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The evolution of Pemphigus publications
A bibliometric analysis with research trends and global productivity

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Abstract

Despite an increase in global research on the subject of Pemphigus, which seriously affects patient health and quality of life, there is no bibliometric research on this subject in literature to date. The aim of this study was to conduct a holistic analysis of scientific articles published on Pemphigus, using bibliometric methods. Articles published on the subject of Pemphigus between 1980 and 2021 were downloaded from the web of science (WoS) database and analyzed using various statistical methods. To determine trend subjects, collaboration between countries, and the most effective studies with citation analyses, visual network maps were obtained with bibliometric analyses. A total of 3034 articles were analyzed. The 3 countries making the greatest contribution to literature were the USA (n:831, 27.3%), Japan (n:402, 13.2%), and Germany (n:221, 7.2%). The 3 most active institutions were Keio University (n:163, 5.3%), Kurume University (n:130, 4.2%) and Tel Aviv University (n:107, 3.5%). The 3 journals publishing the most articles were the British Journal of Dermatology (n: 88), Journal of the American Academy of Dermatology (n:171) and the Journal of Investigative Dermatology (n:143). The 3 leading journals according to the mean number of citations (NC) per article (citation count: CC) were the New England Journal of Medicine (CC:246), the Lancet (CC:143) and the Journal of Cell Biology (CC:133). The author with the most articles published was Hashimoto Takashi (n.168, 5.5%). As a result of cluster analysis, it was seen that 9 different main clusters had been studied on Pemphigus subjects to date (1: desmoglein, 2: paraneoplastic Pemphigus (PNP) – Pemphigus types-desmosome, 3: desmoglein 1 ve 3-autoimmunity, 4: treatment-rituximab, 5: acantholysis-apoptosis, 6: quality of life-remission-relapse, 7: autoantibodies, 8: epidemiology-mortality, 9: corticosteroids). The most commonly studied subjects were determined to be pemphigus vulgaris (PV), pemphigus foliaceus (PF), autoimmunity, rituximab, PNP, desmoglein (desmoglein3-desmoglein1), autoantibodies, acantholysis, autoantibody, treatment, autoimmune disease, desmosome, ELISA, and immunofluorescence. The primary trending topic was rituximab drug, which is used in the treatment of Pemphigus. The other most studied trend topics were azathioprine drug used in treatment, intravenous immunoglobulin treatment, quality of life, mortality rates, Pemphigus herpetiformis, and wound healing.

Abbreviations: AC = average citation per article, CC = citation count, CI = confidence interval, GDP = gross domestic product, HDI = human development index, NC = number of citations, PF = pemphigus foliaceus, PNP = paraneoplastic Pemphigus, PV = pemphigus vulgaris, UK = United Kingdom, USA = United States of America, WoS = web of science.

Keywords: bibliometric analysis, paraneoplastic pemphigus, Pemphigus foliaceus, Pemphigus vulgaris, trends.

1. Introduction

Pemphigus is an uncommon, severe, autoimmune disease affecting the skin and mucosa, which manifests with fluid-filled blisters.[1–4] IgG autoantibodies are characteristically elevated against desmoglein 1 and desmoglein 3, which are cell-cell adhesive molecules found in desmosomes.[3] Pemphigus can be classified into 3 main sub-forms: Pemphigus vulgaris (PV), Pemphigus foliaceus (PF), and paraneoplastic Pemphigus (PNP).[3]

In PV, blisters develop immediately over the basal cell layer and are associated with autoantibodies against desmoglein 3,

which is a keratinocyte cell surface adhesive molecule. PV is the most common form of the disorder, and the wounds generally start in the mouth and make eating difficult. Although PV can emerge at any age, it is seen most often between the ages of 40 and 60 years.[5] In PF, the blisters are higher immediately below the stratum corneum in the epidermis and are associated with desmoglein 1, which is another cell surface adhesive molecule.[2] Of the 3 types, PF is the least severe. PF usually starts on the scalp, and is characterized by scabbed wounds which can move to the chest, back and face. Intra-oral wounds do not form, it is not as painful as PV, and are often confused with

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dermatitis or eczema.[5] The phenotype of PNP is typically characterized by blisters in the deep epithelial layers and interface dermatitis, and originates from a combination of humoral and cellular reactions.[3] PNP is the least frequently seen and most severe Pemphigus type. This disorder is generally a complication of cancer, primarily lymphoma and Castleman disease. It may develop before diagnosis of the tumor, with painful sores in the mouth, on the lips, and in the esophagus. This disease process in Pemphigus usually includes the lungs and causes constrictive bronchiolitis.[6]

The disease is diagnosed from clinical symptoms (loose blisters and erosions on the skin and oral mucosa), and histological and immunochemical tests.[2,3] Skin lesions caused by Pemphigus can led to fatal infections, and therefore treatment is extremely important. Pemphigus, which is usually fatal when not treated, is generally treated with topical, oral, or intralesional corticosteroids. Other treatment options include immunosuppressive agents (micophenolate mofetil and azathioprine), intravenous immunoglobulin (IVIG), and adjuvant treatments including plasmapheresis and immunoadsorption.[2,3,7] Biological agents such as rituximab, which is an anti-CD20 antibody, have been found to improve severely resistant PV cases and have been approved as first-stage treatment for moderate and severe PV in Europe and the USA.[3,4,8,9]

Pemphigus is a rarely seen disease and the global incidence varies significantly. In most populations, PF is less common than PV.[10] In Europe, the USA, and Japan, PV is the most common subtype, whereas PF is the endemic form in South America and North Africa, and thus the most often seen subtype.[11] Although all ethnicities can be affected by the disease, it is most common in those of Mediterranean and Jewish origin.[2] PV incidence has been reported at varying rates; as 0.7 (0.6–0.8) per 100,000 per year in the UK,[12] 0.5 per million in Germany, 8 per million in Greece, 16.1 per 100,000 in Israel, 0.076 per 100,000 in Finland, and 1.61 per 100,000 in Jerusalem.[10,13–15] The incidence of PNP is unknown but it is lower than for PV and PF.[3]

Bibliometry is the analysis of scientific publications using various statistical methods.[16–18] Due to bibliometric studies, researchers can have greater knowledge of the literature by reading the summarized findings of thousands of studies.[16] By showing the previous and current subjects of research, bibliometric studies can also offer ideas for new studies.[17] In parallel with the increasing number of publications in literature, bibliometric research has been conducted on many subjects in the field of medicine.[16–18]

As a result of a meta-analysis and systematic examination of 16 studies from 8 different countries, it was reported that health-related quality of life was seriously diminished in patients with Pemphigus and the decrease in health-related quality of life was clearly associated with high disease activity, anxiety and depression.[19] Despite the increase in the number of studies worldwide on the subject of Pemphigus, which seriously affects patient health and QoL, there has been no bibliometric research on this subject to date. The aim of this study was to holistically analyze scientific articles published on the subject of Pemphigus between 1980 and 2021 using various statistical and bibliometric methods.

2. Material and methods

2.1. Research strategy

Web of Science Core Collection (WoS by Clarivate Analytics) database was used for literature review. The search process was determined as 1980 to 2021 (publications before 1980 are not available in WoS). All publications containing any of the words related to "Pemphigus" (PV, PF, PNP, Pemphigus vegetans etc) in the title were accessed. The search was conducted in all research areas, but studies published in the Veterinary Sciences, Entomology, Ecology, Agriculture, Zoology, Plant Sciences research field were excluded and not included in the analysis. Repeatability codes (search findings may change depending on different access dates) for researchers to access similar documents: (*Title: ("Pemphigus") Refined by: NOT Research Areas: (Veterinary Sciences or Entomology or Ecology or Agriculture or Zoology or Plant Sciences) Timespan: 1980–2021*).

2.2. Statistical analysis

VOSviewer (Version 1.6.16, Leiden University Center for Science and Technology Studies) software was used for bibliometric network visualizations, citation, trend and cluster analyses.[20] Statistical analyses were performed with SPSS (Version 22.0, SPSS Inc., Chicago, IL, License: Hitit University) software. The website (https://app.datawrapper.de) was used to create the world map showing the distribution of publications by country. The Exponential Smoothing estimator was used in Microsoft Office Excel to estimate the number of articles that could be published in the next 5 years based on past publication trends. The normal distribution test of the data was performed with the Kolmogorov-Smirnov test. Correlation analyses between world publication productivity on Pemphigus and some economic development indicators of countries (gross domestic product [GDP], GDP per capita, Human Development Index [HDI]) were analyzed with Spearman correlation coefficient since the data were not normally distributed (data obtained from world bank[21]). $P < .05$ was accepted for a statistically significant correlation.

This article does not include any studies with human participants or animals by any of the authors. Therefore, ethics committee approval is not required.

3. Results

As a result of the literature review, there were a total of 6516 publications on Pemphigus published in all research areas in the WoS database during the 1980 to 2021 period. A total of 251 publications published in the research fields of Veterinary Sciences, Entomology, Ecology, Agriculture, Zoology and Plant Sciences were excluded and 6265 publications were obtained. Of these publications, 48.4% (n = 3034) were Articles, 24.8% (n = 1553) were Meeting Abstracts, 15.1% (n = 947) were Letters, 4.4% (277) were Review Articles, 1.4% (90) were Proceedings Papers and the rest were in other publication types (Editorial Materials, Notes, Early Access, Book Chapters, News Items, Corrections, Additions, Discussions). Bibliometric analyses were carried out with 3034 articles published in the article category out of a total of 6265 publications. 90.7% (n = 2753) of these articles were published in English and the remainder in other languages (French (n = 96), German (71), Russian (43), Spanish (27), Turkish (21), Polish (9), Portuguese (9), Hungarian (2), Czech (1), Estonian (1), Serbian (1)). The h-index of 3034 articles was 100, average citations per article 21.47, sum of times cited 70007 (without self-citations: 40062). The majority of the articles were indexed in the SCI-expanded (n = 2820, 92.9%). 6.7% (n = 203) were indexed in the Emerging Sources Citation Index (ESCI). In addition, 0.8% (n = 24) of the articles were indexed in the Social Sciences Citation Index (SSCI) (as some studies indexed in the SCI-expanded are also indexed in the SSCI, the number and percentage of articles may be higher than the total number).

3.1. Research areas

After Dermatology (1969, 64.9%), the other top 10 research areas with the most research on Pemphigus were Immunology

(273, 8.9%), General Internal Medicine (196, 6.4%), Pathology (131, 4.3%), Dentistry Oral Surgery Medicine (95, 3.1%), Research Experimental Medicine (88, 2.9%), Cell Biology (64, 2.1%), Biochemistry Molecular Biology (56, 1.8%), Pediatrics (52, 1.7%), Infectious Diseases (50, 1.6%), and Pharmacology Pharmacy (41, 1.4%) respectively.

3.2. Development of publications over the years

The distribution of the number of published articles by year is shown in Figure 1. The estimation values of the results of the Exponential Smoothing estimation model used to predict the number of articles that can be published in the next 5 years are shown in Figure 1. According to the estimation model results, it is estimated that 112 (Confidence Interval %: 96–129) articles will be published in 2022 and 126 (CI%: 105–147) articles will be published in 2026 (Fig. 1).

3.3. Active countries

The distribution of the number of articles by world countries is shown in Figure 2. The top 20 countries with the highest

number of articles published were USA (831, 27.3%), Japan (402, 13.2%), Germany (221, 7.2%), Italy (206, 6.7%), France (188, 6.1%), Brazil (169, 5.5%), Israel (168, 5.5%), Iran (140, 4.6%), UK (138, 4.1%), India (129, 4.2%), China (112, 3.6%), Turkey (91, 2.9%), Spain (70, 2.3%), Poland (69, 2.2%), Switzerland (57, 1.8%), Australia (46, 1.5%), Netherlands (46, 1.5%), Greece (40, 1.3%), Canada (39, 1.2%), and South Korea (39, 1.2%) (Fig. 2).

Cluster analysis was performed among 50 countries that produced at least 2 articles from 83 countries that published articles on Pemphigus and had international cooperation among their authors, and it is shown in Figure 3A. According to the results of the cluster analysis, 8 different clusters were formed for international cooperation. In addition, the total link strength (international cooperation score) scores, which show the cooperation power of 64 countries, were calculated and the international cooperation density map created according to these scores was shown in Figure 3B (Top 20 countries with the highest score: USA = 358, Germany = 210, Japan = 206, Italy = 163, Israel = 143, England (in UK) = 136, France = 128, Switzerland = 117, Netherlands = 105, Australia = 97, Poland = 84, Brazil = 83,
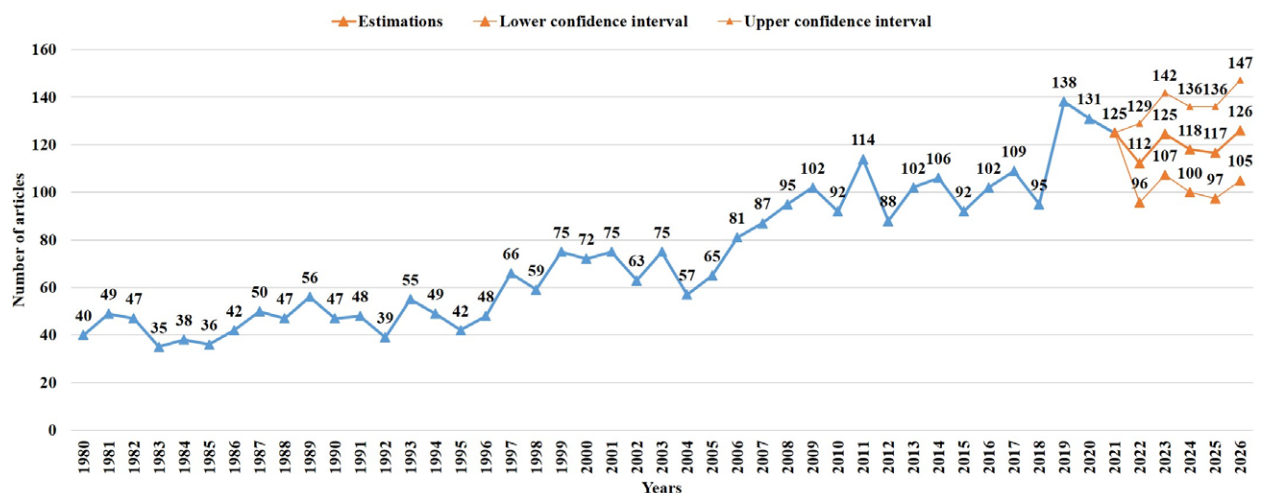

Figure 1. Distribution of articles published on Pemphigus by yr and predictions for the next 5 yr.
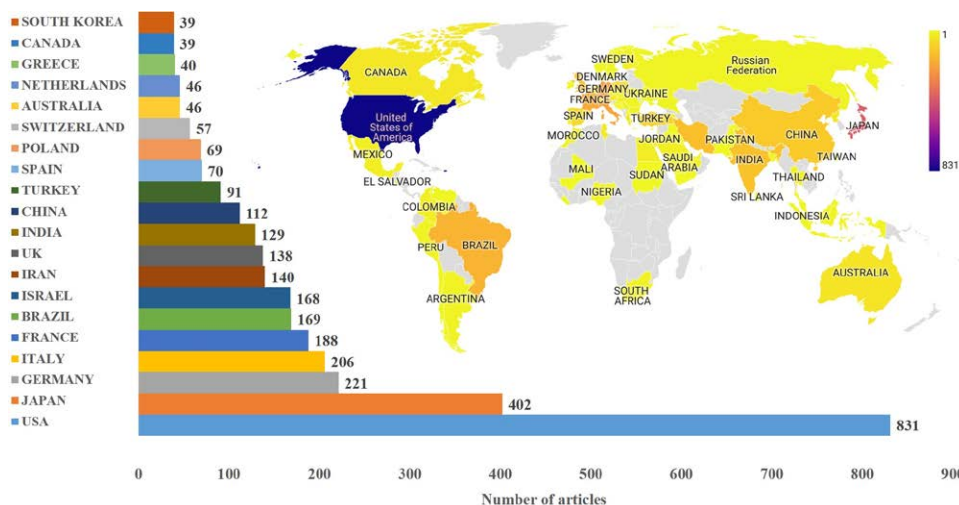

Figure 2. World article productivity density map for all countries that have published articles on Pemphigus and bar graph for the top 20 countries with the most articles.
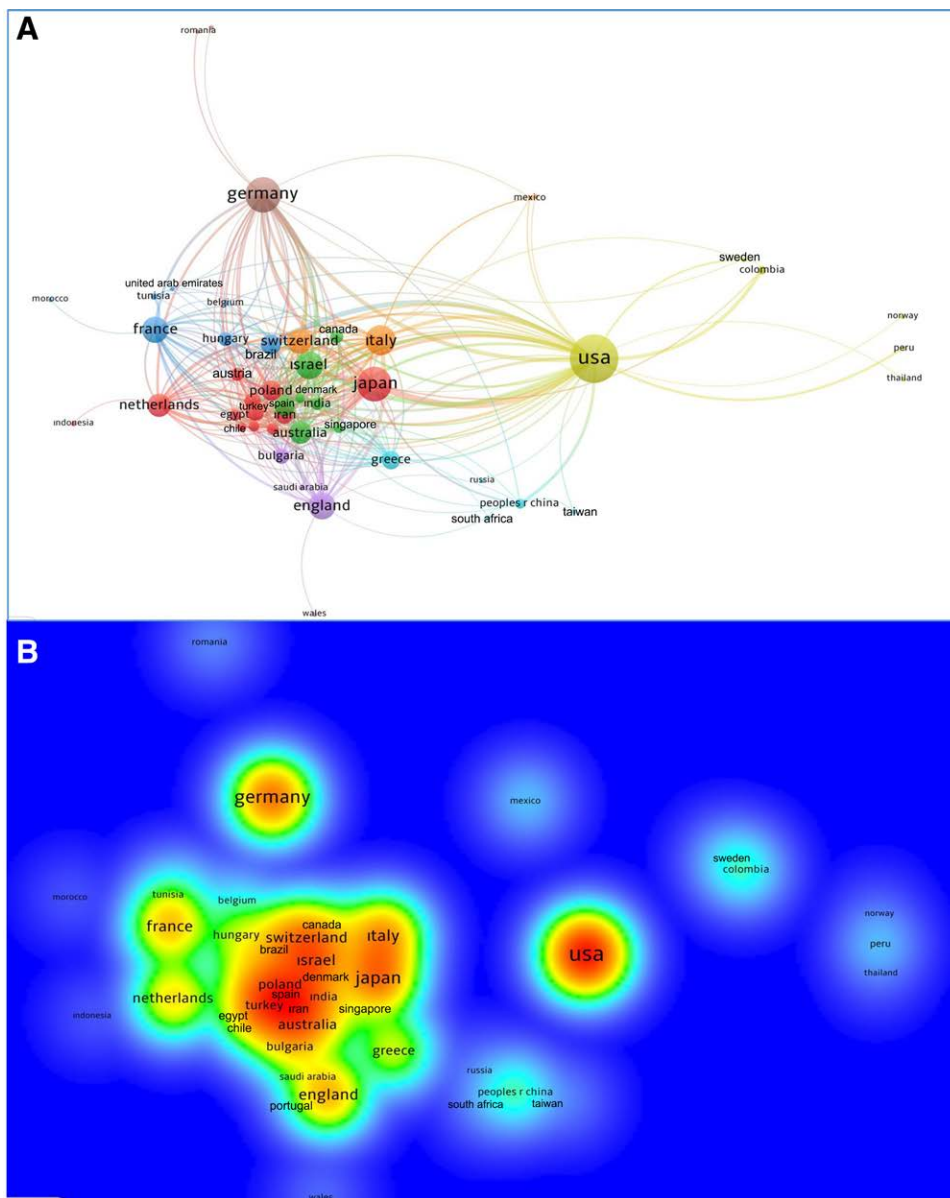
Figure 3. (A) Network visualization map of results of cluster analysis showing international cooperation between countries on Pemphigus. Each color represents a different cluster. As the number of articles published by the countries increases, the size of the circle in which the countries are located increases. The lines show the countries with which they cooperate. (B) Density map showing the intensity of international cooperation of countries on Pemphigus. The strength of international cooperation score increases from blue to red (blue-green-yellow-red).

Spain = 82, Greece = 71, Iran = 68, Turkey = 64, Croatia = 58, Bulgaria = 55, Hungary = 47, Austria = 43).

3.4. Correlation analysis

A statistically significant correlation was found between the number of articles produced by countries on Pemphigus and GDP and GDP per capita values at a moderate level, and a weak correlation with HDI values (respectively, $R = 0.670$, $P < .001$; $R = 0.661$, $P < .001$, $R = 0.450$, $P < .001$).

3.5. Active authors

The top 10 most active authors who published 60 or more articles on Pemphigus were Hashimoto T. (168, 5.5%), Amagai M. (134, 4.4%), Diaz LA. (91, 2.9%), Nishikawa T. (78, 2.5%), Ahmed AR. (76, 2.5%), Anhalt GJ. (65, 2.1%), Joly P. (63, 2%), Daneshpazhooh M. (61, 2%), Hertl M. (61, 2%), and Zillikens D. (60, 1.9%), respectively.

3.6. Active institutions

The top 15 institutions that published the most articles on Pemphigus were Keio University (163, 5.3%), Kurume University (130, 4.2%), Tel Aviv University (107, 3.5%), Sackler Faculty of Medicine (98, 3.2%), Tehran University of Medical Sciences (95, 3.1%), Universidade de Sao Paulo (83, 2.7%), University of Pennsylvania (82, 2.7%), Johns Hopkins University (76, 2.5%), University of California System (76, 2.5%), Assistance Publique Hopitaux de Paris (71, 2.3%), University of Lubeck (67, 2.2%), Harvard University (65, 2.1%), CHU de Rouen (64, 2.1%), University of North Carolina (60, 1.9%), and University of London (57, 1.8%), respectively.

3.7. Active journals

3034 articles on Pemphigus were published in 593 different journals. The first 76 most active journals that contributed the most to the literature that published 6 or more articles from these

journals are presented in Table 1. The total number of citations (NC) received by the journals and the average NC per article are presented in Table 1. The citation network visualization map between these journals is presented in Figure 4. When the citation analyses of the journals were evaluated according to the average NC per article they published, the most influential journals were determined as the New England Journal of Medicine (Average citation per article, AC = 246), Lancet (AC = 143), Journal of Cell Biology (AC = 133), Proceedings of the National Academy of Sciences of the United States of America (AC = 131), Journal of Clinical Investigation (AC = 131), Journal of Immunology (AC = 70), Journal of Biological Chemistry (AC = 63), Journal of Investigative Dermatology (AC = 54), and American Journal of Pathology (AC = 53), respectively.

3.8. Citation analysis

Among the 3034 articles published on Pemphigus, the first 25 articles with the highest NC (over 200 citations) according to

the total NC are presented in Table 2. In the last column of Table 2, the average NC the articles received per year is given.

3.9. Co-citation analysis

There were a total of 28271 studies cited in the references section of all 3034 articles published on Pemphigus. Among these studies, the 5 most influential studies with the most co-citations (more than 200 citations) were Amagai et al (1991) (NC = 358), Anhalt et al (1990) (NC = 288), Anhalt et al (1982) (NC = 239), Ishii (1997) et al (NC = 213), and Murrell et al (2008) (NC = 204), respectively.[1,6,10,22,23]

3.10. Trend topics and co-occurrence analysis

2701 different keywords were used in all of the 3034 articles published on Pemphigus. Among these keywords, 100 different keywords used in at least 7 different articles are shown

Table 1

The 76 most active journals that have published 6 or more articles on Pemphigus.

Journals	RC	C	AC	Journals	RC	C	AC
British Journal of Dermatology	188	6028	32.1	Frontiers in Medicine	14	56	4.0
Journal of the American Academy of Dermatology	171	6541	38.3	Human Immunology	14	447	31.9
Journal of Investigative Dermatology	143	7679	53.7	JAMA Dermatology	14	332	23.7
International Journal of Dermatology	139	2669	19.2	Indian Journal of Dermatology	13	43	3.3
Archives of Dermatology	101	4199	41.6	Actas Dermo-Sifiliograficas	12	99	8.3
Clinical and Experimental Dermatology	98	1284	13.1	American Journal of Pathology	12	637	53.1
Journal of the European Academy of Dermatology and Venereology	80	1492	18.7	Australasian Journal of Dermatology	12	71	5.9
Annales de Dermatologie et de Venereologie	71	465	6.5	Przeglad Dermatologiczny	12	15	1.3
Dermatology	71	1210	17.0	Zeitschrift fur Hautkrankheiten H&G	12	45	3.8
European Journal of Dermatology	58	717	12.4	Clinical Immunology	11	368	33.5
Journal of Dermatology	51	527	10.3	Journal of Autoimmunity	11	220	20.0
Archives of Dermatological Research	43	628	14.6	Journal of Drugs in Dermatology	11	99	9.0
Hautarzt	43	202	4.7	New England Journal of Medicine	11	2705	245.9
Dermatologica	42	648	15.4	Postepy Dermatologii I Alergologii	11	32	2.9
Vestnik Dermatologii I Venerologii	39	50	1.3	Clinical and Experimental Immunology	10	259	25.9
Acta Dermato-Venereologica	38	556	14.6	Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics	10	324	32.4
Dermatologic Therapy	37	144	3.9	Annals of Dermatology	9	81	9.0
Experimental Dermatology	36	632	17.6	Dermatologica Sinica	9	13	1.4
Journal of Cutaneous Pathology	34	354	10.4	Giornale Italiano di Dermatologia e Venereologia	9	45	5.0
Cutis	31	282	9.1	Plos One	9	318	35.3
Frontiers in Immunology	31	268	8.6	Proceedings of the National Academy of Sciences of the United States of America	9	1182	131.3
Anais Brasileiros de Dermatologia	30	223	7.4	Journal of Clinical Immunology	8	212	26.5
Pediatric Dermatology	27	266	9.9	International Immunopharmacology	8	102	12.8
Journal of Immunology	26	1825	70.2	Acta Cytologica	7	82	11.7
Indian Journal of Dermatology Venereology & Leprology	26	267	10.3	Cureus	7	1	0.1
Autoimmunity	25	524	21.0	Dermatology Practical & Conceptual	7	5	0.7
Journal of Dermatological Science	25	555	22.2	Diagnostic Cytopathology	7	68	9.7
Journal of Clinical Investigation	23	3008	130.8	Genes and Immunity	7	155	22.1
Journal of Dermatological Treatment	23	129	5.6	Journal of Cutaneous Medicine and Surgery	7	55	7.9
Clinics in Dermatology	22	893	40.6	Oral Diseases	7	65	9.3
Journal of Oral Pathology & Medicine	21	216	10.3	American Journal of Clinical Dermatology	6	81	13.5
American Journal of Dermatopathology	20	147	7.4	Autoimmunity Reviews	6	212	35.3
Dermatologic Clinics	20	457	22.9	Chinese Medical Journal	6	37	6.2
Journal of Biological Chemistry	20	1268	63.4	Clinical Case Reports	6	7	1.2
Turkderm-Turkish Archives of Dermatology and Venerology	17	17	1.0	Journal of Cell Biology	6	799	133.2
Acta Dermatovenerologica Croatica	16	55	3.4	Lancet	6	856	142.7
Journal der Deutschen Dermatologischen Gesellschaft	16	368	23.0	Mediators of Inflammation	6	111	18.5
Tissue Antigens	16	548	34.3	Immunology	6	51	8.5

AC = Average citation per document, C = Record count, C = Number of citations.
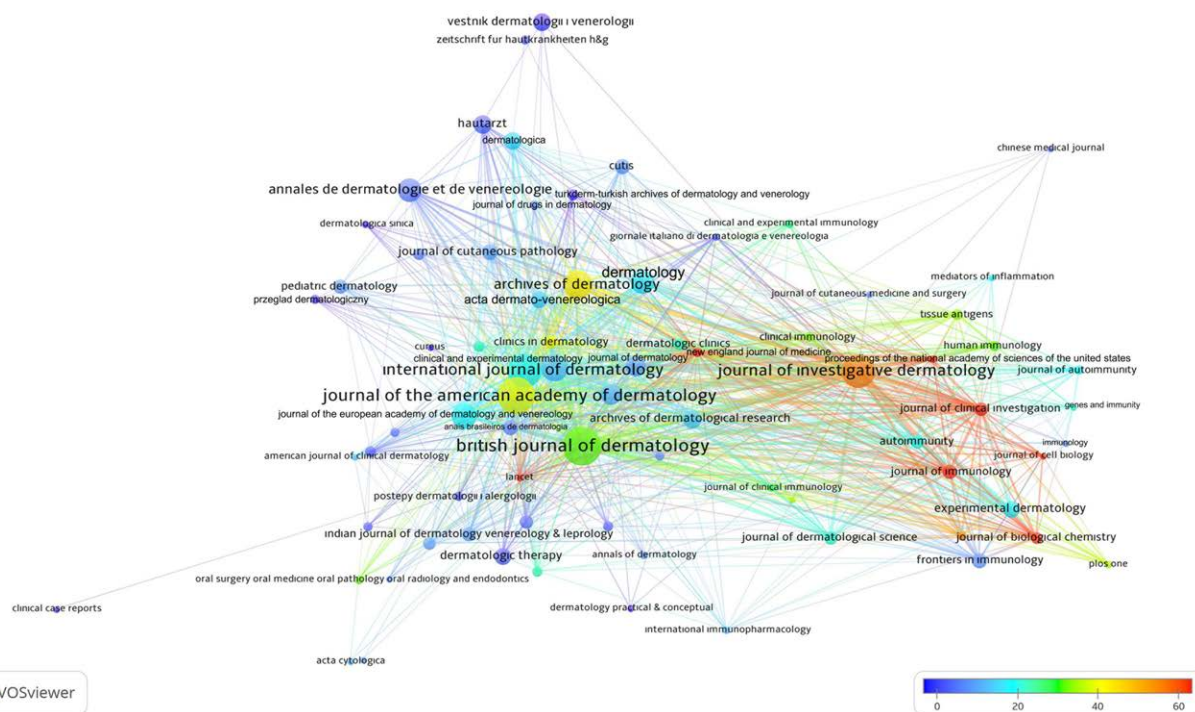
Figure 4. Network visualization map for analysis of citations per article of active journals that publish the most articles on Pemphigus. As the number of articles published by the journals increases, the size of the circle in which the journals are located increases. The average number of citations per article by journals increases from blue to red (blue-green-yellow-red).

in Table 3. The most studied topics from past to present were PV, PF, autoimmunity, rituximab, PNP, desmoglein-desmoglein 3-desmoglein 1, autoantibodies, acantholysis, autoantibody, treatment, autoimmune disease, desmosome, ELISA, and immunofluorescence, respectively.

The cluster network visualization map showing the results of cluster analysis performed between these keywords is shown in Figure 5. As a result of cluster analysis, it was seen that Pemphigus topics formed 9 different main clusters (General topics in which the clusters are divided: 1: desmoglein (red), 2: PNP – Pemphigus types- desmosome (green), 3: desmoglein 1 ve 3-autoimmunity (blue), 4: treatment-rituximab (yellow), 5: acantholysis-apoptosis (purple), 6: quality of life-remission-relapse (turquoise), 7: autoantibodies (orange), 8: epidemiology-mortality (brown), 9: corticosteroids (pink).

The trend network visualization map performed to identify trend topics is shown in Figure 6. According to the results of the analysis performed to determine the trend topics, it was determined that the trend keywords studied in recent years are rituximab, azathioprine, mortality, quality of life, remission, relapse, psoriasis, skin diseases, vesiculobullous, disease severity, Immunology, autoimmune bullous disease, Pemphigus herpetiformis, wound healing, and intravenous immunoglobulin.

The citation network visualization map performed to reveal the most cited topics is shown in Figure 7. It was determined that the most cited keywords were desmosomes, autoantibody, therapy, diagnosis, cadherin, cell adhesion, autoantigen, autoimmunity, desmoglein, keratinocyte, and enzyme-linked immunosorbent assay.

4. Discussion

The number of articles published on the subject of Pemphigus was between 35 and 56 (mean 45) in the period 1980 to 1996, between 57 and 75 (mean 67) for 1997 to 2005, between 81 and 114 (mean 97) for 2006 to 2018, and between 125 and 138 (mean 131) for 2019 to 2021. When the number of articles that

could be published in the next 5 years was evaluated, obtained with Exponential Smoothing estimation based on time series taking seasonal correction into consideration, it can be said that the number of articles on the subject of Pemphigus will continue to increase.

When the distribution of publications of countries was examined, 16 of the 20 most active countries providing the greatest contribution to the literature were determined to be developed countries. The other 4 of these most active countries are classified as developing countries but are countries with large economies (Iran, India, China, Turkey). When the correlation analysis results were evaluated, there was determined to be a moderate level correlation between productivity of Pemphigus articles and GDP and GDP per capita values, and a weak level correlation with HDI values, showing that the size of the economy and level of development of a country were effective factors in publication productivity. The density map formed according to the total collaboration scores between countries was evaluated, and the 10 countries with the most intense collaboration were determined to be the USA, Germany, Japan, Italy, Israel, England (in UK), France, Switzerland, Netherlands, and Australia, respectively.

When author collaborations have been examined in bibliometric studies in literature, geographical proximity has been seen to be effective in international collaboration of article production.[16,17] However, in the current study, it was seen that in author collaboration on the subject of Pemphigus, international collaboration was not based on geographical proximity, but global collaboration was more common (Austria, Chile, Croatia, Czech Republic, Egypt, Iran, Japan, Poland, South Korea, Turkey, Indonesia, Netherlands), (Australia, Canada, Denmark, India, Israel, Singapore, Spain), (Belgium, Brazil, France, Hungary, Morocco, Tunisia, United Arab Emirates), (Colombia, Norway, Peru, Sweden, Thailand, USA), (Bulgaria, England (in UK), Portugal, Saudi Arabia, Wales (in UK)), (Greece, China, Russia, South Africa, Taiwan), (Italy, Mexico, Scotland (in UK), Switzerland), (Germany, Romania, Slovakia).

Table 2

The top 25 most cited articles on Pemphigus by total number of citations.

No	Article	Author	Journal	PY	TC	AC
1	Autoantibodies against a novel epithelial cadherin in pemphigus vulgaris, a disease of cell adhesion	Amagai, M. et al[1]	Cell	1991	769	24.03
2	Paraneoplastic Pemphigus - an autoimmune mucocutaneous disease associated with neoplasia	Anhalt, GJ. et al[6]	New England Journal of Medicine	1990	744	22.55
3	Induction of Pemphigus in neonatal mice by passive transfer of igg from patients with the disease	Anhalt, GJ. et al[22]	New England Journal of Medicine	1982	509	12.41
4	Characterization of autoantibodies in Pemphigus using antigen-specific enzyme-linked immunosorbent assays with baculovirus-expressed recombinant desmogleins	Ishii, K. et al[23]	Journal of Immunology	1997	386	14.85
5	Bullous pemphigoid and pemphigus vulgaris - incidence and mortality in the UK: population based cohort study	Langan, SM. et al[12]	BMJ-British Medical Journal	2008	379	25.27
6	Consensus statement on definitions of disease, end points, and therapeutic response for Pemphigus	Murrell, DE. et al[10]	Journal of the American Academy of Dermatology	2008	344	22.93
7	Targeted disruption of the pemphigus vulgaris antigen (Desmoglein 3) gene in mice causes loss of keratinocyte cell adhesion with a phenotype similar to pemphigus vulgaris	Koch, PJ. et al	Journal of Cell Biology	1997	339	13.04
8	Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin	Ahmed, A. et al[8]	New England Journal of Medicine	2006	333	19.59
9	Explanations for the clinical and microscopic localization of lesions in pemphigus foliaceus and vulgaris	Mahoney, MG. et al	Journal of Clinical Investigation	1999	328	13.67
10	A single cycle of rituximab for the treatment of severe Pemphigus	Joly, P. et al[9]	New England Journal of Medicine	2007	313	19.56
11	The clinical phenotype of Pemphigus is defined by the anti-desmoglein autoantibody profile	Amagai, M. et al	Journal of the American Academy of Dermatology	1999	290	12.08
12	Usefulness of enzyme-linked immunosorbent assay using recombinant desmogleins 1 and 3 for serodiagnosis of Pemphigus	Amagai, M. et al	British Journal of Dermatology	1999	279	11.63
13	Pemphigus	Bystryn, JC and Rudolph, JL[2]	Lancet	2005	275	15.28
14	Autoantibodies against the amino-terminal cadherin-like binding domain of pemphigus vulgaris antigen are pathogenic	Amagai, M. et al	Journal of Clinical Investigation	1992	273	8.81
15	Absorption of pathogenic autoantibodies by the extracellular domain of pemphigus vulgaris antigen (dsg3) produced by baculovirus	Amagai, M. et al	Journal of Clinical Investigation	1994	266	9.17
16	Detection of pemphigus vulgaris and pemphigus foliaceus antigens by immunoblot analysis using different antigen sources	Hashimoto, T. et al	Journal of Investigative Dermatology	1990	255	7.73
17	First-line rituximab combined with short-term prednisone vs prednisone alone for the treatment of Pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomized trial	Joly, P. et al[24]	Lancet	2017	242	40.33
18	Desmoglein 4 in hair follicle differentiation and epidermal adhesion: Evidence from inherited hypotrichosis and acquired pemphigus vulgaris	Kljuic, A. et al	Cell	2003	239	11.95
19	Antibodies against desmoglein 3 (Pemphigus vulgaris antigen) are present in sera from patients with paraneoplastic Pemphigus and cause acantholysis in vivo in neonatal mice	Amagai, M. et al	Journal of Clinical Investigation	1998	234	9.36
20	Demonstration of an adhering-junction molecule (plakoglobin) in the auto-antigens of pemphigus foliaceus and pemphigus vulgaris	Korman, NJ. et al	New England Journal of Medicine	1989	227	6.68
21	The pathogenic effect of igg4 autoantibodies in endemic pemphigus foliaceus (fogo selvagem)	Rock, B. et al	New England Journal of Medicine	1989	224	6.59
22	Induction of Pemphigus phenotype by a mouse monoclonal antibody against the amino-terminal adhesive interface of desmoglein 3	Tsunoda, K. et al	Journal of Immunology	2003	223	11.15
23	Anti-cell surface Pemphigus autoantibody stimulates plasminogen-activator activity of human epidermal-cells - a mechanism for the loss of epidermal cohesion and blister formation	Hashimoto, K. et al	Journal of Experimental Medicine	1983	222	5.55
24	Distinction between epidermal antigens binding pemphigus vulgaris and pemphigus foliaceus autoantibodies	Stanley, JR. et al	Journal of Clinical Investigation	1984	215	5.51
25	Antigen-specific immunoadsorption of pathogenic autoantibodies in pemphigus foliaceus	Amagai, M. et al	Journal of Investigative Dermatology	1995	210	7.5

AC = average citations per year, PY = publication year, TC = total citation.

The journals that published the most articles on Pemphigus are presented in the results section. We can suggest that authors who are in the research process or want to publish on Pemphigus should consider the journals presented in Table 1, primarily these journals. We can also recommend that researchers who want to have more impact on their work to be published should primarily consider influential journals according to their citation numbers.

The analyzed articles were evaluated according to the total citation count (CC) received. The study with the highest NC was "Autoantibodies against a novel epithelial cadherin in Pemphigus vulgaris, a disease of cell-adhesion," published in Cell by Amagai et al (1991).[1] This was followed by "Paraneoplastic Pemphigus - an autoimmune mucocutaneous disease associated with neoplasia," published in the New England Journal of Medicine by Anhalt et al (1990),[6] "Induction of Pemphigus in neonatal mice by passive transfer of IgG from patients with the disease" published in the New England Journal of Medicine by Anhalt et al (1982),[22] "Characterization of autoantibodies in Pemphigus using antigen-specific enzyme-linked immunosorbent assays with baculovirus-expressed recombinant desmogleins" published in the Journal of Immunology by Ishii et al (1997),[23] and "Bullous pemphigoid and PV - incidence and mortality in the UK: population based cohort study" published in the British Medical Journal by Langan et al (2008).[12]

Table 3

The 100 most frequently used keywords in articles on Pemphigus.

Keywords	Number of uses	Keywords	Number of uses	Keywords	Number of uses
Pemphigus	544	Castleman disease	19	bullous diseases	9
pemphigus vulgaris	508	IGA Pemphigus	18	dermatology	9
pemphigus foliaceus	142	keratinocytes	18	envoplakin	9
autoimmunity	116	azathioprine	17	epitope	9
rituximab	112	cytokines	17	immunoblotting	9
paraneoplastic Pemphigus	107	diagnosis	17	oral mucosa	9
desmoglein	102	remission	17	Pemphigus herpetiformis	9
autoantibodies	70	cyclophosphamide	16	psoriasis	9
acantholysis	50	dapsone	16	quality of life	9
desmoglein 3	49	autoimmune bullous diseases	14	skin diseases	9
autoantibody	44	direct immunofluorescence	14	vesiculobullous	9
treatment	43	intravenous immunoglobulin	14	blistering disease	8
autoimmune disease	41	prognosis	14	desmocollin	8
desmosome	41	bronchiolitis obliterans	13	drug-induced Pemphigus	8
desmoglein 1	37	endemic pemphigus foliaceus	13	herpes simplex virus	8
ELISA	36	indirect immunofluorescence	13	immunoadsorption	8
immunofluorescence	31	mycophenolate mofetil	13	Immunology	8
desmogleins	28	castleman disease	12	mouse model	8
autoimmune	27	HLA	11	Pemphigus erythematosus	8
bullous pemphigoid	27	human leukocyte antigen	11	periplakin	8
corticosteroids	26	polymorphism	11	pregnancy	8
enzyme-linked immunosorbent assay	26	pulse therapy	11	thymoma	8
epidemiology	26	cell adhesion	10	autoantigen	7
apoptosis	24	immunohistochemistry	10	chronic lymphocytic leukemia	7
desmosomes	23	immunosuppression	10	dexamethasone	7
Pemphigus vegetans	23	keratinocyte	10	disease severity	7
therapy	23	lymphoma	10	genetic susceptibility	7
pemphigoid	22	mortality	10	IGA	7
autoimmune bullous disease	21	oral Pemphigus	10	methotrexate	7
autoimmune diseases	21	plasmapheresis	10	pathogenesis	7
bullous disease	21	polymerase chain reaction	10	Pemphigus foliaceous	7
cadherin	21	relapse	10	wound healing	7
skin	21	systemic lupus erythematosus	10		
fogo selvagem	20	blister	9		

The analyzed articles were also evaluated according to the mean NC received per year. The most effective article in this respect was "First-line rituximab combined with short-term prednisone versus prednisone alone for the treatment of Pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomized trial" published in the Lancet by Joly et al (2017),[24] followed by the consensus statements on Pemphigus of Murrell et al (2008).[10] The third most effective study was an article by Kasperkiewicz et al (2008),[3] the fourth was by Langan et al (2008)[12] and the fifth was by Amagai et al (1991).[1] According to the co-CCs of all the articles analyzed, the most effective articles were determined to be by Amagai et al (1991), Anhalt et al (1990), Anhalt et al (1982), Ishii (1997) et al (NC = 213) and Murrell et al (2008).[1,6,10,22,23] It can therefore be recommended that dermatologists, other clinicians, and researchers interested in this subject should read these articles first.

When evaluating the findings of keyword analysis in Pemphigus research from the past to the present, a wide spectrum of key themes has emerged, focusing on various aspects such as different types of disease, immune system reactions, treatment methods, cellular structures, and analysis techniques used for diagnosis. These subjects have been extensively examined to provide a comprehensive understanding of the origins, progression, and effective treatments of the disease. Furthermore, recent research trends indicated by keyword analysis have centered on the management and effects of autoimmune bullous diseases, addressing topics including treatment options, disease severity, mortality rates, patients' quality of life, remission, and relapse cycles. Additionally, studies related to vesiculobullous conditions associated with other dermatological diseases, the immunological foundations of specific conditions like Pemphigus herpetiformis, wound healing processes, and research on treatment methods such as intravenous immunoglobulin, have seen an increase. Encompassing a wide array of autoimmune bullous diseases, these topics have garnered attention in both clinical and research domains.

Pemphigus typically initiates in middle to later ages but can occur at any age, albeit rarely manifesting during childhood.[25] In Germany, the prevalence of autoimmune bullous diseases in the pediatric population under 18 years was estimated at 101.1 per million children (approximately 1351 patients) in 2015. The highest prevalence among all autoimmune bullous diseases was observed for PV (30.5 per million children), followed by linear IGA disease (24.5 per million children) and bullous pemphigoid (4.9 per million children).[26] Jelti et al (2019) observed an increase in the incidence of Pemphigus with age in France, with the highest incidence occurring in individuals aged 80 and above.[27] The age of onset for the most common type of Pemphigus, PV, constituting 70% of cases, ranged between 36.5 years in Kuwait to 72.4 years in Bulgaria.[28]

A recent prevalence study conducted in the USA with 1795 Pemphigus patients reported an increasing prevalence in older age groups. The overall standardized prevalence was reported to be similar between women (5.7 per million; 95% CI, 5.3–6.0) and men (4.6 per million; 95% CI, 4.3–5.0) and across racial groups.[29] While the disease can occur in both genders, some studies suggest a slightly higher prevalence among females than males. Finland reported the lowest female-to-male sex ratio at 1.01, whereas Kuwait reported the highest at 5.75. The global average female-to-male ratio was reported as 1.87.[30]
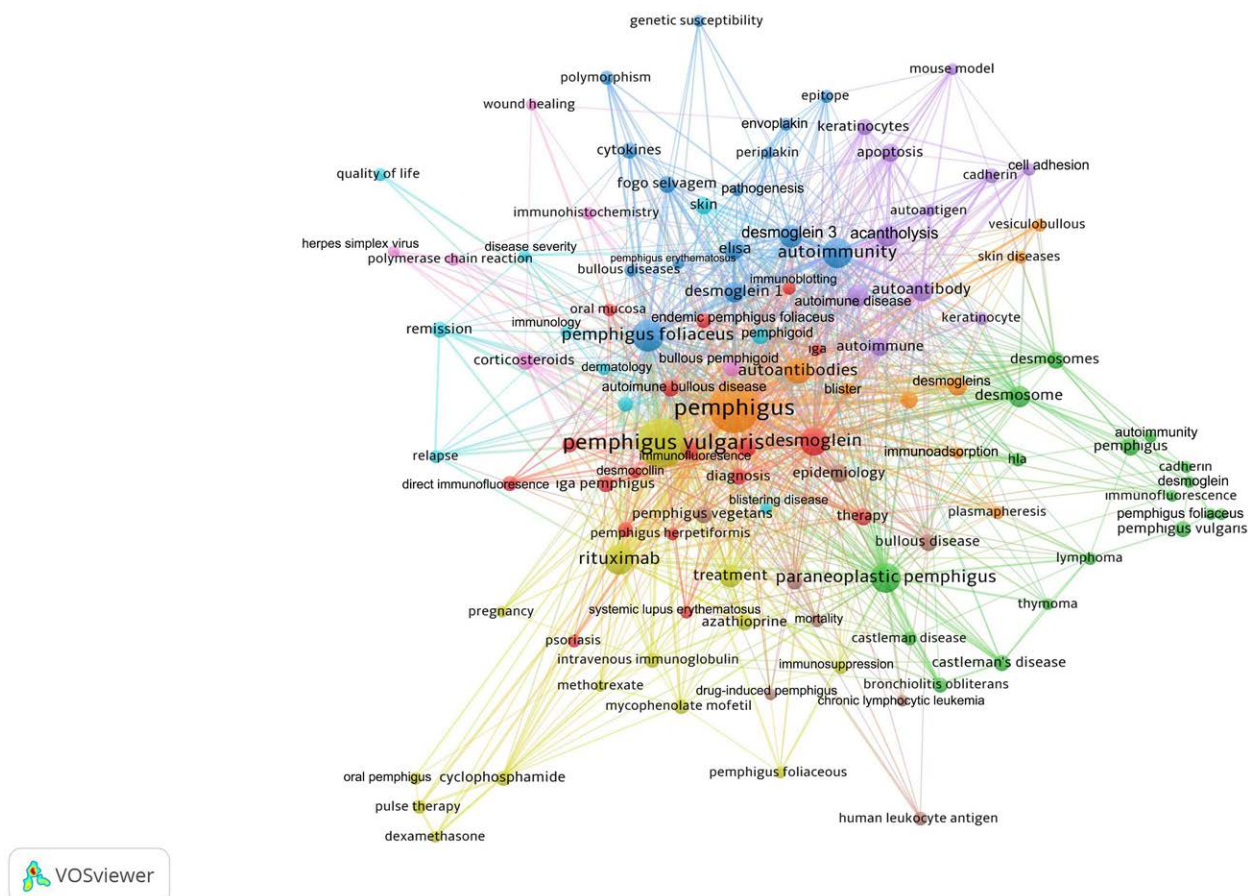
Figure 5. Network visualization map for cluster analysis based on keyword analysis performed to identify clustering of Pemphigus. Each color represents a different cluster. Keywords in the same cluster are of the same color. The size of the circle represents the number of times the keyword has been used.

Figure 6. Network visualization map based on keyword analysis to identify past and current trends on Pemphigus. In the indicator given in the lower right corner of the figure, the topicality of the article increases from blue to red (blue-green-yellow-red). The size of the circle represents the number of times the keyword has been used.
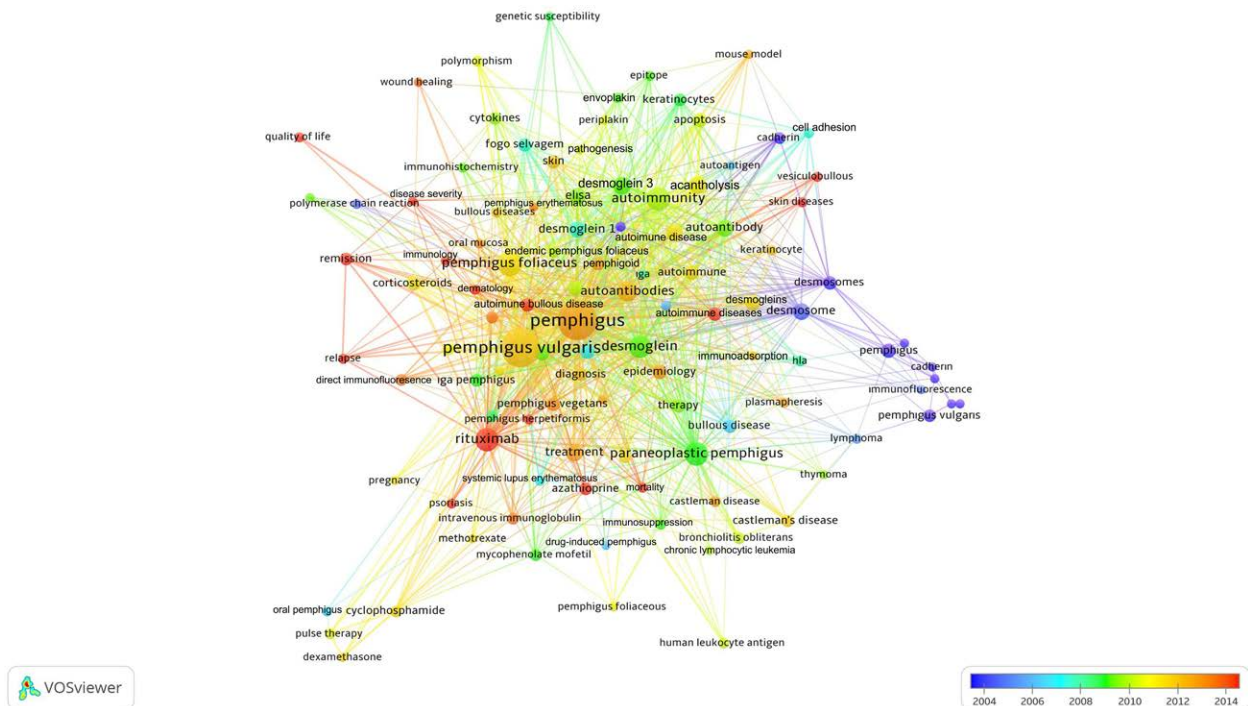
Figure 7. Network visualization map based on keyword analysis performed to identify the most cited topics on Pemphigus. In the indicator given in the lower right corner of the figure, the number of citations received by the subject increases from blue to red (blue-green-yellow-red). The size of the circle represents how many times the keyword is used.

Pemphigus epidemiology displays variations among racial populations worldwide, being more prevalent in certain ethnic groups. However, the disease can manifest in any ethnic group globally. The higher frequency of autoimmune bullous diseases in certain ethnic groups such as Pemphigus in Ashkenazi Jews or PF in specific regions of Brazil has been associated respectively with genetic and environmental factors. However, conclusive evidence regarding why certain ethnic groups experience a higher incidence remains elusive.[11]

Pemphigus treatment is typically carried out with immunosuppressive drugs such as corticosteroids and other immunosuppressive agents. The goal of treatment is to reduce disease severity, control lesions, and achieve remission.[31,32] However, there might be some variations in response to Pemphigus treatment among individuals from different ethnic groups. The underlying reasons for these variations are not entirely clear, but it is believed that genetic and environmental factors can influence the response to treatment. Some studies suggest that different genetic variations can affect individuals' immune system responses, hence altering their responses to treatment. Additionally, various ethnic groups' exposure to different environmental factors and lifestyles may impact their responses to treatment. Nevertheless, research in this area is ongoing, and there is currently no definitive consensus regarding responses to Pemphigus treatment among individuals from diverse ethnic backgrounds.[3,32]

As a result of a scan of literature on Pemphigus, no comprehensive bibliometric study was found on this subject. A systematic review on the subject of Pemphigus has only been conducted by Yang et al (2021), in which the 100 studies on Pemphigus that received the most citations between 2011 and 2020 were examined.[33] The current study can be said to be more comprehensive than that study both in terms of the period examined and the number of articles analyzed. In addition to citation analyses, the current study used several other statistical approaches such as trend keyword analysis, cluster analysis, and correlation analyses.

A limitation of this study can be said to be that only the WoS database was examined in the literature scan. However, the citation and co-citation analyses were conducted using the PubMed database.[17,34] Moreover, compared to the Scopus database, the WoS database indexes articles published in journals with more impact (only journals scanned in the SCI-expanded, ESCI and SSCI index).[17,34]

5. Conclusion

In this comprehensive bibliometric study on the subject of Pemphigus, the information is presented from the statistical analysis of 3034 articles published from 1980 to 2022. According to the results of the analysis to determine trend subjects, the subject most studied in recent years was determined to be rituximab, a drug used in Pemphigus treatment. Other trend subjects being studied are azathioprine drug used in treatment, intravenous immunoglobulin treatment, quality of life and mortality rates of patients with Pemphigus, Pemphigus herpetiformis, and wound healing. The existing research on Pemphigus addresses a broad spectrum of subjects both in dermatology clinical research and in the fields of autoimmunity and cell adhesion. According to the findings of global productivity on the subject of Pemphigus obtained in this study, there is a need to support Pemphigus research in economically less developed countries. This study can be considered to be a useful resource for dermatologists and other scientists in respect of the global output on the subject of Pemphigus.

Authors contributions

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Supervision: Aynure Öztekin.

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Writing – review & editing: Aynure Öztekin, Coşkun Öztekin.

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