Analyzing the Research Trend of Vitiligo in Dermatology From 1963 until 2023: A Bibliometric Analysis

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Abstract

Background: Vitiligo is one of the most common skin pigmentation disorders, which could significantly impact the possessor's quality of life. Scholars have devoted considerable effort to advance the understanding of vitiligo but until now the treatment modalities often fall into a suboptimal condition. There are abundance of scientific updates which challenges healthcare providers to catch up with all the vast knowledge. **Objective:** This study aims to provide a global picture of vitiligo research and the trend of vitiligo research. **Methods:** This study was a bibliometric analysis study that used Scopus as the primary article database. A total of 1374 articles were analyzed using VOSviewer and Biblioshiny. **Result:** There was an increasing number of vitiligo articles published annually from 1963 until 2023. The most productive counties were United States of America, India, and the United Kingdom. There were four major global vitiligo research topics including epidemiology, psychology, conventional treatment, and advanced treatment. Evaluating the psychological aspects of vitiligo patients using DLQI (Dermatological Life Quality Index) is one of the recent research topics. The treatment for vitiligo shifting towards on targeting specific molecular, such as biological agents and janus kinase inhibitors. Understanding the pathogenesis of vitiligo is needed to find a better treatment modality that is specific, effective, and has minimum adverse effects. **Conclusion:** Current global research efforts in vitiligo shifting towards the modality of treatment that targeting specific molecular based on the pathogenesis, with also encompassing the management psychological aspect to ensure better quality of life of the possessors.

Keywords: advanced treatment; bibliometric analysis; psychologic aspects; vitiligo

Review Article

INTRODUCTION

Vitiligo is an acquired autoimmune skin disease caused by melanocyte dysfunctions (Dwiyana et al., 2017). Vitiligo is the most common skin pigmentation disorder, characterized by well-defined hypopigmentation macules.(Dillon et al., 2017) Its prevalence ranges from 0.5% to 2% globally and varies considerably by geographic location.(Dillon et al., 2017; Dwiyana et al., 2017) The etiology of

vitiligo is not understood clearly (Dwiyana et al., 2017). Current understanding suggests a multifactorial origin of vitiligo, implicating genetic predisposition, imbalanced biochemical pathways, autoimmune process, melanocyte dysfunction, and disrupted neurological systems as the pathogenesis of Vitiligo.(Dillon et al., 2017) Beyond its physical manifestation, vitiligo exerts a profound psychological impact that often leads to a decrease in the possessor's self-esteem, depression, and social stigma (Dillon et al., 2017; Manga et al., 2016). Approximately 6-25% of patients with vitiligo ended up with suicidal ideas (Padmakar et al., 2022).

Conventional therapies for vitiligo encompass topical treatments, systemic immunomodulators, and phototherapy (Dillon et al., 2017). These conventional therapy modalities usually have a suboptimal result in treating vitiligo, failing to achieve complete re-pigmentation or prevent disease recurrence (Manga et al., 2016). Consequently, there is a pressing need for further research into vitiligo to understand deeper about this disease. Magnificent updates on the pathogenesis of vitiligo increase to development of better therapy modalities (Padmakar et al., 2022).

Rapid knowledge development challenges the healthcare provider to follow abundant scientific updates. A bibliometric analysis is quantitative research that contains an analytical, statistical study method using a bibliography of published documents. It served as a valuable tool for comprehensively assessing the landscape or a big picture of research, deciphering, and mapping the cumulative research fields (Donthu et al., 2021; Şenel, 2020). Several aspects included in the bibliometric analysis are co-occurrence keywords, scholar's name, affiliations name, and country's productivity (Şenel, 2020). This method is different with other literature review methodology such as metaanalysis and systematic review. Meta-analysis is quantitative research that aims to estimate the strength and direction of effect and the variance across studies, this method tried to summarize empirical evidence and uncover new relationships. Systematic review is the type of literature review which summarize and synthesizes existing literature review which have narrower scope of research (Passas, 2024).

Bibliometric analysis has long been used as one of the research methods in many research fields including dermatology. A study used bibliometric analysis to recognize dermatology research and researcher performance in dermatology (Maymone et al., 2020), another study used bibliometric analysis to understand the hotspot research topic in dermatology (Lee et al., 2023). Bibliometric analysis was different from other literature review based on the objective of this research such as unravelling the emerging trends, collaboration patterns, and research constituent (Donthu et al., 2021). Meanwhile, the literature review is a research methodology which has several types; one of the types of the literature review is a narrative review, which is different from bibliometric analysis. A narrative review is subjective research that aims to review all the articles that could be relevant to the topic (Snyder, 2019). The aims of this research is to provide a global picture and trend of vitiligo research from the first publication until recently, conducted from 1963 to 2023. It also provided the future direction of vitiligo research that could provide basic data for further research.

MATERIALS AND METHODS

A bibliometric analysis was conducted utilizing Scopus as the primary article database. The search strategy employed a Boolean operator with "Vitiligo" and "Dermatology" as the keywords. The author used a broad keyword to retrieve more publication data. Data was downloaded on July 15, 2023. Inclusion criteria encompassed articles published from 1963 to 2023, written in English, including observational study, experimental study, literature review, systematic review, and meta-analysis. Collected articles were analyzed using VOSviewer, Biblioshiny by R Studio, and Scopus-based bibliography analysis tools.

Biblioshiny and scopus based bibliography analysis tools facilitated the examination of publication productivity across timelines and geographical locations. VOSviewer is a tool that already developed for visualizing bibliometric netrworks. This tool provides an easy and basic functionality, and by default it is providing not only network or interrelation between nodes but also to cluster. The cluster was made based on the closely related nodes (van Eck & Waltman, 2014). Overlay analysis

provided insights into the temporal distribution of research topics, with brighter colors indicating recent publications and darker colors indicating former publications. In cluster-based analysis, the graphic size denoted the volume of published documents, while line thickness and distance between graphics represent the correlation between topics. Graphic colors of the represent the cluster which the nodes have been assigned (van Eck & Waltman, 2014).

There were two approaches that we used in this study, the performance analysis and the science mapping. The performance analysis will provide the total publication produced based on the counties and the total publications per years. The science mapping approach this study used co-citation analysis to understand the interrelation between reference work (Passas, 2024).

RESULTS

There are 1374 articles was retrieved from Scopus. The annual publication productivity of vitiligo research (Figure 1) reveals an increasing number of publications from 1963 until 2023, with a notable peak in production observed from 2020 to 2021. Figure 2 displays country-specific productivity, with the United States of America, India, and the United Kingdom emerging as the top three most prolific contributors in vitiligo research, followed by Itali, China, France, Germany, Turkish, Iran, and the United Arab Emirates.

Global research in vitiligo is depicted in Figure 3, where four prominent clusters emerge from cluster-based analysis based on the keyword co-occurrence. The four clusters included epidemiology, psychological aspects, conventional treatment, and advanced treatment modality. Notably, recent publications predominantly focus on advanced treatment.

The epidemiology cluster, characterized by its substantial graphical size, encompasses various topics such as gender distribution, prevalence rates, age demographics, risk factors, disease duration, onset, and prognosis. The second cluster was the psychological aspect with several topics, including depression, psycho-dermatology, quality of life, DLQI (Dermatological Life Quality Index), and stigmatization. Publication in this cluster was identified by the brighter colors in the overlay analysis, which mostly concentrated primarily between 2014 and 2016.

Conventional treatment topics encompass corticosteroids, pimecrolimus, psoralen, methoxalen, vitamin D, excimer laser therapy, and phototherapy. These publications were predominantly dated between 2010 and 2012, with darker graphic colors in overlay analysis. Conversely, the advanced therapy cluster focuses on topics such as Janus Kinase (JAK) inhibitor, tofacitinib, methotrexate, and signal transduction pathways, with publications displaying brighter colors in overlay analysis, indicative of more recent research endeavors.

Global research trends in vitiligo are shown in Figure 4 based on the overlay analysis provided based on the VOSviewer. The brighter yellow coloured picturing the newest/ more recent topics in vitiligo. The most recent topics in vitiligo were psychologic aspect of vitiligo and also the advance treatment modality in vitiligo including molecular targeted therapy, nivolumab, JAK inhibitor.
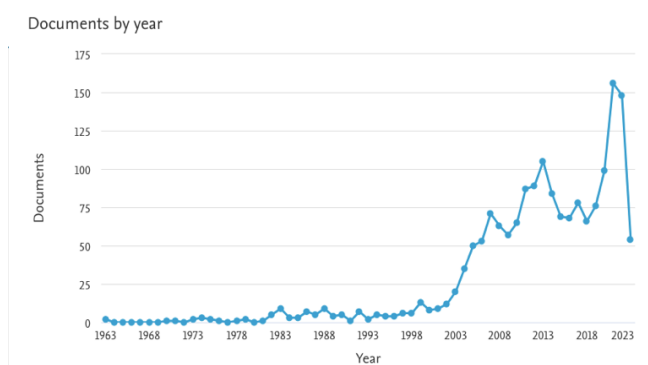

Figure 1. Global Article Publication Productivity of Vitiligo in Dermatology from 1963 to 2023
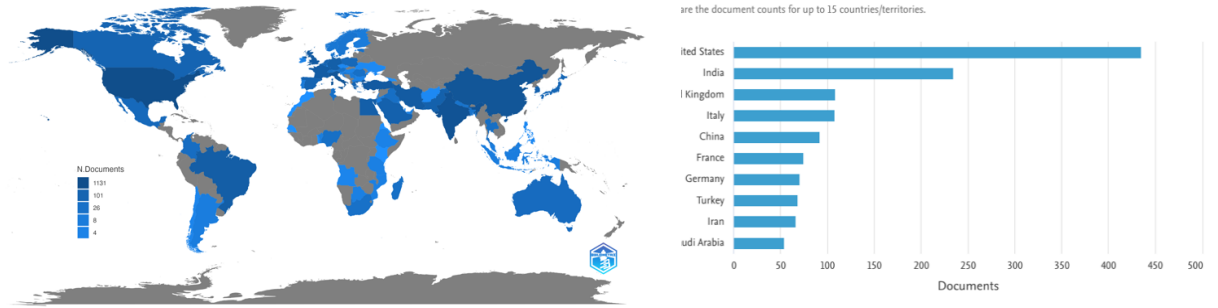
Figure 2. Global Country-based Article Productivity of Vitiligo in Dermatology from 1963 to 2023
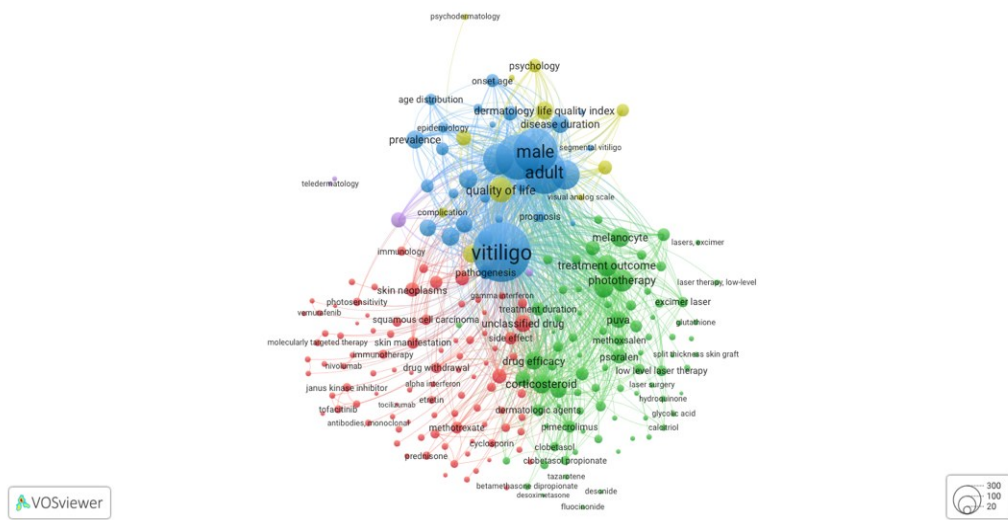

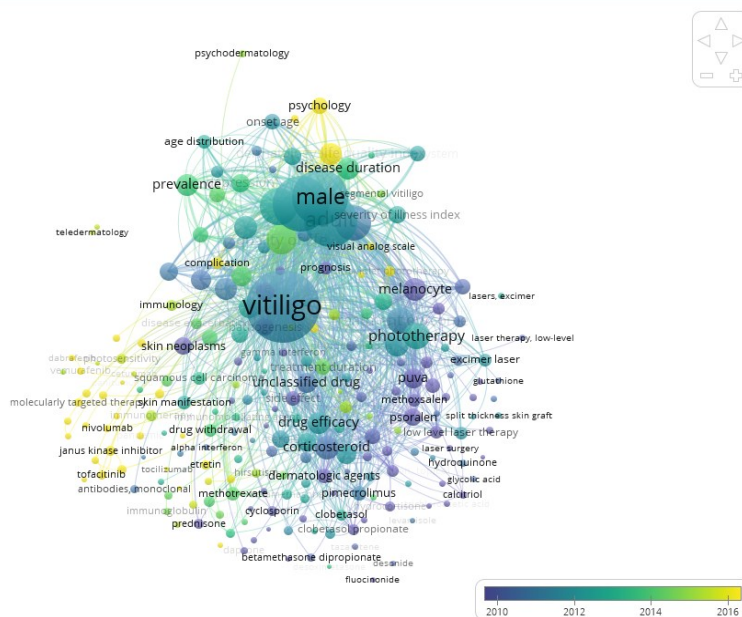**Figure 3.** Global Research Mapping of Vitiligo in Dermatology Cluster-Based Analysis from 1963 to 2023

Figure 4. Global Research Mapping of Vitiligo in Dermatology Overlay Analysis from 1963 to 2023

DISCUSSION

A bibliometric analysis of the dermatology research hotspot highlights vitiligo as one of the top ten most published skin disorders (Lee et al., 2023) Despite being commonly perceived as a cosmetics issue, vitiligo imposes substantial burdens on the individuals affected by this condition.(Picardo et al., 2022) Thus, continual scientific advancements remain crucial to alleviate these burdens comprehensively.

This study shown that the annual article production of vitiligo has shown an increasing trend since the first publication in 1963, with peak production observed during the pandemic of COVID-19 from 2020 to 2021. The pandemic of COVID-19 prompted an acceleration in the publication process, especially on the issues that correlated with COVID-19 (Amerio et al., 2023; Raynaud et al., 2021; Rousseau et al., 2023). It was reported that some journal maintain the number of non-COVID related medical article publication thus increasing the total number of publication, meanwhile other journals decrease the proportion for non-COVID related medical article publication (Raynaud et al., 2021; Rousseau et al., 2023).

Various medical field try to explore the association between their field and the COVID-19 infection including dermatology, even though dermatology is not directly associated in the management of COVID-19 (Amerio et al., 2023). Dermatologist interested in assessing the cutaneous consequenses of infection and the implication of COVID-19 infection in dermatological patient (Amerio et al., 2023). especially in vitiligo disease, there were several cases reported a coincidence of de novo vitiligo following COVID-19 infection and vaccination, especially in individuals with susceptible predisposing genetic factors (Shi et al., 2023; Tiwari et al., 2023) There was also reported the progressive state of vitiligo after the COVID-19 infection and vaccination, especially in an individual with an active disease it was reported to have a higher risk of disease progression (Shi et al., 2023). The occurrence of COVID-19 pandemic restrict many patient to visit the outpatient clinic, including vitiligo. A study had reported that the delayed of treatment is risk factor for vitiligo progression and recurrency for active vitiligo (Xu et al., 2021).

The United States of America, India, and the United Kingdom predominantly lead the top ten countries contributing to vitiligo research articles. Publication is the major output for scientific research, and traditionally USA was reported as the leading country of publication. The number of publications varied within nation but the exact reason is yet to be explained (Man et al., 2004). Countries with strong research funding and English proficiency are overrepresented to have a higher number of publications (Man et al., 2004). Indonesia's productivity ranking was outside of the top ten countries with highest number of publications. The prevalence of vitiligo in Indonesia needs to be more reported and well documented. The number of vitiligo visits at the cosmetic division of the outpatient clinic in Dr. Soetomo General Academic Hospital from 2018 until 2020 was 1.4% of all clinic visits (Saiboo et al., 2023). Even though vitiligo patient may not be as prevalent in Indonesia compared to other diseases, its significant psychological impact underscores the importance of increasing research efforts and fostering collaboration between developing and developed nations (Şenel, 2020).

Various demographic characteristics, including gender and age distribution, exhibit geographical variation in vitiligo prevalence (Zhang et al., 2016). Africa and India report the highest vitiligo prevalence rates (Zhang et al., 2016), while other studies indicate that Europe and the United States of America lead in estimated prevalence on a continental scale (Al-smadi et al., 2023). There is a suspected genetic contribution to varying prevalence rates among populations based on the geographical area (Said-Fernandez et al., 2021; Spritz & Andersen, 2017). Therefore, there is the urge need for ongoing epidemiological surveillance. Vitiligo commonly reported higher incidence in female even though it is not significantly different (Saiboo et al., 2023; Suseno et al., 2018). A study had reported that vitiligo in male present with a longer duration of disease and more likely to report a family history of vitiligo (Patil et al., 2014). Beside that vitiligo in female reported to have a higher predominance of having a higher stress level (Samela et al., 2023).

The psychological aspect is one of the aspects that need to be monitored during vitiligo treatment. Vitiligo does not just affect the physical aspects but also the psychological aspects of the individuals. Vitiligo is classified as one of the psycho-dermatology or a secondary psychiatric disorder (Bidaki et al., 2018). Psychological stress can exacerbate vitiligo severity and vice versa, as the condition's visible manifestation often leads to disturbance in private and social life, diminished quality of life, and societal stigmatization. Unfortunately, healthcare providers frequently are negligent in evaluating and treating the psychological aspects (Bidaki et al., 2018). Vitiligo patients with visible cutaneous lesions are more likely to have a higher negative impact. A survey of 600 vitiligo patients shows that 59% of vitiligo patients experience negative impacts on daily activities (Al-smadi et al., 2023). One of the tools for assessing the quality of life is DLQI. It is important for healthcare workers to do early surveillance to detect psychological disturbance in the possessor, including suicidal ideas, and do early referral (Padmakar et al., 2022).

Conventional treatment modalities for vitiligo involve immunosuppressant agents that have nonspecific or nontargeted molecular mechanisms (Karagaiah et al., 2023). Abrupt cessation of the conventional treatment often results in disease relapse (Karagaiah et al., 2023). Limited understanding of vitiligo pathogenesis has constrained treatment options to generalized and nonspecific approaches. Therefore, one of the future directions of vitiligo research aims to elucidate the underlying pathogenic mechanism, paving the way for safer and more effective treatment modalities (Karagaiah et al., 2023).

Contemporary research has shed light on the underlying pathogenesis of vitiligo, revealing the cytokines and signaling pathways involvement. Advanced treatment modalities are now tailored to target specific molecular mechanisms (Migayron et al., 2020). These include a biological agent that works by inhibiting specific cytokines and small molecule inhibitors that target intracellular signaling molecules (Feng & Lu, 2022).

Janus kinase (JAK) inhibitor represents a promising avenue in vitiligo treatment, functioning by inhibiting the enzyme called Janus kinase. Tofacitinib and ruxolitinib are two such agents currently undergoing clinical trials for vitiligo (Karagaiah et al., 2023). Ruxolitinib is the only JAK Inhibitor agent that has already been approved by the FDA (Food and Drug Administration) for non-segmental vitiligo aged 12 years above. This agent offers a new possibility for repigmentation for vitiligo patients, hence increasing the quality of life and reducing the number of phototherapy sessions with minimum adverse events (Siddiq et al., 2022). Nevertheless, the biological agent that could be the potential agent for vitiligo is anti-TNF (Tumor Necrosis Factor) –α these include adalimumab, etanercept, and infliximab. The other agent is IL17/23, currently under further research, such as ixekizumab and secukinumab. The immune checkpoint modulator, abatacept, is also currently under further research (Karagaiah et al., 2023).

Amidst these research advancements, research has also explored the possible paradoxical effect of certain treatments. Tofacitinib, a JAK inhibitor agent that works by inhibiting the JAK1 and JAK3 receptors, is associated with the occurrence of de novo vitiligo in a patient with rheumatoid arthritis under tofacitinib treatment. Even though this coincidence has not been confirmed to be related (Nguyen et al., 2020). Another case reported a paradoxical effect on the use of antiTNF-α, which has been linked to an increasing risk of vitiligo twice higher after antiTNF-α consumption. Several hypotheses were proposed as the explanation; the disequilibrium of cytokine might be the underlying mechanism of de novo vitiligo (Bae et al., 2018). Larger clinical trials are necessary to validate these findings and provide more comprehensive insights.

This study offers a comprehensive overview of global research on vitiligo since the first published article. There are many unfinished burdens about vitiligo especially on the treatment modality, the impact on psychological aspects, and understanding the pathogenesis of vitiligo. While this bibliometric analysis provides beneficial insights, further research incorporating additional databases is warranted to broaden the scope and provide a more holistic picture.

CONCLUSION

Current global research efforts in vitiligo are increasingly directed towards comprehensive case management, encompassing psychological aspects along with the quest for safe, effective, and specific treatment modalities rooted in a deeper understanding of vitiligo pathogenesis. Notably, Ruxolitinib stands as the sole FDA-approved specific molecular therapy for vitiligo. However, scientists and healthcare providers must recognize the dual nature of targeted molecular treatments, as they may pose both benefits and risks. Hence, ongoing research with vigilant monitoring and fostering collaboration between developing and developed nations is imperative to navigate the complexities of vitiligo treatment successfully.

CONFLICT OF INTEREST

None.

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