed inappropriate (Benard-Laribiere et al., 2017). Similarly, India reported that out of 113 patients, 88.4% of glucocorticoid use was considered inappropriate, involving improper diagnoses and indications not aligned with clinical standards and evidence-based practice guidelines (Masih et al., 2015). Furthermore, systemic glucocorticoids are utilized in more than 11% of cases of acute respiratory infections in the United States (Dvorin et al., 2018). China also experiences prevalent inappropriate glucocorticoid use, particularly in primary care institutions, where a study revealed that 63.5% of inappropriate prescriptions in 27 primary care facilities involved glucocorticoids (Luo et al., 2022). This trend raises concerns about potential adverse effects, particularly the development of secondary osteoporosis.

The analysis indicates a notable surge in the impact of glucocorticoids on osteoporosis in 2021, possibly attributed to the COVID-19 pandemic. Glucocorticoids are frequently employed as part of the treatment regimen for inflammation associated with COVID-19 (Lindou-Renalt et al., 2022).

Fracture stands out as the most severe complication arising from osteoporosis. Projections

indicate a substantial increase in the global incidence of hip fractures by 2050, with an anticipated rise of 240% in women and 310% in men (Gullberg, Johnell, and Kanis, 1997). In Europe, fragility fractures stand as the fourth most prevalent cause of chronic illnesses, trailing ischemic heart disease, dementia, and lung cancer (Hernlund et al., 2013). The top five countries contributing to the incidence of osteoporosis worldwide are India, China, the United States, Japan, and Germany (Shen et al., 2022). This aligns with the distribution of countries that prioritize research on osteoporosis, particularly glucocorticoid-induced osteoporosis (GIOP). China takes the lead, followed by the United States and Japan in subsequent positions.

This analysis thoroughly investigated publications focusing on glucocorticoid-induced osteoporosis (GIOP) using data from Scopus. However, it is important to recognize certain limitations in this study, which offer valuable insights for future research endeavors. Primarily, this study exclusively relied on English-language journals, potentially overlooking significant contributions countries with large populations of from glucocorticoid users or osteoporosis sufferers, such as India. This limitation stems from the exclusion of journals published in local languages from the analysis. Additionally, the study was constrained by the inherent limitations of the selected software. To enhance the examination of result variations and the visual presentation of additional data, the use of supplementary software may prove beneficial for future bibliometric analyses.

5 CONCLUSIONS

In summary, this investigation focused on articles related to Glucocorticoid-Induced Osteoporosis (GIOP) published from 2014 to 2023. The study delineates the temporal distribution, emphasizing notable countries, institutions, authors, and journals. It also outlines primary reference sources and conducts a keyword analysis. The research landscape in this domain has displayed stability in recent years, with prominent areas of interest revolving around the pathogenesis and treatment of GIOP. Looking ahead, there is a call for increased basic and preclinical in vivo research, particularly exploring potentially effective drugs for GIOP. Additionally, a heightened emphasis on high-quality clinical trials is warranted. The outcomes of this bibliometric study offer valuable insights into the status and evolving trends of GIOP research over the past decade. This

information can aid researchers in swiftly identifying key focal points and contemporary frontiers, thereby fostering further advancements in the field.

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