## Journal of Surgery and Medicine •-ISSN: 2602-2079

# A bibliometric analysis of *Bacillus anthracis* research published between 1975 and 2018

1975 ve 2018 yılları arasında yayınlanan Bacillus anthracis araştırmalarının bibliyometrik analizi

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<sup>1</sup> Department of Medical Microbiology, Hitit University, Erol Olcok Education and Research Hospital, Corum, Turkey ORCID ID of the author(s) ÜS: 0000-0003-2319-8171	Abstract Aim: Bibliometrics is a recent field and is performed to quantitatively assess the academic quality of journals or authors using statistical procedures such as citation rates, contents, authorship relations and productivity. Although anthrax still remains important globally, the scientific literature lacks a bibliometric assessment of the anthrax literature. In this study, it is aimed to perform the bibliometric analysis of anthrax. Methods: The data in this study were extracted from the Thomson Reuters Web of Science database (Thomson Reuters, New York, NY, USA) from 1975 to December 2018. The database is accessible back to 1975 and we searched all documents using keywords [Bacillus anthracis OR anthrax] in the "Title" field. Results: WoS database search recorded a total of 5557 publications. More than half of the publications were original articles (n=3828, 68.8%). The country with the greatest number of publications was the United States of America (n=3203), followed by England (n=301) and France (n=264). The Center for Disease Control and Prevention had the most published documents about anthrax with 210 papers and 3.7% of the total literature. The most productive authors are Leppla SH, Collier RJ, and Mock M (n=236, 124, 101 documents), respectively. The most productive journal was Infection and Immunity, which covered 4.3% of the publications with 241 manuscripts. Conclusion: In this first bibliometric study in the literature about anthrax we found that nonendemic developed countries dominated the anthrax literature. This study will encourage further studies about the investigation of anthrax, which is endemic in some parts of the
Corresponding author / Sorumlu yazar:	world. Keywords: Bibliometrics, Citation analysis, Anthrax, Bacillus anthracis
Ünsal Savcı Address / Adres: Hitit Üniversitesi, Tibbi Mikrobiyoloji Anabilim Dalı, Erol Olcok Eğitim ve Araştırma Hastanesi, Çorum, Türkiye e-Mail: unsalsavci@gmail.com Ethics Committee Approval: This study is not a clinical and experimental study. The data in this study were extracted from the Thomson Reuters Web of Science database (Thomson Reuters, New York, NY, USA) from 1975 to December 2018. Author declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki. Etik Kurul Onayı: Bu çalışma klinik ve deneysel bir çalışma değildir. Bu çalışma klinik ve deneysel bir çalışma değildir. Bu çalışma klinik ve veri tabanından (Thomson Reuters, New York, NY, ABD) çıkarıldı. Yazar, araştırmanın Helsinki Dünya Tıp Birliği Deklarasyonu ilkelerine göre yapıldığını açıkladı.	<ul> <li>Öz</li> <li>Amaç: Bibliyometri, atıf oranları, içerik, yazar ilişkileri ve üretkenlik gibi istatistiksel prosedürleri kullanarak dergilerin ve yazarların akademik kalitesini kantitatif olarak değerlendiren bir alandır. Her ne kadar şarbon küresel olarak hala önemli olsa da, bilimsel literatürde şarbon literatürünün bibliyometrik bir değerlendirmesi yoktur. Bu çalışmada, şarbonun bibliyometrik analizinin yapılması amaçlanmıştır.</li> <li>Yöntemler: Bu çalışmadaki veriler, 1975 - Aralık 2018 tarihleri arasında, Thomson Reuters Web of Science (Thomson Reuters, New York, NY, USA) very tabanından elde edildi. Veritabanında 1975 yılına kadar erişilebilir ve "Title" bölümünde [Bacillus anthracis veya anthrax] anahtar kelimeler kullanılarak tüm dökümanlarda aradık.</li> <li>Bulgular: WoS (Web of Science) veritabanında toplam 5557 yayın bulundu. Yayınların yarısından fazlası orijinal makalelerdi (n=3828, %68,8). En fazla yayını olan ülke Amerika Birleşik Devletleri'ni (n=3203), İngiltere (n=301) ve Fransa (n=264) takip etti. The Center for Disease Control and Prevention, şarbon ile ilgili 210 yayın ve literatürün %3,7'si ile en fazla yayın yapan kurumdu. En üretken yazarlar sırasıyla Leppla SH, Collier RJ ve Mock M (n=236, 124, 101 yayın) oldu. En üretken dergi, 241 yazı ile yayınların %4,3'ünü kapayan Infection and Immunity dergisiydi.</li> <li>Sonuç: Şarbon ile ilgili literatürdeki bu ilk bibliyometrik çalışmada, endemik olmayan gelişmiş ülkelerin şarbon literatürün hâkim olduğunu bulduk. Bu çalışma, dünyanın bazı bölgelerinde endemik olan şarbonun araştırılmasıyla ilgili ileri çalışmaları teşvik edecektir. Anahtar kelimeler: Bibliyometri, Atıf analizi, Şarbon, Bacillus anthracis</li> </ul>
Conflict of Interest: No conflict of interest was declared by the authors. Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir. Financial Disclosure: The authors declared that this study has received no financial support. Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir. Published: 9/19/2019 Yayın Tarihi: 19.09.2019	
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#### J Surg Med. 2019;3(9):666-671.

## Introduction

Infectious diseases continue to be the biggest public health problem for centuries in all countries of the world [1]. Anthrax is a zoonotic infectious disease caused by the grampositive bacteria Bacillus anthracis which forms endospores and produces exotoxins [2,3]. The disease occurs in humans, wild and domestic mammal species, especially in herbivores [4]. Anthrax cases in humans are classified in three forms based on clinical features and transmission routes; cutaneous form, comprising nearly 95% of all human cases reported in the world in general, gastrointestinal form, and pulmonary form [5]. There is no evidence of human-to-human transmission of B. anthracis and humans develop the disease due to direct contact with animals infected with anthrax or animal products contaminated with anthrax [6-8]. B. anthracis spores may remain viable for tens of years due to their resistance to extreme pH and temperature, drying and some chemical materials [8].

Although *B. anthracis* is generally an organism that is environmentally stable and found everywhere, it is known as a potential pathogen for use in biological weapons. Anthrax is observed in the world in generally, with lower rates in developed countries. It is endemic in Africa and Asia and WHO estimates the global incidence is from 2000 to 20,000 [9,10]. Due to animal and human epidemics in a variety of regions on earth, it has a potential for use as a biological weapon and it is very difficult to monitor information related to anthrax which is still endemic in some regions.

Bibliometrics is a recent field and is performed to quantitatively assess the academic quality of journals or authors using statistical procedures such as citation rates, contents, authorship relations and productivity. Bibliometrics is used in collaboration with the broader term "infometrics" [11-13], and the narrower term "scientometrics" [13-15]. Pritchard was the first author to suggest the term "statistical bibliography" in 1969 [16]. Scientometrics and bibliometrics often involve the scientific contribution of journals or specific works, citation analysis and a content analysis of words in titles, abstracts or the full text of journals. They also focus on authorship, social network analysis, co-word and keywords assigned to published articles. Nowadays, a number of tools have apparently made it much easier to produce these reports. Databases such as Web of Science (WoS), Scopus or Google Scholar have added and incorporated reference handling features [17]. Bibliometrics could be considered knowledge of science because the scientific literature itself becomes the subject of analysis.

Bibliometric analysis is a commonly used tool to assess the productivity and growth of research in the health sciences. Bibliometric analyses have been performed and published in a variety of research areas like cancer [18], respiratory medicine [19], tuberculosis [20-22], and public health [23,24].

Though bibliometric studies in the health area are increasing with each passing day, there is no bibliometric study related to anthrax found in the literature.

### **Materials and methods**

The data for this study were extracted from the Thomson Reuters Web of Science database (Thomson Reuters,

New York, NY, USA) from 1975 to December 2018. The database is accessible back to 1975 and we searched all documents using keywords [Bacillus anthracis OR anthrax] in the "Title" field. We used VOSviewer software tool to arrange and set the bibliometric networks (VOSviewer 2018). Data were transferred from WoS in the "Full Record and Cited References" content pattern.

## Results

#### Numbers of published items

The WoS database search recorded a total of 5557 publications between 1975 and December 2018. More than half of the publications were articles (3828, 68.8%), followed by meeting abstracts (522, 9.3%), news items (290, 5.2%) and reviews (251, 4.5%) (Table 1).

lications on	anthrax literatur
Number	%
3828	68.8
522	9.3
290	5.2
251	4.5
212	3.8
202	3.6
179	3.2
54	0.9
51	0.9
39	0.7
34	0.6
6	0.1
2	0.03
1	0.01
1	0.01
5672	100
	Number 3828 522 290 251 202 179 54 51 39 34 6 2 1

<sup>a</sup>Total percentage may exceed 100% because certain items were included in more than one category

The number of publications between 2003 and 2012 varied between 250 and 290. There was a decrease in the number of publications after 2012. 2018 is the poorest year with only 137 publications. The most productive year was 2002 with 387 records.

The total number of articles cited in this field was 121,382 and the number is 56,878 if we exclude self-citations. Before the 2000s, the citation numbers were between 200 and 600, but after this time they clearly increased. After 2005, citation records are over 5,000, with the highest number of 9,446 in 2012. The number of publications and citations according to year for anthrax are shown in Figure 1.

The country with the greatest number of publications was the United States of America (n=3203), followed by England (n=301) and France (n=264). Publication density and distribution of the manuscripts is shown on the world map (Figure 2).



Figure 1: Number of anthrax publications and citations by year

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Figure 2: Distribution chart for documents published between 1975 and 2018

## Authors and institutions

The co-authorship network for the countries in relation to anthrax was interrogated using the WoS database. The relationship network is described by at least 20 joint publications. In 130 countries, VOSviewer returned these criteria with 25 countries in 7 clusters. This network shows the productivity power of the countries with the size of the point and the connections between the countries and authors publishing together. Seven colored clusters mean that each color group worked with each other significantly. Connected countries with co-authorship relations were located closely in the same color as the clusters. The USA has the biggest point size and the highest number of publications about anthrax. For example, authors from USA worked with the authors from Australia, India, the People's Republic of China and South Korea. USA had 31 links with over 20 joint publications, while England had 20, France 18 and Germany 17 links (Figure 3).

We also created a citation network for these countries with VOSviewer. We defined the cut off boundary as 300 citations and found 26 countries in nine clusters. In this classification, the USA was again the most cited country (86,340) followed by France (10,497), England (7,079), Italy (3,363) and Germany (2,860).

The Centers for Disease Control and Prevention had the most published documents about anthrax with 210 papers and 3.7% of the total literature. This was followed by National Institute of Allergy and Infectious Diseases (186, 3.3%), Harvard University (163, 2.9%), Institut Pasteur (157, 2.8%), and the US Food and Drug Administration (96, 1.7%) (Table 2).

Co-authorship relations were identified between 2990 institutes, and with at least 40 as the minimum document number threshold this decreased to 28 centers. There are seven clusters and connections are located closely in the same color (Figure 4). For example, in the blue cluster the Centers for Disease Control and Prevention has 206 documents with other institutes and worked closely with Northern Arizona University, Emory University, University of California Berkeley, University of Maryland and United States Navy. The National Institute of Allergy and Infectious Diseases shown in red has 185 documents together and most of them clustered at the upper right side of the infographic.

The most productive authors are Leppla SH, Collier RJ, and Mock M (n=236, 124, 101 documents, respectively) (Table 3). The five most cited authors were Leppla SH, Mock M, Collier RJ, Friedlander AM, and Keim P (n=11707, 6966, 5968, 4087, 3711 citations respectively).







Figure 4: Co-authorship relations between institutions for anthrax

We also made a chart for the ten journal names with most published anthrax papers (Table 4). This showed 4.3% of the papers were printed in Infection and Immunity with 241 manuscripts, followed by Journal of Bacteriology (n=155, percentage 2.7%), Vaccine (n=143, percentage 2.5%), Plos One (n=138, percentage 2.4%), and Abstracts of Papers of the American Chemical Society (n=133, percentage 2.3%).

The most cited article is "Proteolytic inactivation of MAP-kinase-kinase by anthrax lethal factor" published in 1998 by Duesbery et al. [25] in "Science". This is also the most-cited study with an average of 35.95 citations per year. The article "Anthrax Toxin Edema Factor - A Bacterial Adenylate-Cyclase That Increases Cyclic-Amp Concentrations In Eukaryotic Cells" is a relatively an old publication by Leppla [2] with an average citation per year of 19.63. This paper was published in 1982 in "Proceedings of the National Academy of Sciences of the United States of America" (Table 5).

Table 2: Most productive institutes in anthrax

Institute	Record Count	Country	% of 5557
Ctr Dis Control Prevent	210	USA	3.768
NIAID	186	USA	3.338
Harvard Univ	163	USA	2.925
Inst Pasteur	157	France	2.817
US FDA	96	USA	1.723
Univ Chicago	94	USA	1.687
NIH	77	USA	1.382
Jawaharlal Nehru Univ	76	India	1.364
Univ Maryland	75	USA	1.346
Univ Michigan	72	USA	1.292
Univ Oklahoma	71	USA	1.274
USN	64	USA	1.148
No Arizona Univ	60	USA	1.077
Univ Texas	58	USA	1.041
Israel Inst Biol Res	53	Israel	0.951

Ctr Dis Control Prevent: Centers for Disease Control and Prevention, NIAID: National Institute of Allergy and Infectious Diseases, NIH: National Institutes of Health, USN: United States Navy JOSAM

Table 3: The most productive 15 authors <sup>a</sup>

Authors	Instution	Country	Records	% <sup>a</sup>
Leppla SH	NIAID	USA	236	4.235
Collier RJ	Harvard Medical School	USA	124	2.225
Mock M	Institut Pasteur	France	101	1.812
Moayeri M	NIAID	USA	82	1.471
Quinn CP	CDC	USA	82	1.471
Bhatnagar R	Jawaharlal Nehru University	India	77	1.312
Friedlander AM	USAMRIID	USA	72	1.292
Keim P	Northern Arizona University	USA	55	0.987
Koehler TM	The University of Texas	USA	50	0.897
Liu SH	Chaoyang University of Technology	Taiwan	47	0.843
Fouet A	Institut Pasteur	France	46	0.825
Little SF	USAMRIID	USA	44	0.790
Tang WJ	University of Chicago	USA	43	0.772
Hanna PC	University of Michigan	USA	42	0.754
Singh Y	University of Delhi	India	42	0.754

<sup>a</sup> Of total documents published in anthrax literature, NIAID: National Institute of Allergy and Infectious Diseases, USAMRIID: United States Army Medical Research Institute of Infectious Diseases Northern Arizona University, CDC: Centers for Disease Control and Prevention

Table 4: The top ten journal source according to the number of published documents

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Journals	Records	% of 5557
Infection and Immunity	241	4.34
Journal of Bacteriology	155	2.79
Vaccine	143	2.57
Plos One	138	2.48
American Chemical Society	133	2.39
Journal of Biological Chemistry	113	2.03
Journal of Applied Microbiology	99	1.78
Proc Natl Acad Sci USA	95	1.71
Applied and Environmental Microbiolog	y 86	1.55
Emerging Infectious Diseases	81	1.46

Proc Natl Acad Sci USA: Proceedings of the National Academy of Sciences of the United States of America

Table 5: The prominent 10 most cited articles

Article	Author	Publication year	Total citation	Average citations per year
Proteolytic inactivation of MAP- kinase- kinase by anthrax lethal factor	Duesbery NS, Webb CP, Leppla SH, et al.	1998	791	35.95
Anthrax toxin edema factor - a bacterial adenylate-cyclase that increases cyclic-amp concentrations in eukaryotic cells	Leppla SH	1982	746	19.63
Anthrax	Mock M. Fouet A	2001	723	38.05
Anthrax	Dixon TC, Meselson M, Guillemin J, et al.	1999	694	33.05
Anthrax as a biological weapon, 2002-Updated recommendations for management	Inglesby TV, O'Toole T, Henderson DA, et al.	2002	673	37.39
Bacillus anthracis, Bacillus cereus, and Bacillus thuringiensis - One species on the basis of genetic evidence	Helgason E, Okstad OA, Caugant DA, et al.	2000	660	33.00
Identification of the cellular receptor for anthrax toxin	Bradley KA, Mogridge J, Mourez M	2001	645	33.95
Bioterrorism-related inhalational anthrax: The first 10 cases reported in the United States	Shepard CW, et al.	2001	605	37.84
The genome sequence of Bacillus anthracis Ames and comparison to closely related bacteria	Read TD, Peterson SN, Tourasse N, et al	2003	595	35.00
Crystal structure of the anthrax toxin protective antigen	Petosa C, Collier RJ, Klimpel KR	1997	587	25.52

#### **Keyword analysis**

The total number of keywords was 4270, when we limited the minimum number of occurrences to15, 40 met the criteria (Figure 5). Most five commonly used keywords were "anthrax (715)", "bacillus anthracis (705)", "protective antigen (165)", "lethal factor (104)", and "vaccine(100)". As seen in the infographic network, there are 5 clusters related to each other. For example, "anthrax" is mostly used with antibody, capsule, toxin, vaccine and virulence.



Figure 5: Keyword network for anthrax publications between 1975 and 2018

#### Discussion

Bibliometric studies provide qualitative and quantitative analysis of the scientific and academic literature and determine the most active and popular trends in a field [26]. Bibliometric analyses reveal the productivity of countries, authors and organizations and analyze the structure of publications [27]. Definition of anthrax disease begins in the antique period, with the oldest from the Roman poet Virgil. During the 19<sup>th</sup> century, anthrax was an infection involved in important medical developments. Robert Koch (1876) found the disease vector and Louis Pasteur (1881) created the first bacterial veterinary anthrax inoculation prepared containing weakened live organisms. Though it is one of the oldest diseases known in humans and animals, anthrax is still relevant today [28]. In recent times, anthrax has been used as a biological war agent both in the USA and abroad. In 1979, anthrax spores were mistakenly released in Sverdlovsk city in the Soviet Union after an accident in a biological weapons facility and 77 humans were infected with definite diagnosis. Of those infected, 66 died within 1 to 4 days after initial symptoms. In 1993, a group called Aum Shrinrikyo released anthrax in Tokyo during an attack. In 2001, a government agent with the US Army Research Institute for Infectious Disease deliberately distributed anthrax spores through the American postal service. Eleven people in contact with infected post had inhalation anthrax diagnosis and 5 of these patients died [29,30].

There is very limited research in the literature about bibliometric analysis of microbiological studies. There is no bibliometric analysis research in the literature about anthrax, causing serious diseases in both humans and animals, with very high transmission risk, used as biological weapon agent with worrying dimensions by some countries, and still endemic in some regions of the globe. Our study is the first international bibliometric assessment of papers published from 1975 to December 2018 about anthrax. The relatively low number of publications in this study is due to the lack of inclusion of publications from before 1975.

Though anthrax is not endemic in the United States of America, it is the most productive country for anthrax research comprising 57.64% of documents. Though they are endemic regions, there is no country from Africa or South America in the list of the top 25 countries, apart from South Africa. Of publications, 88% (4877/5557) were published after 2000. *B.* 

*anthracis* spores may live in soil for many years and though the disease is endemic to Africa, Central Asia, Middle East and South America, it has spread around the world [31,32].

Our graph for anthrax research after the year 2000 shows highest number of publications were reached in 2002, with a continuous reduction in publication numbers until 2018. The promotion and common use of effective veterinary inoculations by the World Health Organization has reduced the incidence of anthrax in humans exposed to cattle, sheep, goat, camel, horses, and pigs and contaminated animal products. Control precautions in animal husbandry are key to low incidence and anthrax is reported to be one of the infectious diseases decreasing in the world [33]. In this context, the reason for the continuous reduction in publication numbers may be explained by the fall in disease incidence and researchers reducing interest in this disease.

The citation number for articles generally reach maximum levels 4-7 years after publication [34,35]. The citation numbers for anthrax articles were very low until the 2000s (200-600), with a rapid increase after the year 2000 to reach highest levels in 2012 with a continuous fall from 2012 to 2018. The reason for the increase in citation numbers is probably due to the citations of publications focusing from 2002-2009. Due to the fall in publication numbers after 2009, it is expected the number of citations will continue to fall in future years.

Analysis of the WoS database for the co-authorship network between countries found 25 countries with at least 20 common publications formed 7 clusters, with the USA the country with most common publications and 31 connections. As expected, the countries with most publications and common publication criteria of at least 20 or more were England, France and Germany with 20, 18 and 17 connected countries, respectively.

The WoS database revealed that most prolific country institutions cooperate mainly at national level and that international cooperation has risen intensely over the past 25 years as shown in this analysis. This finding simply shows only the publication relationships between countries, because research is only good if performed internationally.

With 12 institutions, American institutions led the published articles as expected. Apart from American institutions, the Pasteur Institute in France (157 articles,  $4^{th}$  place), the Jawaharlal Nehru University in India (76 articles,  $8^{th}$  place) and the Israel Biological Research Institute in Israel (53 articles,  $15^{th}$  place) were among the top 15 institutions. The Centers for Disease Control and Prevention was the institution with most publications at 210 (3.7%), with the unexpected inclusion of the military institution of the United States Navy in the top 15 institutions with 64 publications.

The most productive 15 authors were identified to be from the USA (n=10), France (n=2), India (n=2) and Taiwan (n=1). Lepla SH was the author with highest number of publications (236) and highest number of citations (11,707).

Among 10 journals publishing most articles about this topic, 9 were from the USA (Table 5). Of the thousands of journals, Infection and Immunity (n=241, 4.34%) and Journal of Bacteriology (n=155, 2.79%) were in the top 2 places, with an

English journal Vaccine (n=241, 42.57%) in third place among the top 10 journals.

The article entitled "Proteolytic inactivation of MAPkinase-kinase by anthrax lethal factor" published in 1998 by Duesbery et al. [25] was the article most cited, with a total of 791 citations and a mean 35.95 citations per year.

Bibliometric analysis is the scientific analysis of countries, organizations, authors, scientific cooperation, citations, key words, journals and time intervals and takes a snapshot of the science. It is a table that allows scientists who deal in details, and sometimes get bogged down in them, to look up and see the big picture. It is an analysis that summarizes the past and history of a scientific area and directs the science.

There are relatively few articles about bibliometric analysis of microbiologic diseases. It is probably due to the need for a sufficient volume of materials to be analyzed and for wellestablished databases. The emergence and widespread distribution of the internet also make data gathering easier [13].

Even though there is improved general awareness, increasing popularity of bibliometric studies, and the need for classification analysis and citation analysis, the number of reports about microbiological diseases is rather limited.

There are some limitations to the current study. We used only one internationally established database to search the literature of the Web of Science, because it is the most reliable scientific database for publications and citations [36], and one bibliometric tool "VOSviewer" to arrange and set networks [37,38]. Although the literature goes back to 1900s in PubMed, we could only reach 1975 by searching the WoS.

## Conclusion

In this first bibliometric study in the literature about anthrax we found that nonendemic developed countries dominate the anthrax literature. This study will encourage further studies about the investigation of anthrax, which is endemic in some parts of the world. It may also be the beginning of a new field in the scientific literature for the evaluation of anthrax.

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#### This paper has been checked for language accuracy by JOSAM editors.

The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine