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## **Bibliometric analysis: Effect of vitamin d in adolescent girls with polycystic ovary syndrome (2005-2022)**

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**Abstract**--The study's main objectives are to highlight and properly assess information about the work done in various dimensions suggesting the impact of Vitamin D deficiency on Polycystic ovary syndrome (PCOS) patients, to suggest the current state of knowledge, and to provide an exhaustive and unbiased assessment of the latest advances, as well as areas in need of improvement, concerns, and possible future research paths. Researchers used the programme R and the bibliometrix codes to conduct a descriptive bibliometric analysis and generate a matrix including all of the documents. The information was gathered from the PubMed database and the entire database between 2005 and 2022 was structured on the phrase "PCOS." Our final dataset consisted of 312 publications. We discovered a link between Vitamin D therapy and a variety of other probable PCOS treatments. The driving themes were found to be connected to "insulin resistance," "dietary supplements," and the "double blind method." In the current scenario research on Anti-mullerian hormone and follicle stimulating hormone investigations have gained a lot of traction. This paper gives a full grasp of the bibliometric parameters that link Vitamin D insufficiency to PCOS patients, and it can aid scientific research in this area.

**Keywords**--Asian girls, PCOS, anti-mullerian hormone, follicle stimulating hormone, human insulin.

## Introduction

Polycystic ovary syndrome (PCOS) is a prevalent female endocrine condition that affects 6-12 % of women of reproductive age across the world [1-3]. Menstrual irregularity, anovulatory infertility, hyperandrogenism, and obesity are among the symptoms, as are metabolic dysfunctions such as insulin resistance, type 2 diabetes, and dyslipidemia [4-8]. These symptoms can have a significant influence on a patient's quality of life and health. However, due to the disease's intricacy, the pathophysiology is unknown, and an optimum therapy has yet to be found. There is an increasing need to explore novel treatments for this condition. Vitamin D insufficiency (VDD) is widespread in PCOS patients, according to recent research, and VDD may be linked to metabolic and endocrine abnormalities in PCOS patients [9-13]. Vitamin D insufficiency affects between 67-85 % of women with PCOS, with serum 25(OH)D values of less than 20 ng/ml. Despite the fact that there is no significant difference in 25(OH)D levels between PCOS and normal control women, a high incidence of vitamin D insufficiency has been linked to metabolic syndrome, which might have a substantial influence on public health. In comparison to the general population, PCOS patients have a greater prevalence of VDD.

Vitamin D is a steroid hormone that aids in calcium phosphate equilibrium and bone mineralization [14]. Vitamin D receptors are found in more than 30 distinct organs, including the pancreas, liver, immune cells, brain, and ovaries, and affect the expression of 229 genes [15,16]. As a result, vitamin D supplementation as a PCOS treatment has gained popularity. Vitamin D alters anti-müllerian hormone signalling, follicle-stimulating hormone sensitivity, and progesterone synthesis in human granulosa cells [17-21], which plays a physiologic function in reproduction, including ovarian follicular development and luteinization. It also plays a variety of roles in glucose homeostasis. The presence of specific vitamin D receptors in pancreatic  $\beta$ -cells and skeletal muscle, the expression of 1- $\alpha$ -hydroxylase enzyme, which can catalyze the conversion of 25-hydroxy vitamin D [25(OH)D] to 1,25-dihydroxyvitamin D, and the presence of a vitamin D response element in the human insulin gene promoter are all potential influences of vitamin D on glucose homeostasis [22-24].

Despite the fact that a rising number of intervention studies have looked at the link between vitamin D supplementation and PCOS, there is still a lack of solid evidence that vitamin D supplementation has an effect on PCOS. As a result, this present bibliometric analysis was undertaken to quantify the existing data in order to study the role of vitamin D supplementation on metabolic and hormonal functioning in PCOS patients. The study's main aims are to (1) outline and provide a comprehensive and unbiased analysis of the current state of the art, as well as areas that need improvement, problems, and possible research paths, in terms of cross-disciplines, journal sources, nations and locations, article citations, and keyword co-occurrence; and (2) provide an impartial analysis of areas that need improvement, problems, and possible research paths. The objectives of this paper are to provide more detailed information to future studies so that they may easily grasp the current state of knowledge about vitamin D supplementation's impact on PCOS patients and encourage more research-based implementations in strategic planning and other areas.

## Materials and Method

### Bibliometric analysis

The effect of vitamin D supplementation on metabolic and hormonal functioning in PCOS patients was quantified and visualized in this study using bibliometric analysis, a prominent approach for quantitative analysis of papers released in certain publication fields [25,26]. It uses a variety of analytical and computational approaches to examine the features of a given topic's literature; authors, institutions, countries/regions, and journals are evaluated, research hot spots are identified, and future research trends are predicted. Analysis of co-authorship, co-occurrence, citations, co-citations, and knowledge domain mapping are examples of such approaches. The bibliometric analysis in this article was performed with the help of Biblioshiny for bibliometrix. It is a Java programme created by Massimo Aria of the Federico University of Naples. This programme combines the bibliometrix package's capabilities with the convenience of web applications built using the Shiny package environment.

### Preliminary research strategy

The information was gathered from the PubMed database, an invaluable resource for bibliometric study. More than 33 million citations for biomedical literature from MEDLINE, life science journals, and online books are available in PubMed®. In addition, data reported in present studies were primarily intervened on the basis of the timeline selected from 2005 to 2022. The whole framework was designed substantially based on key terms "Polycystic ovary syndrome," "PCOS," "Vitamin D," "Deficiency," and "Patients." Besides, key terms were assembled by the utility of "AND" and "OR" Boolean operators. Only publications available in the English language were included in the search. As shown in Table 1, our final dataset included 312 papers with 1127 author-defined keywords published between 2005 and 2022. There were a total of 1453 contributors. There were 9 contributors for single-authored publications and 1444 contributors for multi-authored documents.

Table 1  
Main information about data

Description	Results
Timespan	2005:2022
Sources (Journals, Books, etc)	157
Documents	312
Average years from publication	5.08
DOCUMENT CONTENTS	
Keywords Plus (ID)	1127
Author's Keywords (DE)	1127
AUTHORS	
Authors	1453
Author Appearances	1848
Authors of single-authored documents	9

Authors of multi-authored documents	1444
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## Dataset extraction and processing mechanism

We started with a single keyword search – 'PCOS' – to view all the accessible studies in the PubMed database without any year limit to ensure the data was exhaustive. We reviewed our data again and weeded out any systematic reviews, review studies, early versions, and articles without citations. We identified 312 research documents using these parameters. A detailed illustrative summary of data extraction, data analysis, and data visualization is shown in Figure 1.

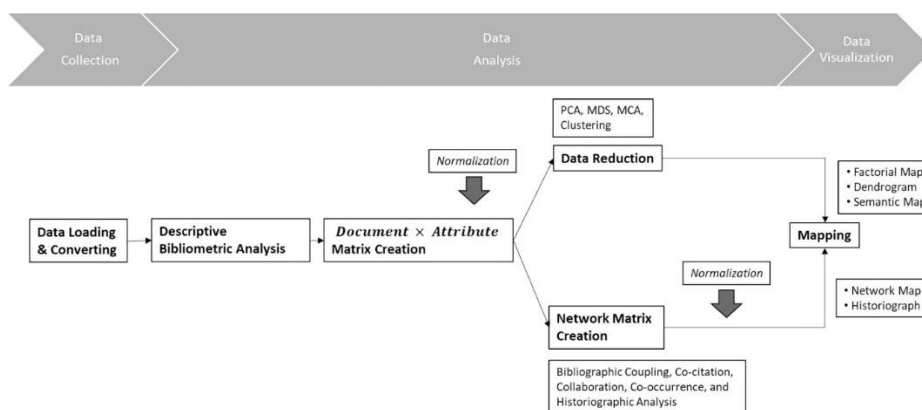


Figure 1. Overview of data processing mechanism

## Network analysis and mapping

Figures and maps are used in the study to analyze research hot zones, research quality, and the characteristics of vitamin D supplementation's influence on metabolic and hormonal functioning in PCOS patients. The analysis' methodological steps include data gathering, processing, visualization, and interpretation. The researchers chose not to impose a time limit on the research because it is focusing on an undeveloped topic and the analysis tries to provide a research trend through time. Researchers used the R programming language and the bibliometrix codes to conduct descriptive bibliometric research and generate a matrix including all of the documents. A conceptual map and a network of co-citations were also created using Biblioshiny.

## Results

### Analysis of research studies

The applied search strategy identified 312 studies from the PubMed database. From the bibliographic citation database, only original papers were examined in this study. Each publication's complete records were converted to a BibTex file and imported into Bibliometrix and Biblioshiny throughout the search. For bibliometric analysis, the article title, author name(s) and affiliation, journal name, number, volume, pages, publication date, abstract, and cited references were retrieved for these publications. Figure 2 depicts scientific papers that

illustrate the impact of Vitamin D insufficiency on PCOS throughout time. In 2012, the number of publications began to rise, then fell in 2013. Until 2016, however, the tendency continued to climb steadily. From 2017 through 2021, which was identified as the peak year of publishing, the graph displays a continuous increase and reduction in publications.

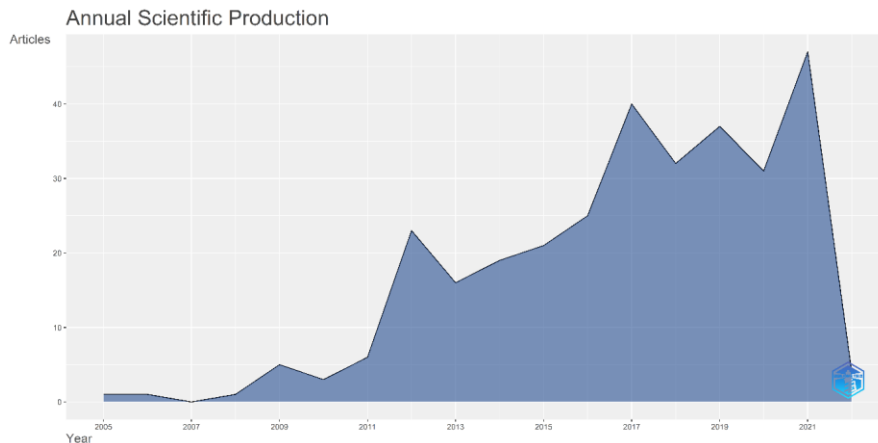


Figure 2. Frequency of publications

The most relevant and well-known publications that have published articles on the impact of Vitamin D insufficiency on PCOS patients have been investigated. Figure 3 illustrates the core collection's ranking of the 20 most fruitful sources on this subject. Gynecological Endocrinology: The Official Journal of The International Society of Gynecological Endocrinology, Nutrients, and European Journal of Endocrinology are the three most productive journals that have focussed publications discussing the impact of Vitamin D insufficiency on PCOS patients.

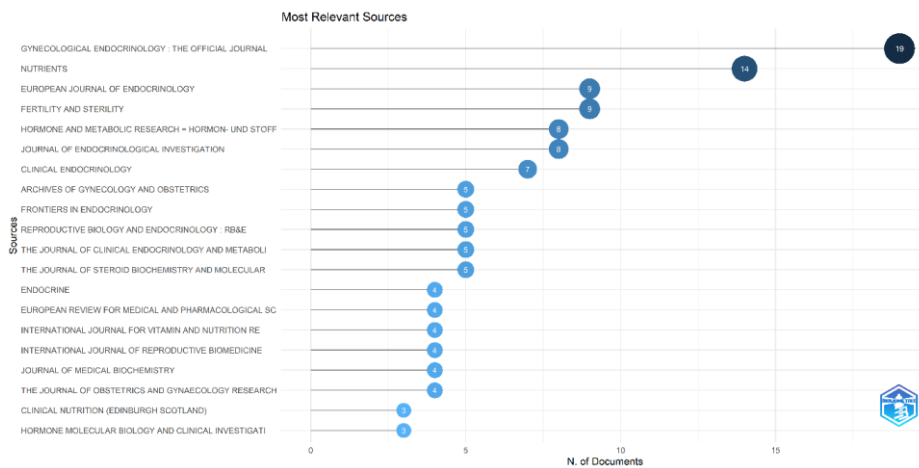


Figure 3. Most productive sources

Bradford's law was used to forecast which periodicals publish papers on the impact of Vitamin D insufficiency on PCOS patients that are the most relevant

and well-known (Figure 4). Bradford presented the theory in 1948, arguing that "for each given topic area, there are a few exceptionally prolific journals, a larger number of more middling producers, and an even greater number of journals with progressively diminishing productivity [27]." The core source area shows the publications which are most frequently referenced within this field's research and, as a consequence, are more likely to appeal to disciplinary scholars [28]. Gynecological Endocrinology: The Official Journal of The International Society of Gynecological Endocrinology, Nutrients, and European Journal of Endocrinology are the three most productive journals for the publications circumventing the impact of Vitamin D insufficiency on PCOS patients.

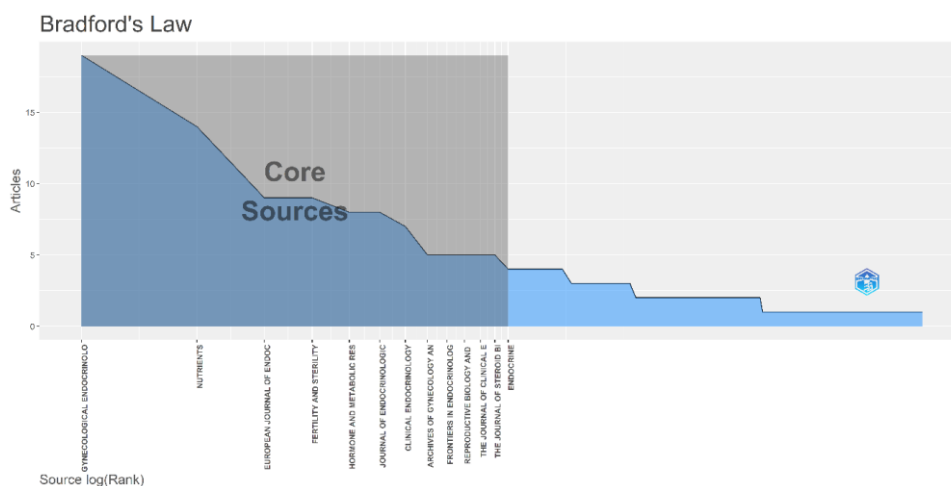


Figure 4. Most productive sources

In the subject of Vitamin D deficiency in PCOS patients, analyses of key phrases in the article, cluster analysis, and multiple correspondence analysis, for example, emphasize the article's theme and literary approach. We used the keywords provided by the authors to create a frequency distribution, as shown in Figure 5. (a). The relevant terms that appear are female (245), humans (228), adult (140), young adult (91), insulin resistance (50), and adolescent (49). They are followed by Body Mass Index, dietary supplements, case-control studies, and some more similar terms. Keywords with a word frequency greater than or equal to 10 were selected and produced as a Word TreeMap using the application biblioshiny (Figure 5(b)) to conduct data mining and data analysis on the high-frequency keywords of the research articles. The figure demonstrates that female, humans, adult, young adult, insulin resistance, adolescent, and body mass index are some of the most commonly used terms while studying the impact of Vitamin D insufficiency on PCOS patients.



### Mapping the scientific collaboration

The most significant authors that have contributed to providing insight into the main challenges and research trends around Vitamin D deficiency and PCOS patients are depicted in Figure 7. Asemi Z has a total of 14 papers, Jamilian M and Obermayer-Pietsch B have 10 publications each, while Masszi G, Lerchbaum E, and Teede HJ have 9, 8, and 7 publications, respectively.

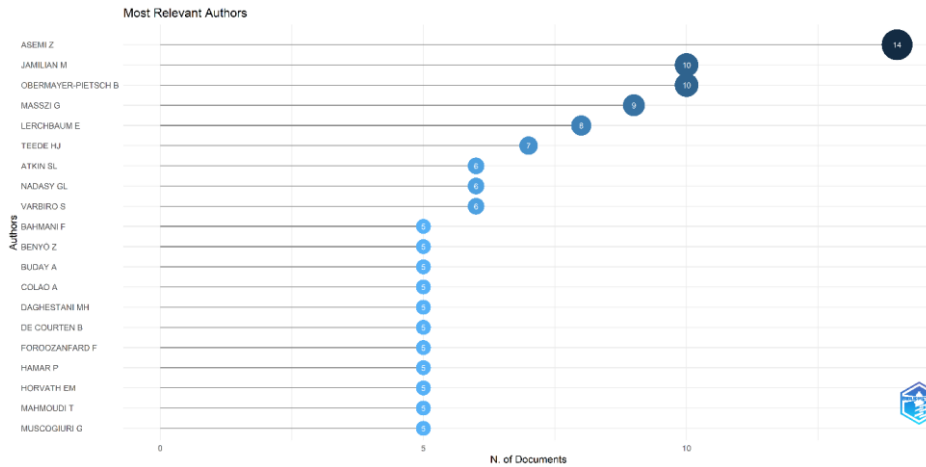


Figure 7. Most relevant authors

When looking at research trends around Vitamin D deficiency and PCOS patients, 56 articles were credited to Monash University, 49 articles credited to Semmelweis University, 39 articles backed by authors from Kashan University of Medical Sciences, 37 articles credited to Medical University of Graz, and 26 articles credited to Tehran University of Medical Sciences are among the most highly cited affiliations (Figure 8).

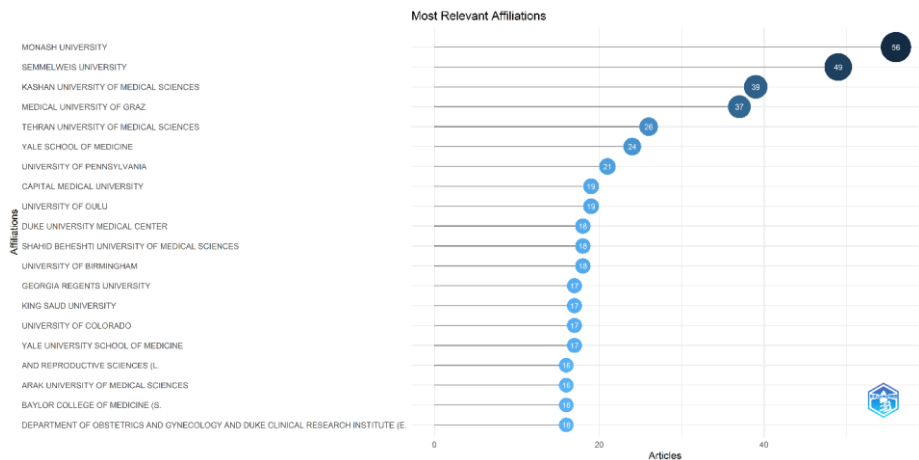


Figure 8. Most relevant affiliation

Figure 9 (a) depicts the collaboration network; independent articles from Iran account for the largest proportion of all publications; followed by China, Turkey, and India. While countries such as Turkey, Hungary, Brazil, Egypt, Greece, Korea, Bulgaria, and Germany concentrate mostly on independent research (Table 2).

Table 2  
Corresponding author's country-wise distribution

Country	Articles	Frequency	Single Country Publications (SCP)	Multiple Country Publications (MCP)	MCP_Ratio
Iran	59	0.23320	53	6	0.1017
China	28	0.11067	25	3	0.1071
Turkey	17	0.06719	17	0	0.0000
India	15	0.05929	13	2	0.1333
Italy	15	0.05929	12	3	0.2000
Australia	14	0.05534	11	3	0.2143
USA	13	0.05138	11	2	0.1538
Austria	12	0.04743	11	1	0.0833
Poland	10	0.03953	8	2	0.2000
Hungary	8	0.03162	8	0	0.0000
Brazil	7	0.02767	7	0	0.0000
Egypt	6	0.02372	6	0	0.0000
Saudi Arabia	6	0.02372	5	1	0.1667
Greece	5	0.01976	5	0	0.0000
Korea	4	0.01581	4	0	0.0000
Pakistan	4	0.01581	3	1	0.2500
Bulgaria	3	0.01186	3	0	0.0000
Germany	3	0.01186	3	0	0.0000
Bangladesh	2	0.00791	0	2	1.0000
Bosnia	2	0.00791	0	2	1.0000

The international coalitions are depicted in Figure 9 (b). The blue tint on the map reflects international research collaboration. The pink lines that link the states represent the level of collaboration among the scholars. Australia and Brazil, Austria with Canada, France, Germany, Greece, Hungary, Netherlands, Qatar and Switzerland, Canada with France, Germany, Netherlands, and Switzerland, and China with Australia and USA are some of the important international ties with countries that are separated by geography. The engagement might lead to policy dialogue and market collaboration.

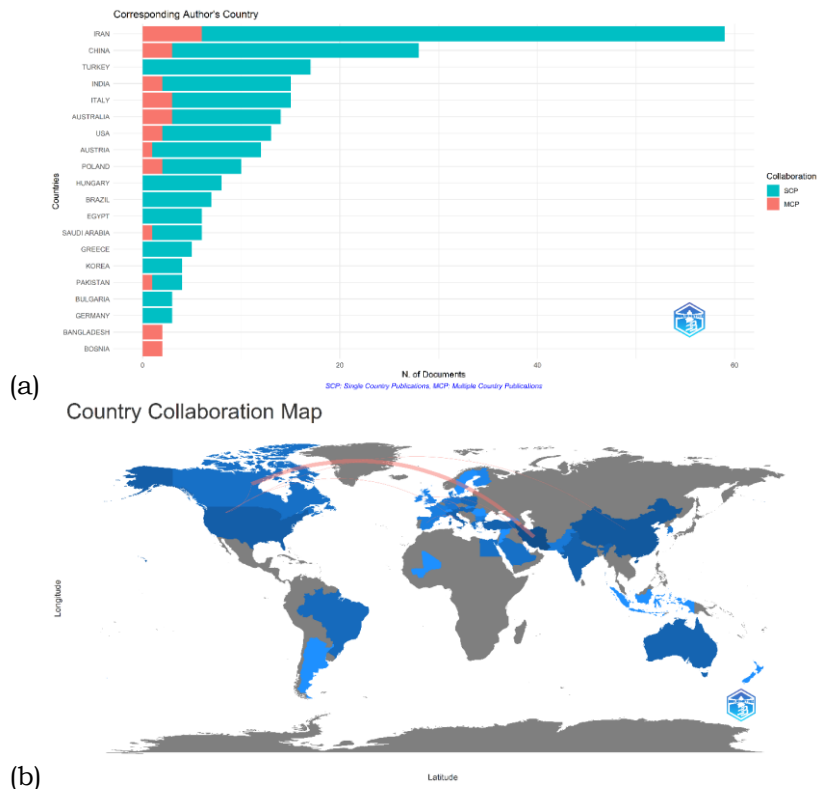


Figure 9. (a) Corresponding author's country and (b) Country collaboration map

### Cluster Analysis

A conceptual structure map was created by employing regional mapping to map the link between two phrases, providing a representation of the contextual structure of each word that appears often in research papers on the Vitamin D and PCOS studies (Figure 10). The values of Dim 1 and Dim 2 were used to sequence each word. Dim is a bibliometric name for a diminutive particle, which results in a mapping of words with comparable values. We used multiple correspondence analysis (MCA) for our study, which is a critical method for dealing with huge and complex datasets. This map is divided into two sections: a red region and a blue region, both of which include related terms. The top three most often appearing phrases ("polycystic," "Vitamin D insufficiency," and "blood") occurred in the red area, which had a large number and variety of words, indicating that many research articles linked the words stated in this location. Less frequently occurring terms ("cholecalciferol," "rats," and "animals") were shown in the blue section.

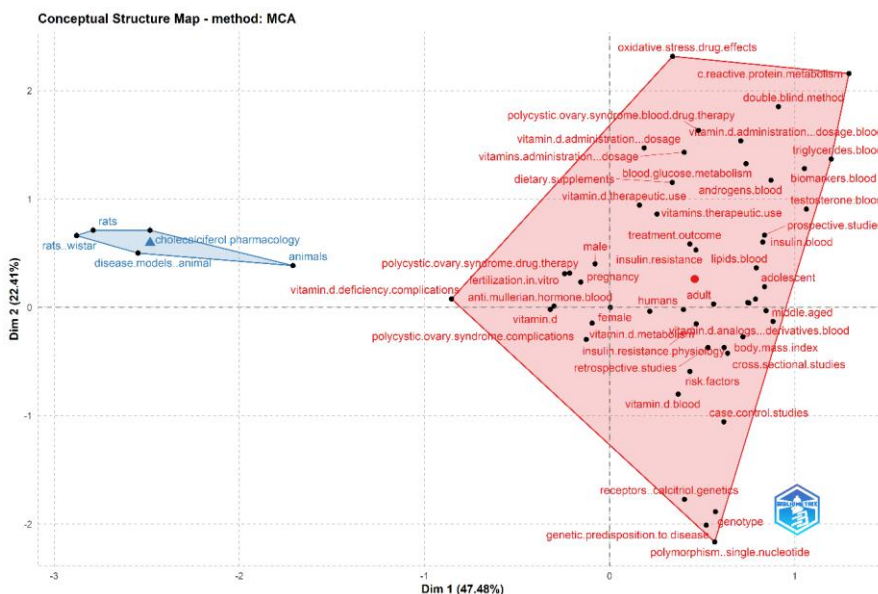


Figure 10. Conceptual Structure Map

The topic dendrogram in Figure 11 depicts the hierarchical order and relationship between the keywords produced from hierarchical clustering. The first strand focuses on calciferol investigations in animals and humans, while the second strand focuses on PCOS, risk factors, cross-sectional studies, and therapy for PCOS patients. We looked at the second block, which also contains the greatest divisions, to determine unique areas of interest and relationships. We notice a relationship between Vitamin D therapy and various other potential therapies for the treatment of PCOS in this dendrogram.

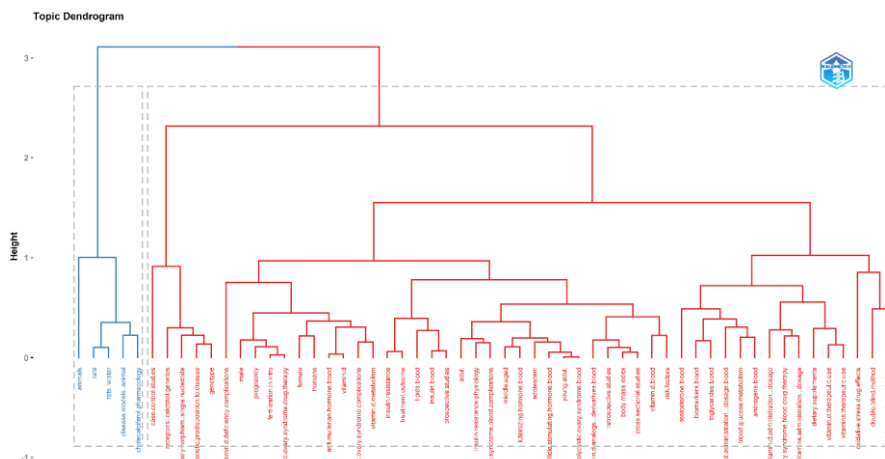


Figure 11. Topic dendrogram

### Three Plots Field

Figure 12 uses a Sankey diagram with arrow width proportionate to flow rate to represent the principal components of three fields (e.g., authors, keywords, affiliation) and their interactions. A schematic plot comprised of rectangles of various colours was used to show the main parts. The total of the relationships that emerged between the element represented by the rectangles and the diagram of the other components is represented by the height of the rectangle. The amount of associations that each element has is determined by the size of the rectangle. Highly cited researchers' work was shown to be linked to vitamin, syndrome, and polycystic. Moreover, the research has been conducted under the supervision of Semmelweis University, Monash University, and Yale School of Medicine.

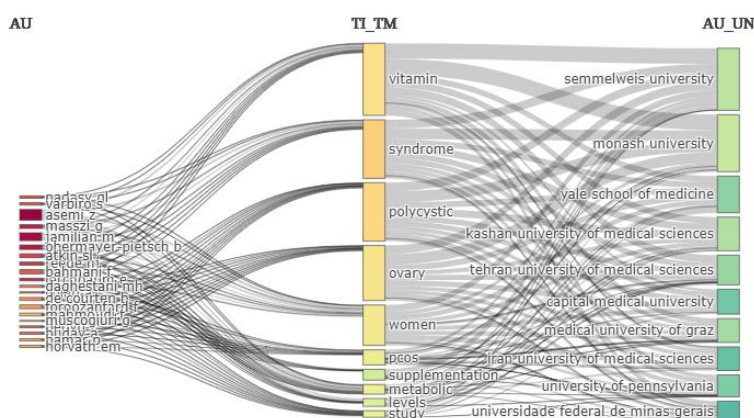


Figure 12. Three Fields Plots

### Thematic analysis and future trend

Thematic evolution analysis is a tool for discovering evolutionary linkages between different evolutionary paths and trends across time [29]. The topic analysis in the domains of Vitamin D and PCOS from 2005 to 2022 is depicted in Table 3 and Figure 13. It also displays the emergence of buildings through time, as well as their strength. Each node is the same size as the number of keywords in the topic.

Table 3  
Thematic evolution analysis

From	To	Words	Weighted Inclusion Index	Inclusion Index	Occurrences	Stability Index
animals--2005-2017	animals--2018-2022	animals; disease models, animal; rats; rats, Wistar; cholecalciferol/pharmacology; vitamins/pharmacology	0.45	0.05	24	0.02
female-	adult--2018-2022	adult; young adult;	0.66	0.03	80	0.01

-2005-2017		adolescent; body mass index; vitamin d/analog & derivatives/blood; middle aged; insulin resistance/physiology; polycystic ovary syndrome/blood; lipids/blood; prospective studies; cross-sectional studies; polycystic ovary syndrome/blood/complications; prognosis; retrospective studies; follicle stimulating hormone/blood				
female-2005-2017	animals--2018-2022	anti-mullerian hormone/blood	0.03	0.04	3	0.01
female-2005-2017	case-control studies--2018-2022	case-control studies; vitamin D/blood; risk assessment	0.33	0.05	18	0.01
female-2005-2017	dietary supplements--2018-2022	polycystic ovary syndrome/blood/metabolism	0.02	0.06	2	0.01
female-2005-2017	female--2018-2022	female; humans; vitamin D/metabolism	0.67	0.03	131	0.01
female-2005-2017	insulin resistance--2018-2022	insulin/metabolism; polycystic ovary syndrome/metabolism; biomarkers/metabolism; prevalence	0.13	0.06	4	0.01
insulin resistance--2005-2017	adult--2018-2022	biomarkers/blood; insulin/blood; testosterone/blood; triglycerides/blood; androgens/blood; anthropometry; vitamin D deficiency/blood/complications/drug therapy	0.19	0.03	12	0.01
insulin resistance--2005-2017	animals--2018-2022	dose-response relationship, drug; polycystic ovary syndrome/physiopathology	0.04	0.04	4	0.02
insulin resistance--2005-2017	dietary supplements--2018-2022	dietary supplements; double-blind method; polycystic ovary syndrome/blood/drug therapy; oxidative stress/drug effects; vitamin D deficiency/blood/drug therapy	0.52	0.06	21	0.02
insulin resistance--2005-2017	female--2018-2022	vitamin D/therapeutic use	0.02	0.03	9	0.01
insulin resistance--	insulin resistance--2018-2022	insulin resistance; blood glucose/metabolism; vitamin d/administration	0.38	0.06	34	0.02

2005-2017		& dosage/blood; c-reactive protein/metabolism; sex hormone-binding globulin/metabolism				
male--2005-2017	adult--2018-2022	treatment outcome; follow-up studies	0.04	0.03	7	0.01
male--2005-2017	animals--2018-2022	receptors, calcitriol/metabolism; vitamin D deficiency/complications	0.06	0.04	3	0.02
male--2005-2017	case-control studies--2018-2022	phenotype	0.02	0.05	3	0.02
male--2005-2017	dietary supplements--2018-2022	vitamin d/administration & dosage; vitamins/administration & dosage	0.14	0.06	8	0.02
male--2005-2017	female--2018-2022	pregnancy; fertilization in vitro; vitamins/therapeutic use; polycystic ovary syndrome/drug therapy; pregnancy rate; polycystic ovary syndrome/complications; infertility, female/etiology; ovulation induction; randomized controlled trials as topic	0.24	0.03	12	0.01
male--2005-2017	insulin resistance--2018-2022	male	0.05	0.06	15	0.02
risk factors--2005-2017	adult--2018-2022	luteinizing hormone/blood	0.03	0.03	3	0.02
risk factors--2005-2017	case-control studies--2018-2022	receptors, calcitriol/genetics; genotype; gene frequency; genetic predisposition to disease; polymorphism, single nucleotide; obesity/complications; polymorphism, genetic; insulin resistance/genetics; alleles; genetic association studies; India; polycystic ovary syndrome/genetics	0.39	0.05	12	0.02
risk factors--2005-2017	granulosa cells/drug effects/metabolism/p pathology--2018-2022	polycystic ovary syndrome/blood/genetics	0.33	0.33	3	0.03
risk factors--2005-2017	insulin resistance--2018-2022	risk factors	0.17	0.06	15	0.02

The "driving" themes in the upper right quadrant, as evidenced by their high density and centrality, are important for future study and should be studied further. "Insulin resistance," "dietary supplements," and the "double blind

approach" were among the subjects discussed. "Animal models," "genetic propensity to disease genotype," and "calcitriol" are among the under-represented subjects in the upper left quadrant, which have a high density but low centrality, indicating that they are still in the early stages of development. The lower left quadrant contains concepts that have been utilized but have witnessed a diminishing trend, as shown by low centrality and density; for example, "therapeutic usage," "metformin," and "hypoglycemic agents." Finally, in the lower right quadrant, fundamental themes with high centrality but low density are seen; these subjects, which include "female," "adult," and "fertilization in vitro," are important for examination as general issues.

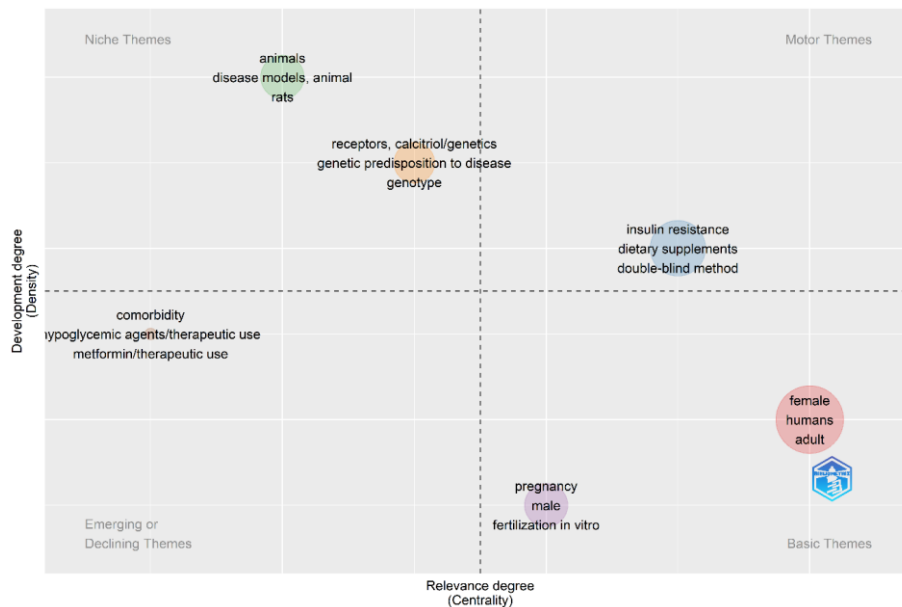


Figure 13. Thematic analysis

Figure 14 depicts the trend themes based on the phrases studied. In 2012, it identified research issues relating to PCOS/therapy/cohort studies/pilot studies/glucose tolerance test; in 2013, it focused on the use of Vitamin D/vasodilation/gene frequency; in 2014, it discovered a large number of publications focusing on cholecalciferol/pharmacology/genotype/studies on Wistar rats; and in 2015, it discovered a large number of publications focusing on Vitamin D deficiency/calcitriol. In 2016, a study on young individuals, insulin resistance, and vitamin D analogues was released. In 2017, studies on young adults and adolescents were published. In 2018, case-control studies, risk variables, and the double-blind approach grew in popularity. By 2019, the majority of the study has been on PCOS, with a focus on leutinizing hormone, vitamin D insufficiency, and some retrospective investigations. Anti-mullerian hormone and follicle stimulating hormone study on the impact of Vitamin D insufficiency on PCOS patients received a lot of attention by 2020 and 2021.

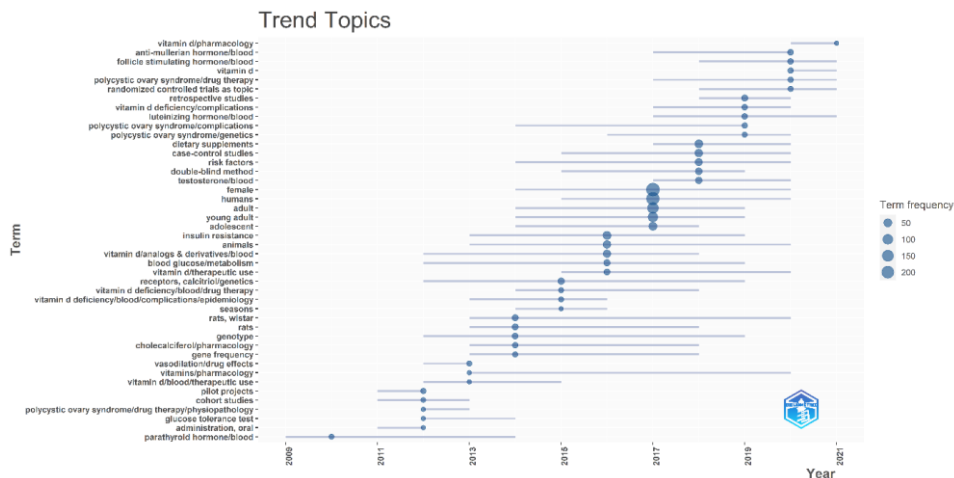


Figure 14. Trend topics

## Discussion

This bibliometric analysis summarizes the overall research trends around Vitamin D deficiency and PCOS patients from the perspectives of cross-disciplines, source journals, regions around the world, article citations, and keyword co-occurrence; and provides a comprehensive and unbiased analysis of the current state of the art, as well as areas that need improvement, problems, and potential research paths. The report demonstrates a continual growth and decrease in publications from 2017 to 2021, which was designated as the peak year of publishing. The three most productive journals that have focused papers regarding the impact of Vitamin D deficiency on PCOS patients were found to be Gynecological Endocrinology: The Official Journal of The International Society of Gynecological Endocrinology, Nutrients, and European Journal of Endocrinology.

Female, people, adult, young adult, insulin resistance, adolescent, and body mass index are some of the most regularly used phrases while researching the impact of Vitamin D deficiency on PCOS patients, according to the keyword analysis. Among the most often referenced connections are Monash University, Semmelweis University, Kashan University of Medical Sciences, Medical University of Graz, and Tehran University of Medical Sciences. Independent articles from Iran account for the biggest share of all publications, according to collaborative statistics from relevant nations, followed by China, Turkey, and India. However, Austria's collaborations with Canada, France, Germany, Greece, Hungary, the Netherlands, Qatar, and Switzerland, as well as Canada's collaborations with France, Germany, the Netherlands, and Switzerland, accounted for the bulk of the collaborative work.

The majority of research papers had words like "polycystic," "Vitamin D deficiency," and "blood," whereas just a few research articles contained words like "cholecalciferol," "rats," and "animals." In the subject dendrogram, we discovered a link between Vitamin D therapy and a variety of other probable PCOS treatments. The work of highly cited scholars has been related to vitamin, syndrome, and polycystic. From 2005 to 2022, the topic analysis in the areas of

Vitamin D and PCOS shows the formation of buildings as well as their strength over time. As indicated by their high density and centrality, the "driving" themes were found to be connected to "insulin resistance," "dietary supplements," and the "double blind method." These niche issues were identified as being relevant for future research and should be investigated further. Anti-mullerian hormone and follicle stimulating hormone studies on the impact of Vitamin D deficiency on PCOS patients gained a lot of attention by 2020 and 2021, according to this study. These methods may aid in a better understanding of the relationship between Vitamin D insufficiency and PCOS.

## **Conclusion**

The purpose of this study is to conduct a bibliometric analysis of publications related to Vitamin D insufficiency in PCOS patients. Anti-mullerian hormone and follicle stimulating hormone investigations were found to be important directions for developing a deeper understanding of the problem, according to the study. This work provides a comprehensive grasp of the bibliometric parameters that link Vitamin D insufficiency to PCOS patients, and it can aid scientific research in this area. Furthermore, scholars may benefit from the analysis and integration of multidisciplinary topics. Moreover, the research uncovers hitherto unexplored issues that researchers might analyze further and address from a managerial approach. In respect of potential research, we believe that this study will aid in the development of an effective PCOS therapy, which will assist PCOS patients. Additionally, the analysis highlights the significance of double-blind trials as an under-represented problem that is critical for making important judgments in PCOS care.

## **Limitations of research**

Our research has significant limitations. One of the limitations is the use of the PubMed database, despite the fact that the Scopus and Web of Science databases are quite comprehensive and reliable. Our research was also confined to English-language publications, while articles in Spanish, Chinese, and French were not included. Another difficulty we observed was that the most recognized and influential writers were rated based on the number of papers they published; as a result, rankings for publications with a single document but numerous citations might be biased.

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