ARTÍCULO ORIGINAL

Research fronts on vitiligo, a Scopus based bibliometric survey

Frentes de investigación sobre vitiligo, un enfoque bibliométrico basado en Scopus

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ABSTRACT

Bibliometrics is frequently used to analyze the structural evolution of research fields, especially in biomedical areas. The present paper provides a macrostructure for scientific research on vitiligo conducted in the last fifty years using bibliometric methods. The data were retrieved from Scopus. A total 6 109 papers related to vitiligo were processed. An analysis was conducted of specialized terms based on the structure of the Medical Subject Headings (MeSH) thesaurus of the US National Library of Medicine. A structural approach was developed using term co-occurrence analysis. Hierarchical cluster analysis was used to identify the macrostructure, applying the CONCOR (CONvergence of iterated CORrelations) algorithm. Global scientific production on vitiligo was found to have increased exponentially in the last fifty years. Structural analysis revealed eight research areas divided in two blocks. On the one hand, an experimental block comprising studies on vitiligo, its relationships with cancer and other autoimmune diseases, its pathophysiology and pathogenesis; and on the other, a block including clinical studies covering various therapeutic approaches as well as the incidence and prevalence of the disease. The methodology applied constitutes a valid tool for the description and classification of biomedical knowledge domains. It also makes it possible to obtain a macrostructure which may be validated through bibliographic reviews.

Key words: vitiligo, bibliometry, term co-occurrence analysis, convergence of iterated correlations, structural analysis, CONCOR algorithm.

RESUMEN

La bibliometría se usa frecuentemente para analizar la evolución estructural de campos de investigación, especialmente en áreas biomédicas. El presente trabajo ofrece una macroestructura de la investigación científica sobre vitiligo durante los últimos 50 años a partir de métodos bibliométricos. Los datos fueron recuperados de Scopus. Un total de 6 109 artículos relacionados con el vitiligo fueron procesados. Fueron analizados los términos especializados basados en la estructura del tesauro *Medical Subject Headings* (MeSH) de la Biblioteca Nacional de Medicina de los Estados Unidos. Se desarrolló un enfoque estructural a partir del análisis de la co-ocurrencia de términos. Se utilizó el análisis de agrupamientos jerárquicos para identificar la macroestructura, a partir de la aplicación del algoritmo CONCOR (CONvergencia de CORrelaciones iteradas). La producción científica mundial sobre vitiligo mostró un crecimiento exponencial durante los últimos 50 años. El análisis estructural reveló ocho áreas de investigación divididas en dos bloques temáticos. En primer lugar, un bloque experimental que agrupa los estudios sobre el vitiligo, sus relaciones con el cáncer y otras enfermedades autoinmunes, su patofisiología y su patogénesis; y en segundo lugar, un bloque de estudios clínicos que agrupa diferentes enfoques terapéuticos, así como la incidencia y prevalencia de la enfermedad. La metodología aplicada ofrece una herramienta válida para la descripción y clasificación de dominios del conocimiento biomédicos. Además, permite obtener una macroestructura que puede ser validada a partir de revisiones bibliográficas.

Palabras clave: vitiligo, bibliometría, análisis de co-ocurrencia de términos, convergencia de correlaciones iteradas, análisis estructural, algoritmo CONCOR.

INTRODUCTION

Metrics are defined as a combination of quantitative techniques associated with a specialised field of scientific knowledge. The aim is to obtain descriptive, evaluative or prospective results from the dynamics of the field.[1]

Bibliometrics, as a metric discipline related to information, has frequently been used to analyze the structural evolution of different research fields and knowledge domains.[2-4] Biomedicine is one of the most studied topics in this regard, and many of medical specialties and specific diseases have been considered by bibliometric studies.[5-11]

Vitiligo is a common skin disease that seriously affects patient's quality of life. It is defined as a depigmenting skin disorder, characterized by acquired, idiopathic, progressive, circumscribed hypomelanosis of the skin and hair, with a total absence of melanocytes. It has an incidence rate of between 0.1% and 2%, with an uncertain cause and an unpredictable course.[12]

Despite a lot of review articles describing and sistematizing the most important research on the disease,[13-18] there are few bibliometric studies reported in the literature.[19-21] In addition, there are none that make a structural analysis of

published articles with the aim to describe the research *corpus* of the most prevalent pigmentary disorder.[22]

The objectives of this short communication are to obtain a domain's macrostructure and to identify research fronts and citation levels of the world scientific literature on vitiligo during the last fifty years using bibliometric methods.

METHODS

Data (retrieved on January the 7th, 2011) were collected from Scopus, the biggest database specialized in Science and Technology developed by *Elsevier*.[23] Scopus covers the entire content of PubMed, which is the most important database of the National Library of Medicine (NLM), as well as different international databases specialized in Medicine. This allows access to a wide range of literature from biomedical areas.

A total of 6 109 articles were identified in the database using the search term "vitiligo" in the fields *Title*, *Keywords* and *Abstract*, without a time limit. Articles were downloaded using the EndNote XIV software, developed by *Thomson Reuters* (http://www.thomsonreuters.com/endnote).

The selected units of analysis were specialized terms describing the articles content, based on the structure of the US National Library of Medicine's Medical Subject Headings (MeSH) Thesaurus. Check tags, main heading and subheadings were also considered. Terms coocurrence Analysis (TCA), a bibliometric technique frequently used for the structural analysis and visualization of knowledge domains, was conducted.[4,24-28] The most used terms (those that covered the 45 % of terms appearance in papers) were selected. A co-occurrence matrix of these most used terms (188 keywords used in more than 100 articles, excluding *vitiligo*) was obtained using the program *Bibexcel* (http://www.bibexel.edu.se).

A structural analysis using the program UCINET (created by Steve Borgatti for the study of social networks) was developed.[29] The analysis of hyerarchical clusters was used as a technique to identify substructures, applying the CONCOR (CONvergence of iterated CORrelations) algorithm.[30]

CONCOR algorithm has been applied in sociology, psyhcology, pedagogy, management, biology, politics and information science.[31-36] Papers from Csigó and Vedres.[37] and Magnusson and Mascia,[32] used the CONCOR algorithm for the discourse (content) analysis, and the bibliometric assessment of patents and research projects. The CONCOR is capable of processing large networks, allowing the organization and visualization of blocks through the analysis of the structural equivalence of terms.

Traditional documental analysis (literature review) was used to identify research areas in the eight groups of articles obtained by hyerarchical clustering. Citation analysis was also used to determine the citation activity of each group, taking into account the percentage of cited articles as an indicator. It is important to remark that citations derived from articles published before 1996 are not covered by Scopus, which would be related to low visibility levels in the early periods studied. The main topics and the most frequently used keywords in articles belonging to each research area were also identified.

RESULTS

The world scientific output on vitiligo has experienced an exponential growth during the last fifty years. From the 6 109 documents published during the studied period, 3 100 articles (50,7 %) belong to the last decade (Fig. 1). The same behavior was also observed in the citations growth, despite 38,2 % of articles published during the last decade belong to the period 2008-2010. These results provide clear evidence of a research field in progress, no matter the limited citations coverage of Scopus (1996-2011).

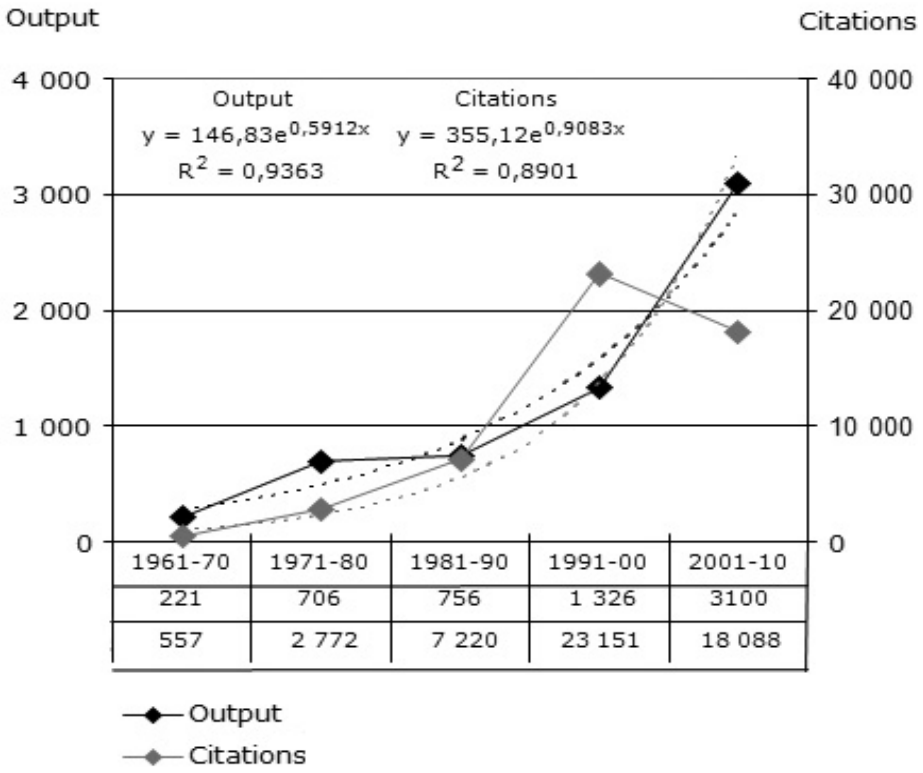

Fig. 1. World scientific research on Vitiligo: behavior of output and citations per decade during the last fifty years.

The linear growth of world scientific production on vitiligo during the period 1996-2010, confirms the increasing importance of this disease within the scientific community (Fig. 2). However, simple output-based indicators are not sufficient to understand the dynamics of the research behavior. A structural analysis of the literature, using keywords as analytical units, may offer a more comprehensive view.

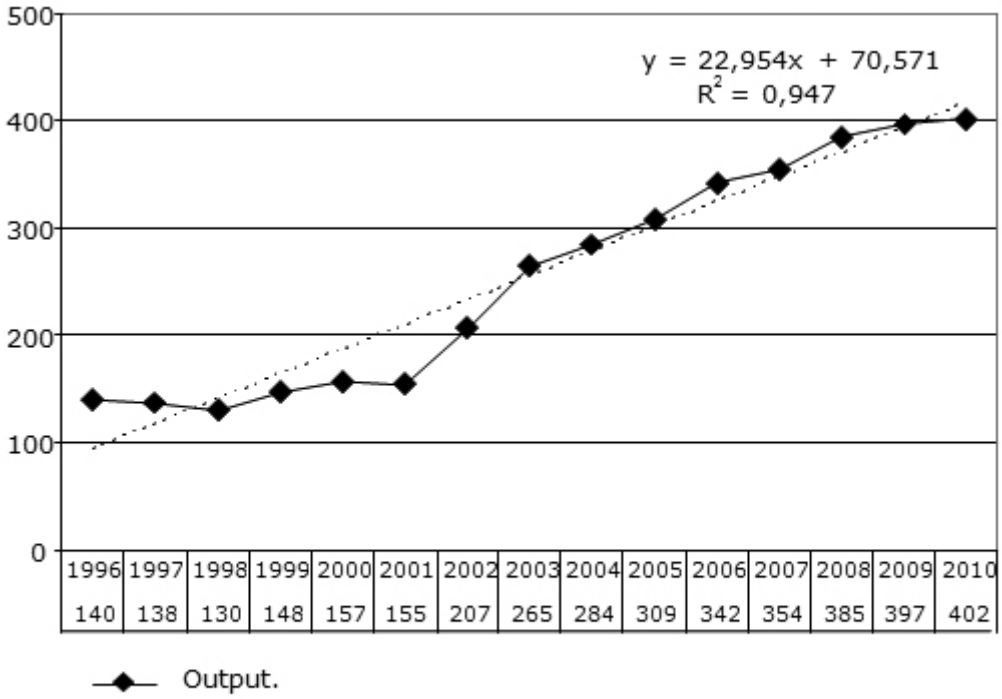

Fig. 2. World scientific output on vitiligo during the period 1996-2010.

IDENTIFICATION OF RESEARCH FRONTS

Bibliometric methods identified eight research areas divided in two blocks: experimental research and clinical research (table 1).

Table 1. Structure of the scientific output related to Vitiligo covered by Scopus

Block 1 Experimental research	Block 2 Clinical research
Area 1.1. *Vitiligo, cancer and autoimmunological disorders*	*Area 2.1.* *Therapeutical assessments*
a) Vitiligo and cancer	a) Drug therapy
b) Vitiligo and autoimmune diseases	b) Phototherapy and combined therapies
Area 1.2. *Pathophysiology of Vitiligo: pathogenesis and in vitro studies*	*Area 2.2.* *Epidemiological studies*
a) In vitro studies of animal models	a) Follow-up studies in age groups
b) Pathophysiology and pathogenesis	b) Incidence and prevalence

The experimental block covers a global area related to the study of vitiligo and its relationship with cancer and other autoimmunological disorders, and also a very important area involving pathophysiology and pathogenesis of this multifactorial disease. The clinical block involves the different therapeutical assessments and interventions of patients with Vitiligo, including an epidemiological front that deal with the incidence and prevalence of the disease, and also with the multiple age groups analyzed on follow-up studies.

The structural view obtained through the automated processing of articles on vitiligo covered by Scopus and the statistical analysis of the specialized terms centrality (in a relatively short time), is relatively similar to those obtained by classic documental analysis developed in the most recently published reviews on the disease.

EXPERIMENTAL RESEARCH

The experimental approach, according to the four areas revealed by the structure (table 2), involved a wide variety of topics. The relation of vitiligo with cancer, especially the coexistence of vitiligo with malignant melanoma, is frequently studied, and is a recurrent research area in the most recently published articles. The most cited articles involved in this area are evidence of this aspect,[38,39] especially those that reported tumor regression and autoimmune vitiligo after immunotherapy against malignant melanoma.[40-46] In this area, vitiligo is usually studied as a factor associated with response to cancer immune therapy. The citation activity of the research area is high (70-80 % of cited articles).

Vitiligo as a marker of autoimmune disorders is a research area that appears very early in scientific literature indexed by Scopus.[47-50] The citation frequency of the area is also high (70-80 % of cited articles), and there are strong links with the previous studies related to cancer research. Different autoimmune diseases (Addison's disease, Hashimoto's thyroiditis, insulin dependent diabetes mellitus, etc.) are specifically studied in this area as well.

Another important area involved in vitro studies of animal models. The citation frequency here is extremely high (80-90 % of cited articles). Melanoma, psoriasis and autoimmune diseases are frequently analyzed in pre-clinical studies and Mice are the most studied animal models. Cell proliferation, melanogenesis, enzyme activity and protein expression are recurrent topics. The most cited article of this area is also the most cited article retated to vitiligo in Scopus (643 citations received since 2001). This influential review on reactive oxygen species, antioxidants and the mammalian thioredoxin system, was developed by researchers of the Medical Nobel Institute for Biochemistry from the Karolinska Institute (Sweden).[51]

Finally, a fourth area involves papers related to pathophysiology and pathogenesis of vitiligo. Despite this area being less visible than others (65-70 % of cited articles), a group of important articles define the impact of the different research fronts involved.[52-56] Immunohistochemical studies are well represented in the area, as well as papers studying the histology and pathology of pigmentation disorders, and research on melanocytes and melanins.

CLINICAL RESEARCH

Therapeutical asessment and epidemiology of vitiligo are dominant subjects in the clinical block (table 3). Drug therapy is the first of the areas covered by this block. Steroids, specially hydrocortisone and corticosteroid-based drugs are well studied. Different skin disorders associated to vitiligo are included (atopic, seborrheic and contact dermatitis). There are a large amount of articles related to adverse effects of drug therapy (rash, fatigue, nausea, etc.). Also, studies on the quality of life in patients with vitiligo are covered. The area shows a low citation activity (65-70 % of cited articles), which is probably related to the fact that oral and topical treatments were highly studied in papers published before 1996. The most cited articles studied topical and oral treatments, but were always compared with phototherapies.[57-60] Psoralen, calcipotriol, clobetasol, fluorouracil are among the most studied drug therapies.

The most important area of this block is related to the use of phototherapy and combined therapy as a treatment for Vitiligo. Ultraviolet (A and B) radiation, and PUVA therapy combined with other therapies (psoralen, calcipotriol, etc.) were the most important treatments studied by randomized controlled clinical trials. The lower citation activity of this area (60-65 % of cited articles) is in contrast to the publications updated (more than 60 % were published in the XXI Century). However, more than 20 % of articles were published during the period 2008-2010, too early to receive a large amount of citations. Ultraviolet therapy, laser treatment and epidermal grafting are the main topics in the area which are clearly revealed by the most cited articles.[61-67]

The epidemiological approach of this clinical block is represented by an area of follow-up studies in age groups. Adolescents, middle aged and aged were the age groups most represented in the research front, but children are also a very important group treated by comparative and follow-up studies. Childhood vitiligo is analyzed in some of the most cited papers.[68-71] Differential diagnosis and prognosis of the disease are also among the main research fronts of an area with a high citation frequency (75-80 % of cited articles). Topics like hypopigmentation, skin defect, family history, disease severity, time factors and risk assessment related to vitiligo were frequently studied in papers.

At the same time, the last obtained area analyzes the incidence and prevalence of vitiligo. Less visible than previous areas (65-70 % of cited articles), this area shows important research fronts related to risk factors, clinical manifestations and different associated diseases. The associated diseases include *systemic lupus erythematosus*, *rheumatoid arthritis*, *thyroid diseases*, *Vogt Koyanagi syndrome*, alopecia areata, diabetes mellitus and many others. The most visible paper of the area is also among the most cited articles of the scientific output on vitiligo in Scopus.[72] The close relation between vitiligo and associated autoimmune diseases is also a relevant topic covered by the most influential literature.[73]

DISCUSSION

The bibliometric approach proposed in this paper, based on the analysis of hierarchical clusters, is one of the different quantitative methods used to obtain a comprehensible macrostructure of a knowledge domain. In this case, the scientific literature on vitiligo was used to explore the dynamics of the concerned biomedical areas as an organic system. The obtained macrostructure is an integral part of this system, developed with the aim to present with simplicity and clarity for scholarly communication and public understanding the main research fronts on the disease.

Bibliometric analysis on research fronts are well established in the literature, and co-citation networks are often used to represent the core structure of a knowledge domain.[2] However, the current paper uses TCA (co-words) techniques to achieve that goal. Co-word analysis is inspired by the actor-network theory.[24] This theory is based on scientists' use of scientific publications as a vehicle for research ideas, hence creating a semiotic network of concepts.[74] Co-word analysis measures the strength of relationships between two documents by the co-occurrence of terms (phrases, descriptors, classification codes, etc) in a chosen domain. In this paper, the clustering of a co-descriptor network is used to illustrate the cognitive structure of the biomedical field.

Cluster analysis encompasses a number of different classification algorithms with the aim to organize big amounts of information into manageable piles, called clusters. A cluster problem involved set of «objects» (e.g. documents, terms) and a similarity or distance function. The goal is to divide the object set into number of sub-sets (clusters) that best reveal the structure of the object sect. These can take the form of partitions or a hierarchically organized taxonomy.[2] Despite no clustering algorithm is particularly better than others when producing the same number of clusters,[75] different experiences suggest that some approaches are more "reliable" than others for generic dataset.[76]

In this case, the CONCOR algorithm was used to process a network of highly used keywords. The resulting image is a reduced representation of the network, divided in hierarchical blocks. Each block shows the interrelationships of keywords in articles. Thus, homogeneous clusters of terms with high density constitute the different domains' areas and research fronts.

The clustering developed by mean of the CONCOR algorithm, allowed the authors to obtain a macrostructure that clearly reveals a research activity strongly focused on the main challenges faced up by physicians devoted to the study of vitiligo.

The main concerns related to the disease are implicit in the clusters obtained: It is the most prevalent pigmentary disorder; it is related to genetic and non-genetic factors; the pathogenesis still is not understood, which is the reason of a plethora of different treatments; it is relatively resistant to most of these treatments; coexists with other autoimmune disorders, including thyroid diseases and malignant melanoma; affects seriously the emotional stability, with a major impact on the quality of patients' life; the course of the disease is unpredictable, but often progressive; and the lack of melanin pigment increased the risk of sunburn and skin cancer within the amelanotic areas.[12] The identified research fronts are mainly covered by epidemiological studies, therapeutical assessments and experimental exercises to analyze the pathogenesis of the disorder and its relation with cancer and autoimmune diseases. This is in accordance with the most relevant reviews on the disease, which validates the effectiveness of the analytical technique proposed in this paper to characterize the major research efforts developed during the last fifty years.

CONCLUSION

The bibliometric approach allowed the structural analysis of a large amount of data (6 109 papers) in a relatively short time. The applied methodology, using the CONCOR algorithm for the analysis of keywords co-ocurrence in the articles, offers a valid tool for information clustering, description and classification in different knowledge domains. In this sense, the international scientific research on Vitiligo

was characterized. It was possible to obtain a macrostructure of the domain, which can be further validated through documental analysis and literature reviews.

Despite the current study identifying research fronts in the whole period, further analysis is needed in order to describe the evolution of the main areas per decades. In the same way, the study of the most relevant authors, the identification of the most productive countries, and the characterization of the most important journals where the scientific output is published, would be a necessary complement to analyze the behaviour of international scientific output related to vitiligo.

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