



Network Analysis on Graves' Ophthalmopathy

Graves Oftalmopatisi İle İlgili Yayınların İşbirliğine Dayalı Ağ Analizi

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Abstract

Aim Graves' ophthalmopathy (GO), sometimes known as Graves' orbitopathy, is an eye illness that can lead to vision loss. Despite significant developments in ophthalmology over the previous few decades, there is no comprehensive bibliometric description of the quality and quantity of GO research in the peer-reviewed literature. The purpose of this study was to examine the trends in GO publications.

Material and Method The bibliometric search was conducted using the Web of Science (WoS) Core Collection advanced search engine. Keywords related to "Graves" and "ophthalmopathy" or "orbitopathy" were used. The time span was set from 1970 to 2021. The researchers looked at data on publishing growth, the most active countries and institutions, the most cited journals, and publishing and keyword mapping. The articles were investigated thoroughly. The maps were visualized using the VOSviewer technique.

Results The WoS database yielded 958 articles about GO. These 958 articles had an average of 29.59 citations each. These items have a H index of 81. The majority of the papers found were in the fields of endocrinology and metabolism (38.83 percent), followed by ophthalmology (25.99 percent), with the United States as the leading country. The articles garnered a total of 28348 citations, averaging 29.59 per article. Annual citation growth of GO was sluggish until the 1990s, then skyrocketed in the subsequent decade.

Conclusion The USA was the leading country but the rest of the world made a significant contribution. The quantity of citations is great, yet global collaboration is required to address this increasing and worrisome issue.

Keywords graves ophthalmopathy; eye; bibliometric analysis; research publications.

Özet

Amaç Graves' orbitopatisi olarak da bilinen Gravesoftalmopatisi (GO), görme kaybına yol açabilen bir göz hastalığıdır. Oftalmolojide son yıllarda önemli gelişmelere olmasına rağmen, literatürlerde GO araştırmasının kalitesi ve miktarına ilişkin kapsamlı bir bibliyometrik tanım bulunmamaktadır. Bu çalışmanın amacı, GO yayınlarındaki eğilimleri incelemektir.

Gereç ve Yöntem Bibliyometrik arama, Web of Science (WoS) Core Collection gelişmiş arama motoru kullanılarak yapıldı. "Graves" ve "oftalmopati" veya "orbitopati" ile ilgili anahtar kelimeler kullanıldı. Zaman aralığı 1970' den 2021' e kadar belirlendi. Araştırmacılar, yayın büyümesi, en aktif ülkeler ve kurumlar, en çok alıntı yapılan dergiler ve yayıncılık ve anahtar kelime eşleme ile ilgili verilere baktılar. Makaleler kapsamlı bir şekilde incelenmiştir. Haritalar VOSviewer tekniği kullanılarak görselleştirildi.

Bulgular WoS veritabanı, GO hakkında 958 makale verdi. Bu 958 makalenin her biri ortalama 29.59 atf aldı. Bu makalelerin H indeksi 81' di. Bulunan makalelerin çoğu endokrinoloji ve metabolizma (%38,83) alanlarında, bunu oftalmoloji (%25,99) izledi ve Amerika Birleşik Devletleri lider bu konuda lider ülkedydi. Makaleler, makale başına ortalama 29.59 olmak üzere toplam 28348 atf aldı. GO' nun yıllık atf büyümesi 1990' lara kadar yavaş, ardından sonraki on yılda hızla arttı.

Sonuç GO ile ilgili çalışmalarda ilk sırada ABD yer almaktadır. Yapılan yayınların alıntılanma sayısı oldukça fazla olmasına rağmen konu ile ilgili bilimsel verilerin elde edilmesi için küresel iş birliğine ihtiyaç vardır.

Anahtar Kelimeler graves oftalmopatisi; göz; bibliyometrik analiz; araştırma yayınları.

INTRODUCTION

Graves' ophthalmopathy (GO), commonly known as Graves' orbitopathy, is a potentially blinding ocular disease that has confused doctors and scientists for nearly 200 years. Thyroid-associated ophthalmopathy, also known as thyroid eye illness, organ-specific autoimmune disease, or thyroid eye illness, is a condition that affects individuals who have hyperthyroidism or have had hyperthyroidism in the past due to Graves' disease.¹ GO is the most common extrathyroidal symptom of Graves' disease and its whole clinical presentation can significantly reduce patients' quality of life.²

Patients with persistent autoimmune thyroiditis, whether euthyroid or hypothyroid, may also be affected. The disease has a yearly adjusted incidence rate of 16 women and 3 men per 100,000 individuals.¹ Intravenous steroids/immunosuppression can effectively cure active inflammation, although this does not always result in complete remission, as inflammation quickly leads to persistent fibrosis and an increase in orbital fat. It's vital to keep risk variables under control in order to avoid progressing to more severe phases (smoking cessation, adequate thyroid function, selenium supplementation). A detailed assessment of GO activity and severity should be used to guide treatment. To restore function and beauty, many people require rehabilitative surgery (orbital decompression, squint surgery, and eyelid surgery). These patients have antibodies against the thyroid-stimulating hormone (TSH) receptor, which have been associated to the advancement of thyroid and ocular disease. At various phases of the disease, antibody levels can be used to guide therapy decisions.²

Despite significant developments in ophthalmology over the previous few decades, there is limited comprehensive bibliometric description of the quality and quantity of GO research in the peer-reviewed literature. As a result, the purpose of this research was to examine the development of GO articles in global contributions since 1970.

MATERIALS and METHODS

Study setting & design

The bibliometric search was conducted using the Web of Science (WoS) Core Collection advanced search engine, which provides a standard dataset for analyzing and tracking bibliographical factors such as author names, country, journal title, affiliation, keywords, number of citations, and subject areas. The data for this bibliometric analysis was gathered from the WoS core collection between 1970 and 2021. In January 2022, data recruiting was completed. There was no need for ethical approval because the data was taken from publicly available research.

Search strategy

Keywords related to "graves" and "ophthalmopathy" or "orbitopathy" were used in a search query in the WOS search engine. The time span was set from 1970 to 2021. Data on publishing growth, the most active countries and institutions, the most cited journals, and publishing and keyword mapping were examined. The articles were analysed in detailed.

The VOSviewer technique was used to visualize the maps, which were evaluated to present several bibliometric indications. VOSviewer (Leiden University, Leiden, Netherlands) is a software application for visualizing bibliographic linking, co-citation, co-authorship, keyword and co-occurrence analysis in publications.³

The Hirsch (H) index was utilized as marker of publication impact.⁴

Data analysis

For analysis, the data was exported into Microsoft Excel (Microsoft® Corp., Redmond, WA). Quantitative data included the total number of publications, articles, citations, journal titles, and organization-enhanced publications. By manually examining the retrieved parameters, the validity of the search method was determined.

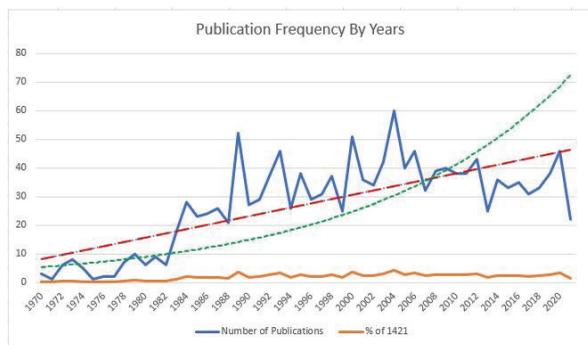
RESULTS

1. Publications

A total of 1421 journal publications were retrieved with an average of 24.26 citations per article. H index was found to be 85. Even if study search the publications in the period between 1970 and 2021 first article was in 1971. Distribution of publications showed in Table 1.

Document Types	Number of Publications	% of 1421
Article	958	67.417
Meeting abstract	150	10.556
Letter	126	8.867
Proceedings paper	90	6.334
Review	72	5.067
Editorial material	65	4.574
Note	11	0.774
Correction	6	0.422
Book chapter	4	0.281
Early access	4	0.281
Discussion	3	0.211
Correction addition	1	0.07
Retraction	1	0.07

During the study period, the annual growth of GO articles showed a rising pattern. The majority of the publications (n=1357; 95.49 percent) were written in English, followed by German (n=37; 2.60 percent) and French (n=15; 1.056 percent). The remaining languages were Portuguese, Serbian, Korean, Russian, and Spanish (Graphic 1).



Graphic 1. The number of publications by the years.

2. Articles

Of the total publications, 958 (67,417) were research articles. The average number of citations of these 958 articles was 29.59. (High H index) The h index of these articles, which were cited 28348 times in total, was 81. And the detailed analysis of the articles was shown as follows. Endocrinology and Metabolism (n=372; 38.83%), Ophthalmology (n=249; 25.99%), General Internal Medicine (n=120; 12.52%), Radiology/ Nuclear Medicine/ Medical Imaging (n=64; 6.68%), Immunology (n=41; 4.28%), and the rest were from diverse fields (Table 2).

Research Areas	Number of Articles	% of 958
Endocrinology Metabolism	372	38.831
Ophthalmology	249	25.992
General Internal Medicine	120	12.526
Nuclear Medicine/ Medical Imaging /Radiology	64	6.681
Immunology	41	4.28
Surgery	33	3.445
Research Experimental Medicine	32	3.34
Oncology	24	2.505
Cell Biology	15	1.566
Otorhinolaryngology	15	1.566
Pharmacology Pharmacy	15	1.566
Biochemistry Molecular Biology	13	1.357
Neurosciences Neurology	12	1.253
Pediatrics	12	1.253
Science Technology Other Topics	12	1.253
Genetics Heredity	9	0.939

•Only main research areas were shown.

2 a. Active countries, institutions, and journals

The leading country on journal number is USA with (n=210; 21.92%), followed by Italy (n=88; 9.18%), China (n=76; 7.93%). Other 50 countries which around the globe were (n=584; 60.96%). Turkey ranked 9th (Table 3).

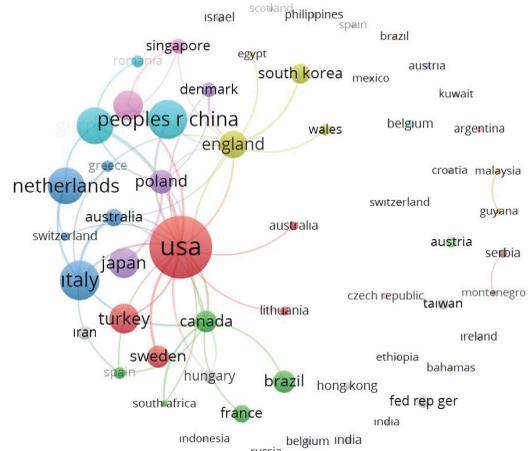
Table 3. The list of top 15 ranked countries in publishing GO articles.

Countries/Regions	Number of Articles	% of 958
USA	210	21.921
Italy	88	9.186
Peoples Republic of China	76	7.933
Germany	75	7.829
Netherlands	75	7.829
Taiwan	50	5.219
Japan	49	5.115
England	47	4.906
Turkey	43	4.489
Poland	29	3.027
Brazil	27	2.818
Sweden	25	2.61
Canada	24	2.505
Australia	20	2.088
South Korea	20	2.088

University of Munich	12	1.253
China Medical University	10	1.044
China Medical University Hospital	10	1.044
University of Insubria	10	1.044
Gazi University	9	0.939
Kurume University	9	0.939
Lund University	9	0.939

2.c. International and author collaboration

Papers co-authored by authors from multiple countries were designated as “international collaborations.”



2.b. Affiliations.

Amsterdam University and Mayo Clinic were the leader affiliations on GO research (Table 4).

Table 4. The list of top affiliations.

Organizations	Number of Articles	% of 958
Amsterdam University	52	5.428
Mayo Clinic	78	8.142
The University of Pisa	40	4.175
National Taiwan University Hospital	42	4.104
The Netherlands Ophthalmic Research Institute	15	1.566
University of Southern California	15	1.566
Stanford University	13	1.357
National Yang-Ming University	12	1.253

Figure 1. Co-authorship network visualization map among nations with at least one GO publication. Collaboration is indicated with lines connecting countries. Stronger cooperation are indicated by thicker lines. Countries with higher circle sizes or font sizes had more articles per capita.

Figure 1 depicts a network map of international collaboration. Using the VOSviewer approach, an investigation of international cooperation for active nations with at least one document revealed that there were clusters of international collaboration (Figure 2 and Figure 3).

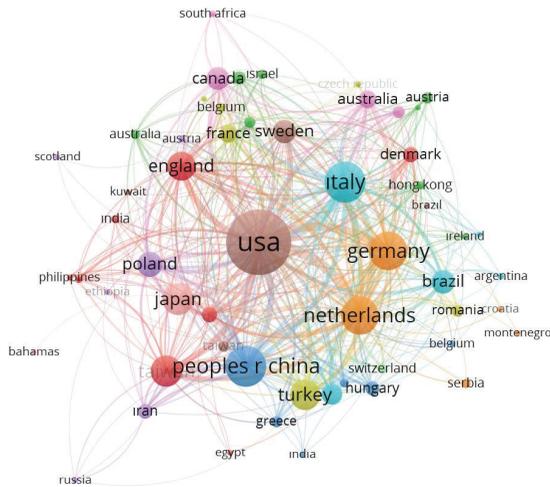


Figure 2. Countries with at least one GO publication are represented in a network visualization map of citations. Collaboration is indicated with lines connecting countries. Stronger cooperation are indicated by thicker lines. Countries with a larger circle or text size had a higher level of international collaboration.

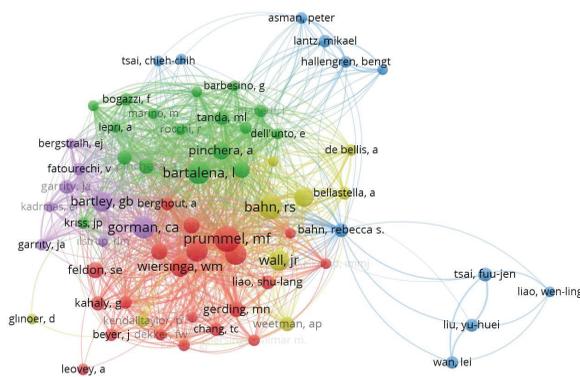


Figure 3. Citation visualization map of the top 66 authors with at least five publications on Google Scholar. Citations are shown by lines connecting nations. Authors with a greater circle size or font size had a higher number of citations.

Keyword analysis

Graves' ophthalmopathy, Graves' disease, and ophthalmopathy were mostly preferred keywords. The keywords other than the name of the disease were mostly about treatment protocols and pathogenesis (Table 5). The keyword mapping was also given in the Figure 4.

keyword	occurrences
graves' ophthalmopathy	199
graves' disease	105
ophthalmopathy	58
graves ophthalmopathy	50
hyperthyroidism	15
exophthalmos	14
thyroid eye disease	14
radiotherapy	13
methylprednisolone	12
orbital decompression	12
thyroid-associated ophthalmopathy	12
clinical activity score	11
graves disease	11
corticosteroids	10
quality of life	10
magnetic resonance imaging	9
smoking	9
adipogenesis	8
glucocorticoids	8
graves disease	8
graves' orbitopathy	8
autoimmunity	7
cytokine	7
graves’	7
graves'	7
polymorphism	7
autoimmune thyroid disease	6
cytokines	6
diagnosis	6
extraocular muscles	6
orbit	6
orbitopathy	6
oxidative stress	6
radioiodine	6
thyroid	6
endocrine ophthalmopathy	5
pathogenesis	5
proptosis	5
rituximab	5
strabismus	5
thyroid disease	5

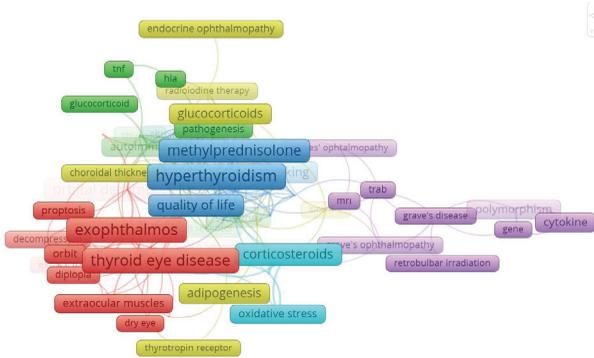
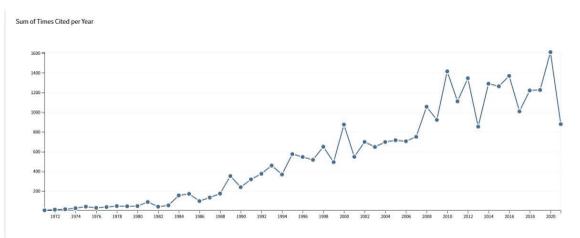


Figure 4. Keyword mapping. *Keyword visualization map of articles on GO with at least one occurrence. In articles, linked lines indicate occurrence relationships. Keywords denoted by a higher circle size or text size appeared in the articles more frequently.

2.d. Citing analysis

The total number of citations for the articles that were found was 28348, with an average of 29.59 citations per article. The H index of the articles that was 81. A total of 885 articles (92.37%) were cited at least once, while 73 articles (7.62%) were not cited at all. The number of citations has risen steadily over time. The annual citation growth of GO was sluggish until the 1990s, but exploded in the subsequent decade. The annual growth of citations on GO was depicted in Graphic 2. The year with the most citations was 2020, with a total of 2080 citations (Graphic 2).



Graphic 2. Graphics of citation by years between 1973 -2021. Line express the citing numbers.

The most cited article was published in the Journal of Clinical Endocrinology and it was cited for 555 times. The summary of the most cited 10 articles were given in Table 6.

Article Title	Journal	Times Cited, All
Clinical activity score as a guide in the management of patients with Graves' ophthalmopathy	Clinical Endocrinology	555
Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy	New England Journal Of Medicine	471
Clinical-criteria for the assessment of disease-activity in graves ophthalmopathy - a novel-approach	British Journal of Ophthalmology	442
Occurrence of ophthalmopathy after treatment for graves hyperthyroidism	New England Journal Of Medicine	401
Thyrotropin receptor autoantibodies are independent risk factors for graves' ophthalmopathy and help to predict severity and outcome of the disease	Journal of Clinical Endocrinology & Metabolism	275
Epidemiology and prevention of Graves' ophthalmopathy	Thyroid	264
Randomized double-blind trial of prednisone versus radiotherapy in graves ophthalmopathy	Lancet	261
Supervoltage orbital radiotherapy for graves ophthalmopathy	Journal of Clinical Endocrinology & Metabolism	259
Prednisone and cyclosporine in the treatment of severe graves ophthalmopathy	New England Journal of Medicine	255
Orbital cobalt irradiation combined with systemic corticosteroids for graves ophthalmopathy - comparison with systemic corticosteroids alone	Journal of Clinical Endocrinology & Metabolism	246

DISCUSSION

The most common cause of hyperthyroidism is Graves' disease. Despite the effectiveness of antithyroid medications and radioactive iodine, surgery is still the preferable treatment for many patients.⁵ GO is an autoimmune orbital disease most commonly associated with Graves' disease that necessitates close interdisciplinary collaboration.² It's a difficult phenomenon that necessitates collaboration among several specialists (endocrinologists, ophthalmolo-

gists, radiologists, radiotherapeutic, and orbital surgeons) for the better clinical outcome. In order to plan an effective treatment for GO, a precise diagnostic assessment is essential. To control the disease, medical therapy, radiation, or surgery may be required. There are numerous therapy techniques, as well as more modern medicines based on pharmacologic immunomodulation.⁶ In summary, GO is a hot topic in multidisciplinary approaches needed.

Systematic reviews, meta-analyses, and bibliometric analyses can be used to describe trends in a field. Systematic reviews and meta-analyses are primarily used to compare the efficacy or side effects of various treatment procedures or pharmaceuticals, and they can provide definitive or suggestive data. They do not, however, provide descriptive statistical analysis of research in a given field.^{7,8} Bibliometric analysis is a statistical tool for defining the features of large-scale data and finding the key development trends based on database searches on a certain topic.^{8,9}

Bibliometric analysis extracts data on the number of publications, countries, institutions, authors, and research areas, resulting in visual findings representing research status.⁹

Despite the fact that many bibliometric analyses have been undertaken in the field of medicine on a variety of issues from Turkey⁹⁻²¹, there are only two studies that are equivalent to our research in the literature^{21,22}. Cao et al.²¹ looked at the GO literature from 1999 to 2019, while Elubous et al.²⁰ looked at the last two decades. The current analysis looked at the literature from 1970 to 2021. Similar to our study, Cao et al.²¹ and Elubous et al.²² employed the same database for analysis.

In this work, we aimed to give a bibliometric review of the literature on GO from 1970 to 2021. To do so, we used the well-known WOS database, which has already been used in published bibliometric research.^{13,16,17} According to our findings, the number of GO articles has been gradually increasing over the last decade. The higher H-index

demonstrates the importance of this topic to a wide range of doctors and academics, despite the modest number of publications. The United States and Italy came in first and second place, respectively. The increased number of GO investigations in these countries is noteworthy and deserves more research. The gap in co-authorship and citation data shows that this is a global problem that needs far more international cooperative research (co-authorship).

The USA also had the most GO research outputs similar to Cao et al.'s study.²¹ In our study, however, the second-leading country was Italy (n = 88; 9.18%). But Cao et al.²¹ reported that China was in second place. In Cao et al.'s²¹ study, all kinds of publications were analyzed, but we also only analyzed research articles. Elubous et al.²² also analyzed research articles too.

In the last two decades, the number of scientific studies on GO has risen. The visualization map shows a strong collaboration between European countries, which forms a cluster; most of any European country's linkages are with other European countries. The United States, on the other hand, collaborates with countries from other clusters, implying that it engages in more worldwide GO research collaboration. The study's two most mentioned articles were authored by a consortium of authors from different European countries (European Group of Graves Orbitopathy [EUGOGO]). Several studies have demonstrated that international co-authorship has a positive impact on citation count. Our findings were similar to Elubous et al.²² reports. In bibliometric analysis, co-citation analysis is a useful approach for identifying publications that are often cited by multiple authors. Articles with a high number of co-citations imply a close link. Co-citation analysis can also help us figure out what the authors have to say about a given issue.²² We examined the topics of highly referenced articles in this study. The most cited article was published in the Journal of Clinical Endocrinology and it was cited 555 times and its topic was about the treatment.

Also in keyword mapping analysis, it was determined that, the keywords other than the name of the disease were mostly about treatment protocols and pathogenesis

CONCLUSIONS

Over the last two decades, the number of publications on GO has risen. According to the findings, the majority of the publications on GO are supplied by the United States, which has a growing number of publications, particularly in North American countries. The rest of the world made a significant contribution. This bibliometric investigation revealed the world's expanding population. The quantity of citations is great, yet global collaboration is required to address this increasing and worrisome issue. As a result of keyword mapping analysis treatment protocols and pathogenesis were hot topics on GO.

Limitatitons

There are some limitations in the current study. It wasn't possible to include papers from journals that weren't indexed in the WOS database. Furthermore, because the keywords were all in English, publications in other languages may have gone unnoticed. Another problem was the lack of other databases such as Scopus and Pubmed. The analyses were carried out using the VOSviewer; however, alternative tools (such as CiteSpace II and Bibexcel) could be used in future studies.

Ethical Approval

For bibliometric investigations, no approval is required.

Conflict of Interest

As there is only one author, there is no need to declare a conflict of interest.

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