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ORIGINAL ARTICLE

The Status and Trends of Human Papillomavirus Research: A Global Bibliometric and Visual Analysis

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OBJECTIVE

This study aimed to make a bibliometric and keyword visualization analysis of the literature on HPV.

METHODS

Scientific publications on HPV were analyzed using the Scopus database between 1975 and 2021. Quantitative and qualitative analyses of the obtained data were reviewed using bibliometric indicators. The VOSviewer program was used to visualize keyword networks.

RESULTS

There were 50362 scientific publications, and most were conducted in 2021 (5,82%). HPV publications have accelerated in the past decades. The United States (USA) ranks first with 31,96 % (n=18128) in terms of the number of publications. Most of the publications were produced as Articles and in the English language. According to keyword network analysis, it was seen that the most popular themes were mostly about immunization and diagnosis of HPV.

CONCLUSION

To the best of our knowledge, this bibliometric analysis includes the widest timelapse on HPV research. This study includes rigorous bibliometric and thematic knowledge of literature related to HPV will be useful for work accordingly for research and development activities.

Keywords: Bibliometric analysis; cervical cancer; HPV; visualization; VOSviewer.

INTRODUCTION

Human Papillomaviruses (HPV) are small, non-enveloped, double-stranded DNA viruses belonging to the Papillomaviridae family. More than 200 HPV types have been recorded by the International HPV Reference Center, and new types are continuously being discovered.[1,2] Type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59 (12 HPV type) have been defined by the World Health Organization (WHO) as high-risk HPV types (hrHPV). hrHPVs are the major causative agent of cervical cancer in women and are also highly associated with oropharyngeal, anal, and lower genital tract cancers in both genders.[2,3]

HPV is the main etiologic agent of cervical cancer which is one of the most common cancer considered the major cause of cancer-related death among women worldwide.[4] All over the world, female deaths due to cervical cancer can be reduced by protection from HPV infection through vaccination.[5] Despite the

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high protective effect of vaccines, cervical cancer remains an important public health issue, especially in low- and middle-income countries.[5,6]

Effective scientific researches are very important in struggling with common public health problems such as HPV. Decades of pioneering research, beginning with the demonstration of an infectious agent that can cause warts, have shown that certain types of carcinogenic HPV can cause cancers.[7] It is obvious that future research on HPV, like previous ones, will lead to new discoveries in the understanding, diagnosis, treatment, and control of health problems caused by HPV. An overview of research trends over the years can help in perceiving the circumstance and current state of HPV-related research to shed light on new studies. Bibliometric data and visualization map analysis are the most common and beneficial methods to overview publications on a scientific subject.[8,9]

Bibliometric analysis can provide a basis for a better understanding of the status and priorities in a specific research area and can shed light on when and where the research area began and where it is heading. Periodically performed bibliometric analyses can encourage researchers to fill gaps in existing knowledge and lay the base for new research.[9,10] Academicians have started increasingly to use and accept bibliometric methodology in scientific studies. Today the importance and value of bibliometric analysis are better understood and known by researchers. Bibliometric analyses can build a solid foundation for advancing a subject in novel and meaningful ways.[9,11,12] Visualizing and mapping the data obtained by bibliometric analysis and creating meaningful information is especially useful in determining the themes of the researched subject. The Vosviewer program is a common application that is used to visualize the data obtained in data mining and bibliometric analysis studies.[13]

To the best of our knowledge, this is the first bibliometric study on HPV from 1975–2021. The objective of this study was to retrieve and analyze global publications on HPV for 1975–2021. In this study, bibliometric indicators and visualized data extracted from the Scopus database have been presented and gaps in research activity on HPV were aimed to be filled. Furthermore, the results of this study will shed light on research and development activities and academics to improve HPV research.

MATERIALS AND METHODS

Various electronic databases can be used for bibliometric studies. Elsevier developed Scopus which provides wider and more accurate data analysis than Pubmed or Google Scholar, combining the characteristics of both Web of Science and PubMed.[14] Scopus allows for exporting documents and initiating new searches from categorized results based on document type, source title, author name, year of publication, and subject area.[15,16] In our study, Scopus was preferred as the database because of all these features and advantages.

On 15 June 2022, 'Human papillomavirus' was searched within the title, abstract, and keywords at Scopus. The study covers publications between 1975 and 2021, owing the oldest HPV article was published in 1975 and the last completed year was 2021. The display of the last search query in Scopus is as follows: (TITLE-ABS-KEY ("human papillomavirus") AND PUBYEAR<2022).

The data that was collected was utilized to create a ratio of the original publications by year, language, document type, country, institution/organization, research area, and author. Statistical analysis of the data was performed by calculating frequency, percentage, and arithmetic mean values with Microsoft Excel 365 program (Microsoft Corp. Washington, USA). In addition, research themes and relationships were determined by analyzing obtained keywords using the VOSviewer version 1.6.16 program (Leiden University's Centre for Science and Technology Studies, Leiden, Holland), which collects all keywords in the data set and visualizes them by creating a common word network map.[13]

Ethics Statement

Ethical approval and informed consent are not required for this bibliometric analysis of published articles. No contact was made with the authors for additional information.

RESULTS

Analysis of Global HPV Publications

A total of 50.362 articles were found in the Scopus database between 1975 and 2021. The first article on HPV was published in 1975. There was an increase in publication numbers on HPV over the years (Fig. 1). The highest number of publications was found in 2021, with 3300 (5,82 %). Table 1 shows the annual number of publications and the growth rate in the annual number of publications in the last 20 years. Between 2002 and 2021, a total of 41.491 (74,15%) publications were published, with an annual average growth rate of 0.08.

More than 159 countries globally have contributed to HPV literature. The United States (USA) ranks

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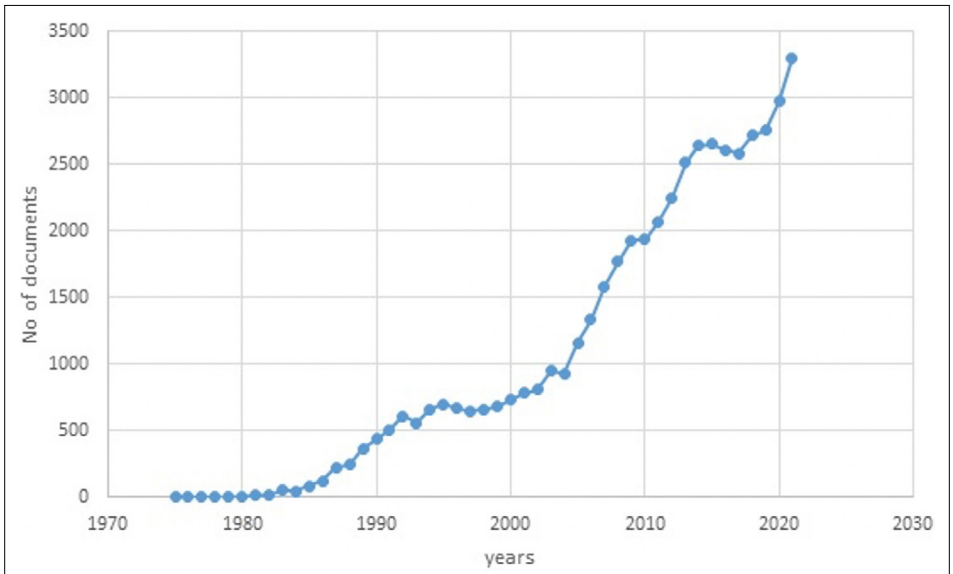

Fig. 1. Distribution of publications on HPV by years.
HPV: Human Papillomaviruses.

first with 31,96 % (n=18128) in terms of the number of publications, followed by China (n=4442; 7,83%) and the United Kingdom (n=3680; 6,49%). The top 20 countries with the highest number of HPV publications in the literature are shown in Figure 2. According to WHO regions; The countries that published the most publications were the USA in the Region of Americas, China in the Western Pacific Region, the UK in the European region, India in the South-East Asian region, South Africa in the African region and Iran in the Eastern Mediterranean Region.

The most commonly used language in publications was English (n: 46548), which was 82,06 % of the total publications. Chinese was the second most popular language (n=1061; 1,87%) followed by other languages (n=2753; 16,07%).

In the selected research period, most of the HPV publications were published in the area of "Medicine" (n=39582; 69,78%), followed by "Biochemistry, Genetics, and Molecular Biology", "Immunology and Microbiology," and "Pharmacology, Toxicology, and Pharmaceutics".

Most of the publications were produced as "Article" (n: 39916; 70,37%), followed by "Review" (n: 5670; 10%) and other publication types (n:4776, 8,42%).

Table 2 shows the top ten institutions/organizations contributing to the literature. National Cancer Institute was the most productive institution in terms of number of publications, with 1402 (2,47%) publications, followed by the German Cancer Research Center (n:951, 1,68%) and National Institutes of Health (n: 835, 1,47%). The top 10 authors who have the most HPV publications are presented in Table 3.

Table 1 Number of documents by year and annual increase rates (2002–2021)

Year	Number of documents	%	AAGRP
2021	3300	5.82	0.11
2020	2977	5.25	0.08
2019	2759	4.86	0.02
2018	2716	4.79	0.05
2017	2583	4.55	-0.01
2016	2612	4.60	-0.02
2015	2653	4.68	0.00
2014	2640	4.65	0.05
2013	2516	4.44	0.12
2012	2248	3.96	0.08
2011	2073	3.65	0.07
2010	1935	3.41	0.00
2009	1931	3.40	0.09
2008	1773	3.13	0.12
2007	1585	2.79	0.19
2006	1336	2.36	0.15
2005	1161	2.05	0.25
2004	932	1.64	-0.02
2003	953	1.68	0.18
2002	808	1.42	0.03

%: The ratio of the total number of articles; AAGRP: Annual average growth rate percentage

Table 2 The top ten most active institutions/organizations (1975–2021)

	Affiliation	Country	Articles (n)	%
1	National Cancer Institute	United States	1402	2.47
2	German Cancer Research Center	Germany	951	1.68
3	National Institutes of Health	United States	835	1.47
4	International Agency for Research on Cancer	France	796	1.40
5	University of California, San Francisco	United States	692	1.22
6	Centers for Disease Control and Prevention	United States	675	1.19
7	Karolinska Institutet	Sweden	667	1.18
8	Albert Einstein College of Medicine of Yeshiva University	United States	629	1.11
9	Amsterdam UMC - Free University Amsterdam	Netherlands	627	1.11
10	Harvard Medical School	United States	613	1.08

The top 10 journals with the most HPV publications and their SJR and IF values are shown in Table 4. A total of 6900 (12,16%) documents were published in the top ten journals listed in Table 4.

Vosviewer Analysis

The Vosviewer program was used to analyze keyword frequency and relationships. Figure 3 shows the network maps of 84 keywords of HPV publications that were used more than 10 times between 1975 and 2021. While the size of the circles is directly proportional to the frequency of use of the keywords, the length of the lines connecting the circles is inversely proportional to the relationship between the keywords. The most common keywords were "human papillomavirus, HPV, cervical cancer, vaccination, HPV vaccine" which occurred 531, 334, 316, 74, and 71 times, respectively.

All of the keywords were classified into seven clusters. Cluster 1 which consists of 21 keywords (red) is mainly about "HPV immunization". Cluster 2 which consists of 20 keywords (green) is mainly about "non-cervical HPV-related cancers". Cluster 3 which consists of 15 keywords (blue) is mainly about "diagnosis of cervical cancers". Cluster 4 which consists of 12 keywords (yellow) is mainly about "molecular diagnosis of HPV". Cluster 5 which consists of 9 keywords (purple) is mainly about "HPV-related cancers among men who have sex with men". Cluster 6 which consists of 5 keywords (pink) is mainly about "HPV-related reviews". Cluster 7 which consists of 2 keywords (orange) is mainly about "Cervical intraepithelial neoplasia and HPV types". Cluster 3 (blue) consists of the most used keywords, followed by clusters 2, 1, 4, 5.6, and 7 respectively.

DISCUSSION

Research on a particular subject, as well as, evaluating studies from a broad perspective is important in terms of determining which subjects are prominent or under-

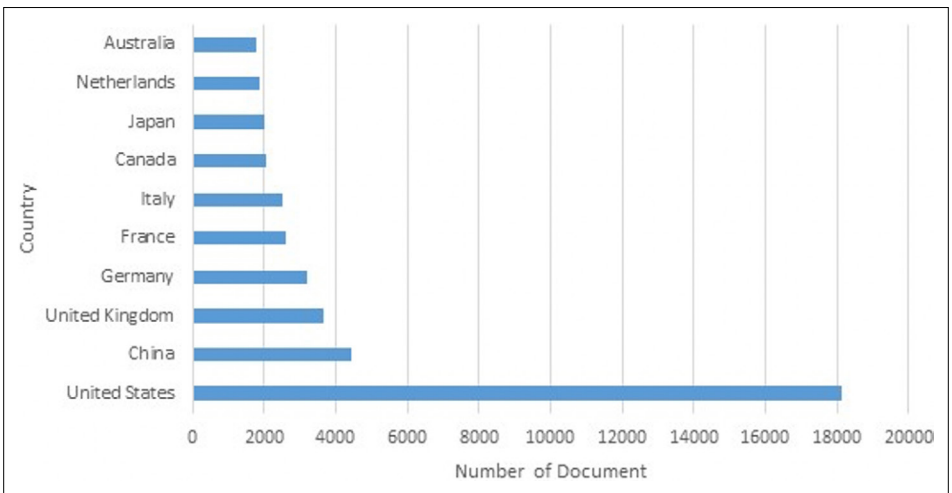

Fig. 2. Distribution of the number of publications by country.

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Table 3 Top 10 most active authors (1975–2021)

SCR	Author	Number of publications	%	Total number of citations (S)	h-index (S)	Country
1st	Meijer, C.J.L.M.	404	0.71	96958	135	Netherlands
2nd	Schiffman, M.	367	0.65	63253	127	United States
3rd	Dillner, J.	352	0.62	29906	79	Sweden
3rd	Snijders, P.J.F.	316	0.56	46636	99	Netherlands
3rd	Castle, P.E.	312	0.55	26526	80	United States
6th	Burk, R.D.	287	0.51	33804	98	United States
6th	Franco, E.L.	284	0.50	27414	84	Canada
6th	Villa, L.L.	280	0.49	21464	68	Brazil
6th	Giuliano, A.R.	265	0.47	21097	71	United States
6th	Franceschi, S.	245	0.43	97199	142	Italy
6th	Meijer, C.J.L.M.	404	0.71	96958	135	Netherlands
6th	Schiffman, M.	367	0.65	63253	127	United States

SCR: Standard competition ranking; S: Sorting; h-index: Hirsh index

Table 4 Top 10 journals most commonly published (1975–2021)

Rank	Journal	Number of articles	%	SJR	IF
1	International Journal of Cancer	1025	1.81	2.056	7.396
2	Vaccine	976	1.72	1.392	4.422
3	Journal of Virology	917	1.62	2.049	3.341
4	Plos One	815	1.44	0.852	3.240
5	Gynecologic Oncology	638	1.12	1.493	5.482
6	Virology	623	1.10	1.112	3.616
7	Journal of Medical Virology	540	0.95	2.656	2.327
8	Journal of Infectious Diseases	504	0.89	2.509	5.226
9	Cancer	442	0.78	2.463	6.860
10	Journal of Lower Genital Tract Disease	420	0.74	0.560	1.925

SJR: SCImago Journal Rank, IF: Impact factor

estimated. Bibliometric analyses and network studies provide information about scientific performance and hot topics by analyzing the structure of publications in a particular research area and showing the productivity of countries, authors, and organizations. As in this study, the evaluation of studies on HPV as a whole is informative about where we are in HPV research and how to proceed. To the best of our knowledge, this study is important as it is the bibliometric analysis that includes the widest timelapse on HPV research.

In this study it is observed that 73.14% of all publications were published in the last 20 years clearly shows that the performance of publications has accelerated in recent years. The fact that the largest number of articles were published in 2020 and 2021 (11,07%) showed that HPV research has not been overshadowed by the coronavirus disease 2019 (COVID-19) pandemic. A previous bibliometric study of joint publications on the HPV vaccine and cervical cancer reported that the publications increased especially since 2018 and the most publications were in 2021 similar to our study.[17] It is possible that the reason for this was the WHO's global call for a cervical cancer elimination program in 2020.

It is markable that the USA is the country with the highest number of publications, the most active authors, and the leading institutions. It was observed that the countries that presented the most HPV research in the literature did not have high HPV incidences.[18] The fact that the countries that produced the most publications are those with relatively low incidence suggests that research activities may be effective in reducing the incidence and prevalence of HPV. To enhance global research on HPV, strong collaborations between developed and developing/underdeveloped countries are needed.

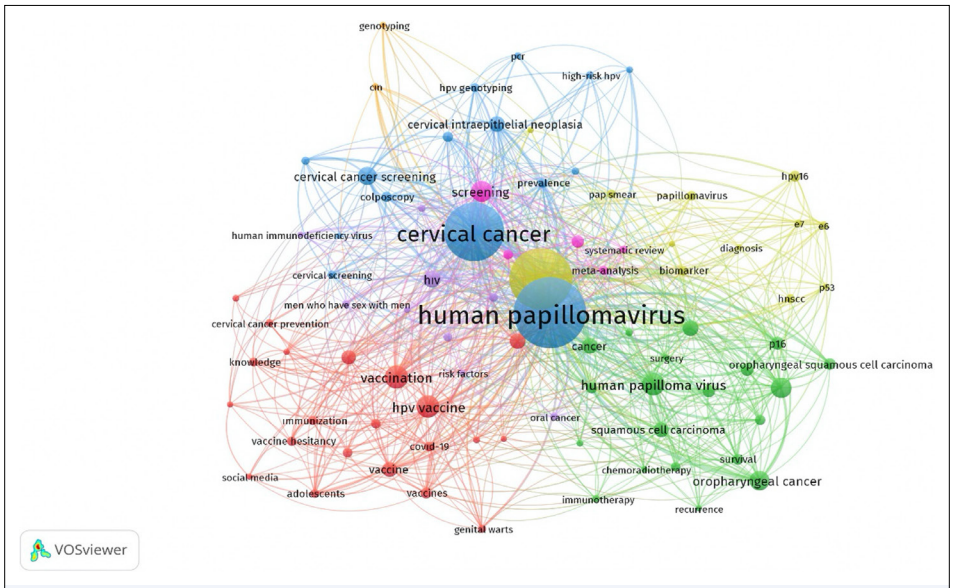

Fig. 3. Keywords network analysis of HPV publications.
HPV: Human Papillomaviruses.

Since English was the most popular language in previous studies, it was expected that English would be the most popular in our study.[8,10] The fact that the USA and the UK are two countries with the most publications, also explains the situation.

Our analysis showed that the majority of the publications belong to the field of medicine. The reason is that HPV has currently been one of the most common sexually transmitted infectious diseases and still remains an important human health issue. Additionally, it is suggested, that WHO's global call for a cervical cancer elimination program and the efforts to control and eliminate HPV at the global level prompt researchers in the field of medicine to conduct research and publications in this direction. As a result of the analysis, it was seen that the greatest number of publications were published as articles. The high number of produced articles shows that new and original studies have been carried out on HPV frequently.

As expected, our analysis shows that journals publishing HPV publications mostly belong to the field of medicine. It is observed that 12.16% of publications were published in the top 10 preferred journals. The scopes of the top 10 journals are in agreement with our keyword network analysis results. The most common themes in network analysis are related to HPV-related cancers, vaccination, and diagnosis, explaining that the top 10 journals have scopes on cancer, vaccines, and virology.

As a result of our analysis, it was seen that major topics were mostly related to HPV diagnosis, immunization, and non-cervical HPV-related cancers. In a study aimed to investigate the research trends and hotspots of HPV research from the top-cited articles between 2003–2012, it was reported that the identification of HPV, epidemiological and laboratory studies, and vaccination are the most studied themes.[19] In another keyword network analysis study covering the years 2014–2018, it was reported that cervical cancer, vaccination, and head and neck cancers were the most studied subjects, similar to our study.[20] Since HPV causes various cancers, especially cervical cancer, and also is a common sexually transmitted disease, it is understandable that intensive studies on the diagnosis of HPV, determination of epidemiology, and immunization are at the forefront. It is thought that in recent years, as a reason of routine screening tests and many countries have started routine vaccination in women and girls, non-cervical cancers, which are more common in men, have come to the fore. The results of our study also support this situation. Although diagnosis and vaccination are the primary themes, it has been observed that research on non-cervical cancers has gained momentum. We think that further research on non-cervical HPV cancers, especially those associated with men, will reveal data on the necessity of male vaccination and will be important in encouraging countries to vaccinate men.

In a review presented in 2018, meta-analyses on vaccines were evaluated and it was reported that the second most frequent pathogens/diseases studied was HPV with a 13% ratio.[21] Results of a study in

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2020 that describes the evolution of studies on HPV vaccination reported a high degree of acceleration in HPV vaccination topics.[22] The third most studied theme in our study is related to immunization, which is in line with previous studies. Especially with the effect of WHO's global call for a cervical cancer elimination program, it is thought that studies on immunization will increase in the future.

Although our study contains useful data covering large-scale HPV publications on a wide range of dates, it has some limitations. First, in this analysis, only a single database (Scopus), through the broadest, was used. In addition, the visibility of important and trending topics that have been studied in recent years, but few, may have been overlooked in big data.

CONCLUSION

In conclusion, the current analysis provides valuable information about the global progress of HPV research, despite some limitations of the study. Our study showed that HPV publications have accelerated in the past decades. This study will be also very helpful in following the developments in HPV research, pioneering topics, and their characteristics. Additionally, this is the most comprehensive bibliometric and visual analysis of HPV on a global scale, despite the existence of several similar studies.

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