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Trends in Drug Resistant Research: A Biblometric Examination of Antibiotic Resistance

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Abstract: **Overview: Antibiotic-resistant (ABR) poses a severe hazard to human health and the environment. As the severity of the problem grew, more countries conducted studies on the ARB, and the number of studies has expanded dramatically, particularly in the last decade. As a result, it is critical to retrace relevant ARB research produced between 2010 and 2020.**

Objectives: This research used bibliometrics to investigate ABR-related papers obtained from the Web of Science (WOS) from 2010 to 2020. Methods: This study performed a statistical analysis of the countries, institutions, journals, authors, research areas, author keywords, Essential Science Indicators (ESI) highly cited papers, and ESI hotspots papers to provide an overview of the ABR field as well as research trends, research hotspots, and future research directions in the field. Results: The results showed that the number of related studies is increasing year by year; the USA is the most published in the field of ARB; China is the most active in this field in recent years; the Chinese Academic Science published the most articles; Science Total Environment. published the greatest number of articles; CM Manaia has the most contributions; Environmental Sciences and Ecology is the most popular research area; and "antibiotic resistance," "antibiotics," and "antibiotic resistance genes" were the most frequently occurring author keywords. Conclusion: A citation analysis showed that aquatic environment-related antibiotic resistance is a key research area in this field, while antimicrobial nanomaterial-related research is a recent popular topic.

Keywords: **Bibliometric Analysis; Multi Drug Resistance; Antibiotic Resistance; Drug Resistance.**

1. INTRODUCTION

Antibiotic resistance (ABR) poses a major global threat to human and animal health, impeding progress made by antibiotics in revolutionizing healthcare practices worldwide [1, 2]. Resistance emerges through mutations and horizontal gene transfer of resistance determinants, including direct inactivation of antibiotics, modification of cellular targets, and modification of the cell wall [3]. The primary driver of resistance is the overuse of antibiotics by humans and animals, which includes antibiotic overuse, demographic changes associated with urbanization and poor sanitation, discharge of antibiotic residues

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through environmental wasting, and biocide use in livestock production [4-6]. The sewage treatment processes create an environment suitable for the development and spread of antibiotic resistance, leading to the spread of antibiotic-resistant bacteria and genes in the environment [7]. Antibiotic misuse, overuse, and poor sanitation also contribute to the development of antibiotic resistance. Antibiotic consumption in livestock is projected to increase significantly by 2030, with a significant increase in the populous developing countries [8-11].

Pathogenic bacteria with properties that enable them to cause diseases, including invasiveness and toxicity, have evolved, with antibiotic resistance being a relatively recent development. Resistance may improve virulence or pathogenicity, making antibiotic resistance a potential virulence factor, particularly in hospitals, where drug-resistant bacteria can cause high mortality and morbidity [12]. Despite attempts to address antibiotic resistance, there is a lack of coordinated action at the political level [13]. Hospital-acquired infections associated with antibiotic-resistant pathogens cause 99,000 deaths annually in the US alone, with economic losses of up to $35 billion [14, 15]. Antibiotic resistance costs are difficult to estimate, and data constraints may lead to incomplete estimates. A worst-case scenario of a world without potent antimicrobial agents could lead to global economic damage of $120 trillion [2, 16].

Bibliometric analysis is an effective method for quantitatively assessing academic papers and can be used to investigate the evolution of certain fields, and the results can provide an overview of a certain field as well as research trends, hot topics, distribution of research power and future research directions [17, 18]. The advantage of bibliometric is that it is not limited by geography, allowing data to be collected by country in a particular area to analyze research globally [19]. In addition, specific data analysis software can process the results of bibliometric analyses and present them in a more three-dimensional form. Therefore, bibliometric analysis have been applied to many fields, such as medicine, chemistry, psychology, computer science, and robotics [17, 20]. In addition, bibliometrics is also widely applied to the aspect of research method, for example the publications related to such research methods as TOPSIS, Analytic Hierarchy Process, and ordered weighted averaging operator can also make knowledge recreation by bibliometrics [21].

2. METHODS

Database

Data was retrieved from the google scholar and PubMed database using a comprehensive search string to reflect the entire Antibiotics resistance (ABR) field (Core Team, 2019). These databases were selected because they are valuable database for antibiotic resistance due to their comprehensive coverage of scholarly literature. The rationale lies in the ability of this database to provide access to a wide range of peer-reviewed articles, academic papers and conference proceedings from various sources. It is favored for its extensive collection that enables thorough and in-depth literature reviews, aiding in identification of current trends, key search findings and emerging perspectives within the field of cardiovascular medicine [22].

Search Strategy

A comprehensive search strategy was used to gather publications and articles related to antibiotic resistance and drug resistance to analyze publication patterns, trends, and treatment strategies in this field. The search string used in gathering the data for the analysis are: ("Anti-Bacterial Agents" [Mesh] OR Anti-Bacterial* [tiab] OR antibacterial*[tiab] OR antibiotic*[tiab] OR antimicrobial*[tiab] OR antimycobacterial*[tiab] OR and ("Drug Resistance" [Mesh] OR resistan*[tiab] OR "Microbial Sensitivity Tests" [Mesh]). The search results formed the text corpus of this study. The extracted variables were: PMID number, author names, affiliations, title, abstract, journal, and database entry year. The keywords used are; "antibiotic resistance", "drug resistance", "bibliometric analysis", "publication patterns", "multi drug resistance", "treatment strategies". Date range; the publications and articles used for this analysis used a 23 years phase that ranged from 2000 to 2023.

Validation of the search strategy

In the current study, the development of the search query was continuously fine-tuned until the top 200 cited documents in the retrieved literature were free of any false-positive results. Furthermore, the search query was tested for missing data (false-negative) by adopting a previously published method which relies on the correlation between the retrieved research output for active authors and their actual research output in this field [23].

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Bibliometric indicators

In the current study, the following bibliometric indicators were presented: (1) volume and growth of publications on antibiotics resistance (ABR) in the environment over the past two decades; (2) research output from different world regions; (3) subject areas of literature on ABR in the environment; (4) most active countries, institutions, and journals involved in publishing scientific articles on ABR in the environment; and (5) the antibiotics drug classes and pathogens mostly encountered in the retrieved literature.

Data Analysis

Retrieved data were exported from Scopus to Microsoft Excel for analysis and table presentation. Graphics were created using Statistical Package for Social Sciences (SPSS, version 21). Geographical distribution of publications was carried out using the World Health Organization (WHO) geographical classification: the region of the Americas; the European region, the Eastern Mediterranean region, the African region, the South-Eastern Asia region, and Western Pacific region). Visualization maps were created using VOS-viewer program [24]. International research collaboration among active countries was assessed using the "link strength" indicator extracted from visualization maps. The normalized citation value was obtained from the network visualization maps created by VOS viewer. The Hirschindex (h-index) was used to measure the scientific impact of authors, institutions, countries, and a body of literature.

3. RESULTS

General trends

From 2010 to 2020, 2,823 papers in the ABR field were published by authors in 116 countries, including 99 ESI highly cited papers and 3 ESI hot papers. These publications can be divided into 11 languages, including 2,793 in English (98.94%), 10 in German (0.35%), 6 in Spanish (0.213%), 3 in French and Polish (0.106%), 2 in Hungarian and Portuguese (0.071%), and 1 in Chinese, Dutch, Italian and Turkish (0.035%). The growth trend of articles related to the ABR field from 2010 to 2020 was described (Figure 1.0). During this period, the number of articles published in this field increased by more than sevenfold, with the number of articles published from 2018 to 2020 increasing significantly. This finding indicates that ABR has attracted increasing concern year by year, and it also shows that the impact of ABR on human beings is increasing.

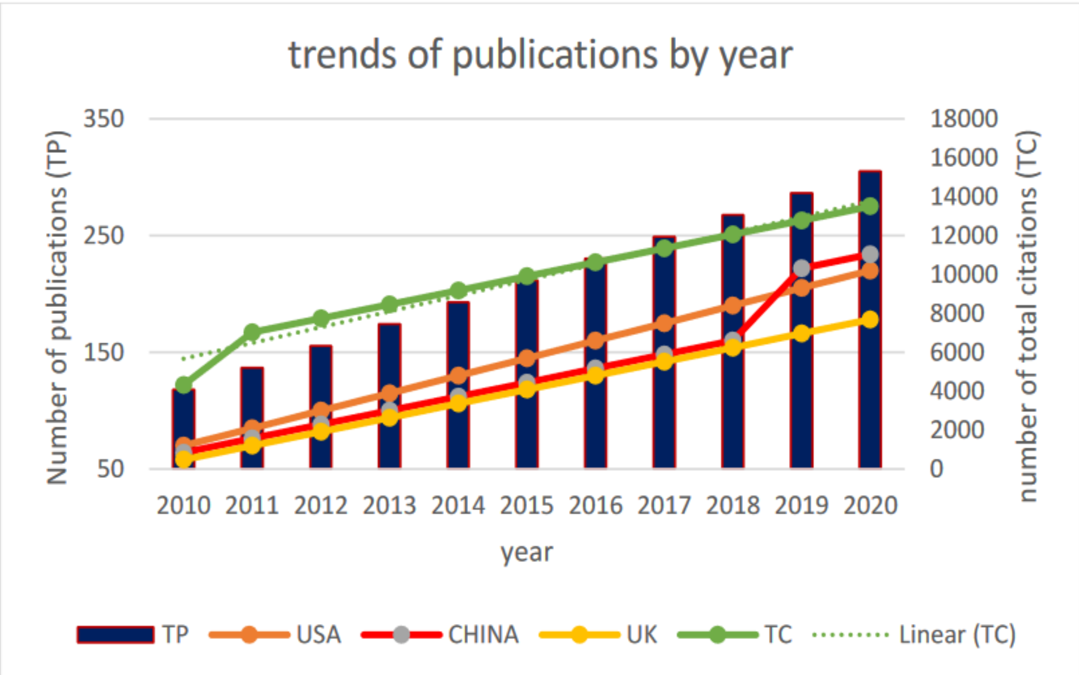

Figure 1.0; Trends in the number of published articles related to ABR by year. TP, total papers; TC, total citations.

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Contribution of leading countries/regions

The top 20 countries in terms of total quantity of publications in the ABR field between 2010 and 2020 were identified (Table 1.0). The USA is the country with the most publications in this field, followed by China and the UK, whose publications account for 25.61, 18.17, and 6.23% of the total publications, respectively. The same result can be seen in the ranking of total citations; that is, the USA is first, followed by China and the UK. Figure 1.1 shows the number of ABR0related publications per year from 2010 to 2020 in the USA, China and the UK. It can be seen that China issued very few publications from 2010 to 2010, less than the UK and the USA, while in 2019 the number of publications in China rose significantly. In 2020 China has already surpassed the USA in the number of relevant publications. This indicates that China is considerably more active in this research field during recent years. It is likely related to the large population in China, the high prevalence of antibiotic abuse, the relevant policies and higher scientific research fund support [25]. Among the top 20 countries, 11 countries were in Europe, 5 countries were in Asia, and 4 countries were in the Americas, which show that ABR have attracted global attention.

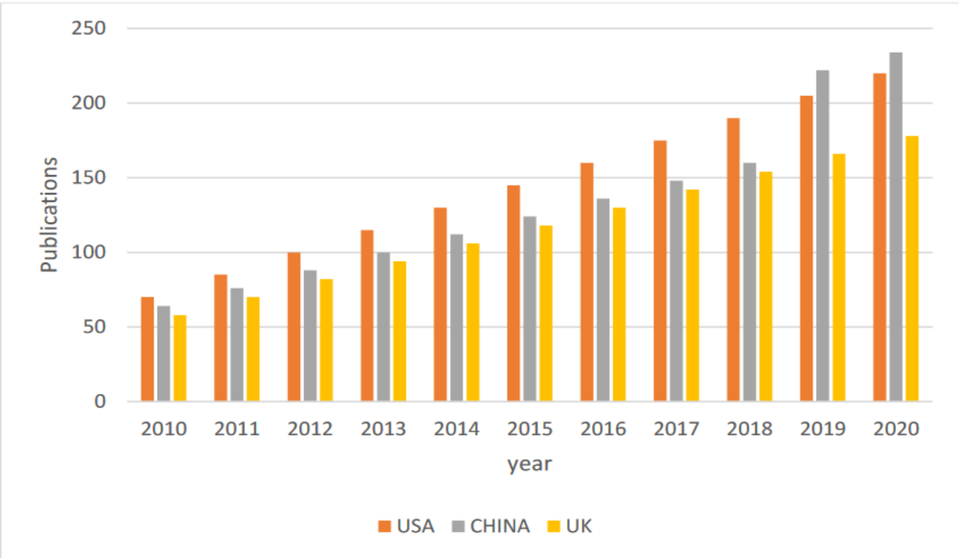

Figure 1:1 Number of ABR-related publications per year from 2010 to 2020 in the USA, China, and the UK

Table 1.0; The top 20 most productive institutions in the ARB field during 2010–2020

Rank	Country	TP	TC	h-index	ACPP	nCC	SP (%)
1	USA	723	27,937	78	38.63	67	40.11
2	China	513	16,157	64	31.5	43	32.75
3	UK	176	10,977	43	62.37	64	69.32
4	Germany	168	10.219	43	60.83	57	61.90
5	Italy	140	8,384	36	59.89	48	52.14
6	Spain	139	6,584	38	47.37	52	64.75
7	India	134	2,941	30	21.95	43	34.33
8	South Korea	121	3,168	32	26.18	35	37.19
9	Sweden	104	7,246	33	69.67	48	59.62
10	Canada	101	6,148	34	60.87	46	64.36
11	France	99	7,044	32	71.15	55	64.65
12	Japan	99	2,317	24	23.4	32	39.39
13	Australia	98	6,120	36	62.45	47	75.51

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14	Portugal	96	6,808	34	70.92	47	44.79
15	Netherlands	79	5,778	32	73.14	45	62.03
16	Poland	79	3,298	27	14.75	39	34.18
17	Brazil	77	1,509	22	19.6	19	41.46
18	Switzerland	67	4,386	28	65.46	39	59.70
19	Iran	55	969	18	17.62	11	18.18
20	Turkey	49	876	15	17.88	17	28.57

TP, total papers; TC, total citations; ACPP, average citations per publication; nCC, number of cooperative countries; SP, Share of publications

Cooperation of leading countries/regions

The most impactful science comes from international collaboration, which is based on the flow and integration of knowledge. Different countries/regions may have different emphases when studying ABR, although resource complementarity and continuous innovation impulses can be achieved by collaboration. International collaborative publications are joint papers written by scholars from multiple countries. The number of cooperative countries (nCC) refers to how many countries a country has cooperated with in a certain field. It can be concluded from Table 1.0 that among all countries, the USA, the UK, Germany, Spain and France have more cooperation with other countries. To better understand the current state of international collaboration in the ABR field, a network graph between the top 10 countries/regions was created using the DDA software (Figure 1.2). The circle size symbolizes the countries' contributions, the lines connecting the circles indicate cooperation between countries, and the thickness of the lines indicates the number of collaborative publications. It can be seen from Figure 1.2 and 1.3 that almost all of the top 10 countries in publications have ever cooperated with each other. The line between the USA and China is the thickest, which indicates that the number of cooperative publications between the USA and China is the largest in this field, followed by the number of cooperative publications between the USA and Canada.

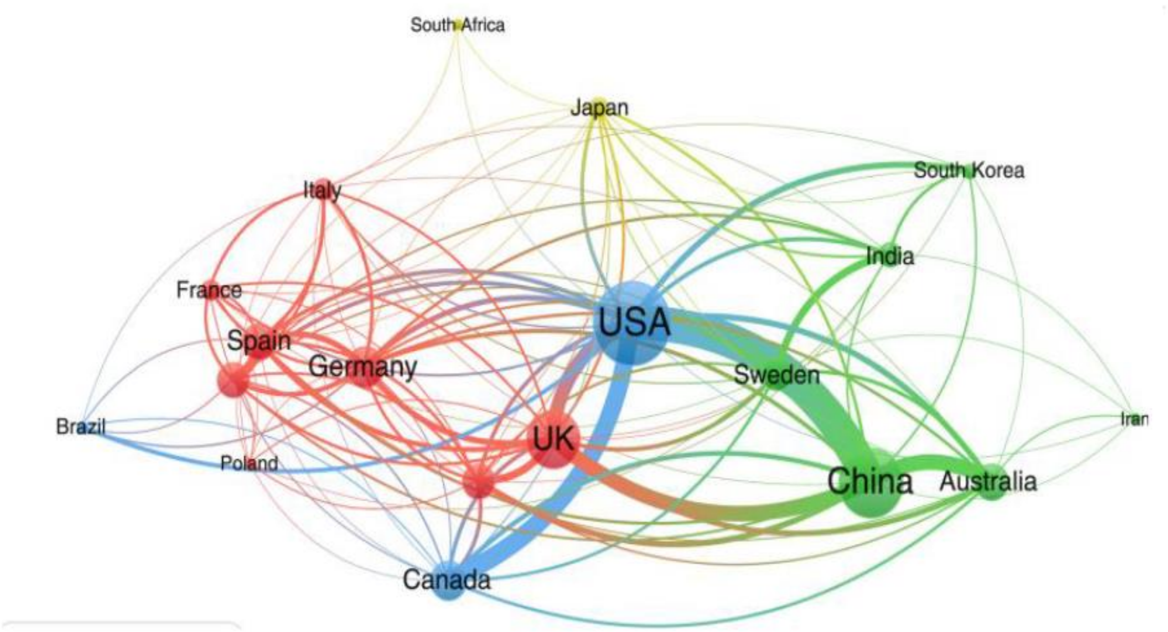

Figure 1.2: Network visualization map of international research collaboration among countries with minimum research output of 50 documents on AMR in the environment. The thickness of the connecting lines represents the strength of research collaboration between any two countries. The connecting line between the USA and China represents the strongest research collaboration due to it thickness relative to other lines.

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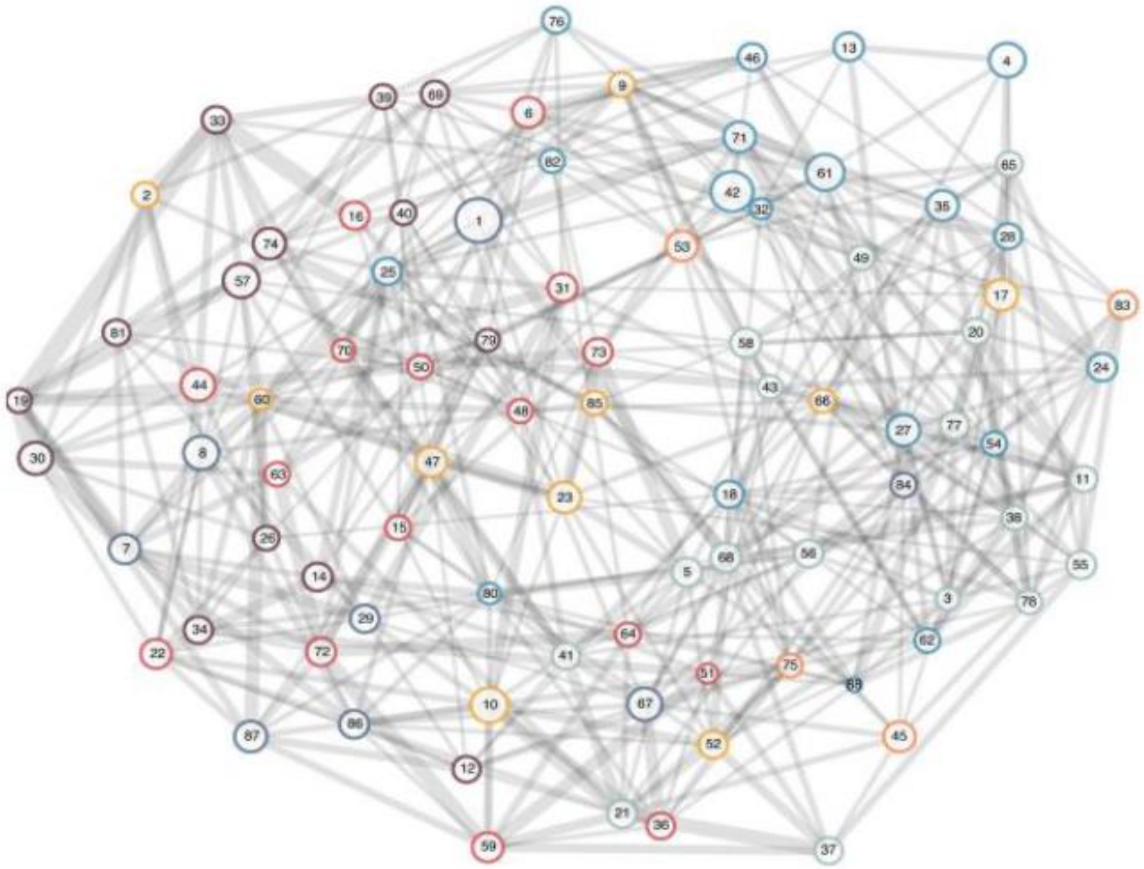

Figure 1.3; Topic network in AMR research based on topic co-occurrence generated. The 88 topics names with their corresponding number are displayed. Colours are used to highlight the 7 thematic groups within the network: clinical (purple), environment (orange), organism (red), system (grey-blue), compound (light blue), methods (yellow), and strategy (dark blue). Line size within the network corresponds to correlation weight (more weight equals thicker lines) and node size corresponds to the proportion of published articles.

Contribution of leading institutions

Statistics on the contributions of leading institutions can help us identify the most authoritative professional institutions in the ABR field. There are 3,430 institutions involved in ABR research, and the top 10 are summarized (Table 1.1). Among these 10 institutions, there are 40% institutions in Europe and Asia, respectively, while the majority of those in Asia are from China. Although the Chinese Acad Sci has published a large number of articles, the total citations and average citations per paper are not the highest. Although several European institutes do not have a large number of publications, such as Univ Catolica Portuguesa and Univ Cyprus, the quality of articles is relatively high, which can be seen from their high total citations and average citations per paper. The output and quality of scientific research were positively correlated with the degree of international collaboration [26]. A cluster map of the collaboration among the top 10 institutions was created with DDA software (Figure 1.4). Obviously, Gothenburg University, the Chinese Acad Sci and Tsinghua University showed the most extensive collaborations with other institutions in the ABR field. In addition, the USDA ARS, Karolinska Inst and Univ Queensland have a greater number of collaborations with institutions in different countries; thus, their degree of internationalization was high. The collaborations between the Chinese Acad Sci and Univ Chinese Acad Sci and between Univ Porto and Univ Catolica Portuguesa were the most frequent. Institutions in European countries were more closely connected with those in neighboring countries/regions, which was similar to that in Asia, possibly because of factors such as institutional relationships and geographical proximity.

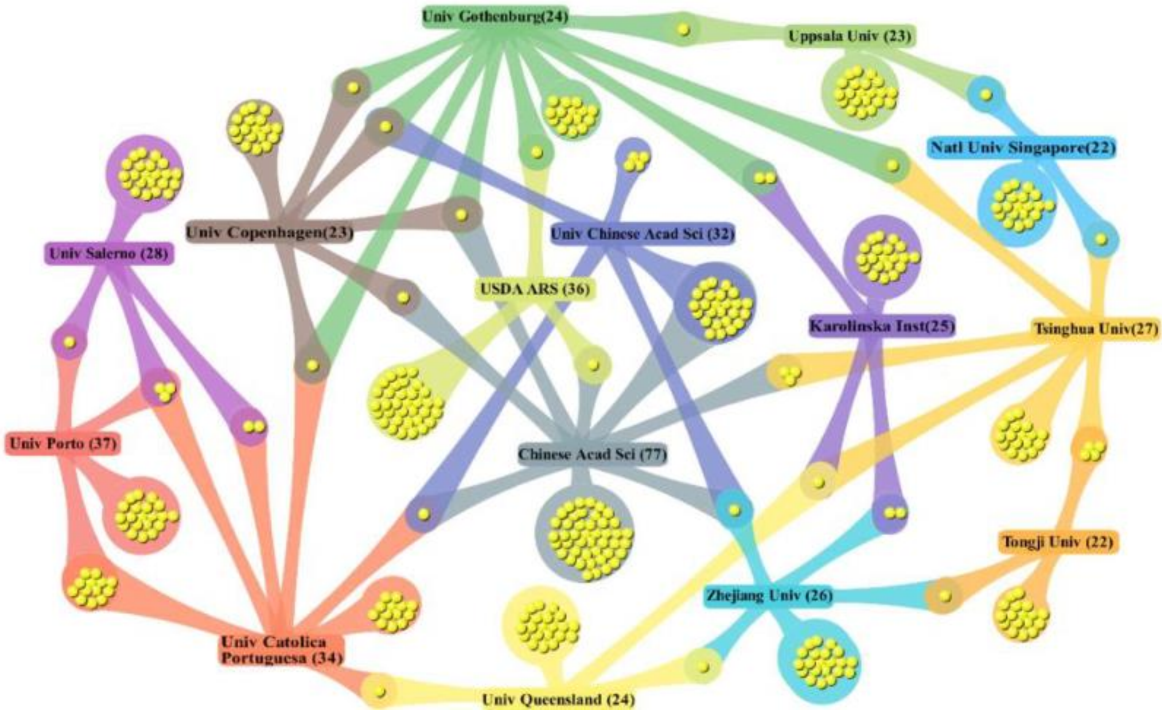

Figure 1:4. DDA cluster map on cooperation of the top 15 institutions

Table 1.1: The top 10 most productive institutions in the ARB field during 2010–2020

Rank	Institutions	TP	TC	ACPP	h-index	TPR (%)	Country/Region
1	Chinese Acad Sci	77	3,443	44.71	31	2.728	China
2	Univ Porto	37	2,046	55.30	21	1.311	Portuguese
3	USDA ARS	36	986	27.39	17	1.276	USA
4	Univ Catolica Portuguesa	34	4,239	124.68	24	1.204	Portuguese
5	Univ Chinese Acad Sci	32	1,455	45.47	18	1.134	China
6	Univ Salerno	28	2,732	2,732	19	0.991	Italy
7	Tsinghua Univ	27	1,355	50.19	18	0.956	China
8	Zhejiang Univ	26	450	17.31	11	0.921	China
9	Karolinska Inst	25	704	28.16	13	0.886	Sweden
10	Univ Gothenburg	24	2,070	86.25	17	0.850	Sweden

TP, total papers; TC, total citations; ACPP, average citations per publication; TPR, the percentage of articles of institutions in total publications.

Contribution of leading journals

The collation of published journals revealed that a total of 983 journals published ABR-related research from 2010 to 2020. The top 20 journals by the number of articles are displayed (Table 1.2). These 20 journals have published a total of 911 articles on ABR, accounting for 45.86% of the total literature. Forty-three percent of these journals were related to the

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environment, 20% were related to microbiology, 13% were related to medicine, 10% were related to engineering technology, and 3% was related to materials and chemistry each. The breadth of disciplines involved reflects that ABR represent an interdisciplinary research field.

Table 1.2: Top 20 journals publishing papers in Antibiotics resistant research

Rank	Journal title	TP	TC	ACPP	IF	TPR (%)
1	Sci. Total Environ.	110	5,546	50.42	7.963	3.897
2	Front. Microbiol.	79	2,656	33.62	5.64	2.798
3	PLoS One	69	1,780	25.8	3.24	2.444
4	Water Res.	65	4,684	72.06	11.236	2.303
5	Chemosphere	40	1,799	44.98	7.086	1.417
6	Sci Rep	40	591	14.78	4.38	1.417
7	Antibiotics-Basel	36	391	10.86	4.639	1.275
8	Environ. Sci. Pollut. Res.	35	936	26.74	4.223	1.24
9	J. Hazard. Mater.	30	992	33.07	10.588	1.063
10	Antimicrob. Agents Chemother.	29	984	33.93	5.191	1.027
11	Environ. Sci. Technol.	28	2,215	79.11	9.028	0.992
12	Int. J. Environ. Res. Public Health	28	772	27.57	27.57	27.57
13	Environ. Pollut.	27	956	35.41	8.071	0.956
14	mBio	26	1,154	44.38	7.867	0.921
15	Environ. Int.	25	1,177	47.08	9.621	9.621
16	Appl. Environ. Microbiol.	22	997	45.32	4.813	0.779
17	ACS Appl. Mater. Interfaces	19	636	33.47	9.229	0.673
18	Appl. Microbiol. Biotechnol.	19	545	28.68	4.813	0.673
19	Microb. Drug Resist.	18	228	12.67	3.431	0.638
20	Clin. Infect. Dis.	17	1,844	108.47	9.079	0.602

TP, total papers; TC, total citations; ACPP, average citations per publication; IF, Impact Factor 2020; TPR, the percentage of articles of journals in total publications.

Contribution of leading authors

Statistics on leading authors can help us understand the top experts in the ABR field. A total of 13,966 authors were counted among 2,823 articles, of which 12,086 authors only published one article, 337 authors published three articles, and 15 authors published 10 or more articles. The top 10 authors in the number of articles and their institutions are summarized (Table 1.3). These authors published 245 articles, accounting for 8.67% of all articles. CM Manaia has published the most articles in this field and made important contributions to the presence and removal process of antibiotics, ABR and ARG in wastewater and antibiotic resistance in the environment. L Rizzo mainly studied sewage treatment processes, such as photocatalysis and UV. In addition to the study of sewage treatment processes, D Fatta-Kassinos also contributed to the reuse of wastewater.

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Table 1.3: Contribution of the top 10 authors in ARB research.

Rank	Author	TP	TAR	TC	ACPP	h-index	Institution (current), country/region
1	Manaia, CM	33	20	3,296	99.88	24	Univ Catolica Portuguesa, Portugal
2	Rizzo, L	26	22	2,704	104	19	Univ Salerno, Italy
3	Fatta-Kassinos, D	21	9	3,754	178.76	16	Univ Cyprus, Cyprus
4	Larsson, DGJ	17	9	2,036	119.76	15	Univ Gothenburg, Sweden
5	Nunes, OC	16	8	1,358	84.44	13	Univ Porto, Portugal
6	Pruden, A	14	6	1,335	95.36	11	Virginia Tech, USA
7	Topp, E	14	6	1,866	133.29	13	Agr and Agri Food Canada, Canada
8	Webster, TJ	13	12	673	51.77	11	Northeastern Univ, USA
9	Schwartz, T	12	2	2,687	223.92	11	Karlsruhe Inst Technol, Germany
10	Boopathy, R	11	11	320	29.09	9	Nicholls State Univ, USA

TP, total papers; TAR, total number of articles for which they are responsible; TC, total citations;
ACPP, average citations per publication.

Contribution of leading research areas

Statistics on the research areas can help us grasp the shift of research emphasis in a specific field. There are 90 study areas associated with ABR, and the top 20 based on the number of articles are concluded (Table 1.4). The research areas of ABR are not only related to microorganisms, diseases, drugs, and chemistry but also related to the environment, engineering, agriculture, materials and oceanography, with the greatest number of publications related to the ecological environment. The top 5 areas accounted for 76.83% of all articles published, indicating that the environment, microbiology, engineering, drug and chemistry are the top research areas in the ABR field. The bubble chart can show the research trends and emphasis in a specific field more stereoscopically [27]. A bubble chart is depicted to showing the top 20 ABR research areas (Figure 1.5). The numbers on the bubbles reflect the number of publications. “Environmental Sciences and Ecology” is the dominant research direction in the ABR field. From 2010 to 2020, the number of publications in this field increased and was the greatest overall, and it showed significant annual growth since 2017. “Microbiology” is also a research direction of increasing concern. The number of publications related to “Microbiology” every year is also on the rise, although a certain gap is observed. Compared with “Environmental Sciences and Ecology,” “Microbiology” received greater attention in the initial stage. Previously, the number of publications in the “Engineering” direction increased slowly but substantially between 2018 and 2020. The number of publications related to “Materials Science” was low in the initial phase but increased significantly after 2015, reaching a peak in the last 2 years.

Table 1.4: Contribution of the top 20 research areas in ARB field.

Rank	WOS research area	TP	TPR (%)	TC	ACPP	h-index
1	Environmental sciences and Ecology	697	24.69	28,631	41.08	83
2	Microbiology	545	19.306	23,188	42.55	71
3	Engineering	317	11.229	13,193	41.62	62
4	Pharmacology and pharmacy	314	11.123	8,238	26.24	46
5	Chemistry	296	10.45	9,583	32.38	51
6	Science and technology—other Topics	279	9.883	8,932	32.01	55
7	Infectious diseases	261	9.246	11,324	43.39	42
8	Biotechnology and applied Microbiology	210	7.439	5,330	25.38	41
9	Biochemistry and molecular Biology	195	6.908	5,829	29.89	41
10	Water resources	159	5.632	6,370	40.06	39
11	Materials science	155	5.491	4,824	31.12	40
12	Public, environmental and occupational health	151	5.349	4,160	27.55	31

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13	Immunology	109	3.861	4,722	43.32	33
14	Food science and technology	98	3.472	2,023	20.64	24
15	Veterinary sciences	82	2.905	995	12.13	18
16	Agriculture	76	2.692	1,978	26.03	24
17	General and internal medicine	71	2.515	3,320	46.76	25
18	Physics	51	1.807	1,490	29.22	21
19	Marine and freshwater biology	49	1.736	725	14.8	17
20	Biophysics	43	1.736	1,213	28.21	21

TP, total papers; **TRP,** percent of total articles in the field; **TC**, total citations**; ACPP**, average citations per publication.

Analysis of author keywords

A keyword collection based on abundant academic findings in a research field over a long period of time can reveal the overall characteristics, developmental trends, and internal connections of such research. The top 30 author keywords from 2,823 publications were sorted and displayed in a bubble chart in this study (Figure 1.5). The number on the bubble represents the times that the author keywords appeared in the corresponding year. In this paper, we combined author keywords with the same meaning through the DDA. Eventually, a total of 5,506 author keywords were obtained. Among them, 4,276 author keywords appeared only once, which accounted for 77.67%; 573 author keywords appeared twice, which accounted for 10.41%; and 6 author keywords appeared more than 100 times, which accounted for ~0.11%. Among them, "Antibiotic resistance," "Antibiotic-resistant bacteria," "Antibiotics," and "Antibiotic resistance genes" had the highest appearance frequency. Much of the research on "Antibiotic resistance" has focused on the existence of "Antibiotics," "Antibiotic-resistant bacteria," and "Antibiotic resistance genes" in "Wastewater" and the environment and associated removal techniques. There are also many related studies on "Antibiotics," "Antimicrobials," "Antimicrobial peptides," "MRSA," "Nanoparticles," and "Mutidrug resistant bacteria".

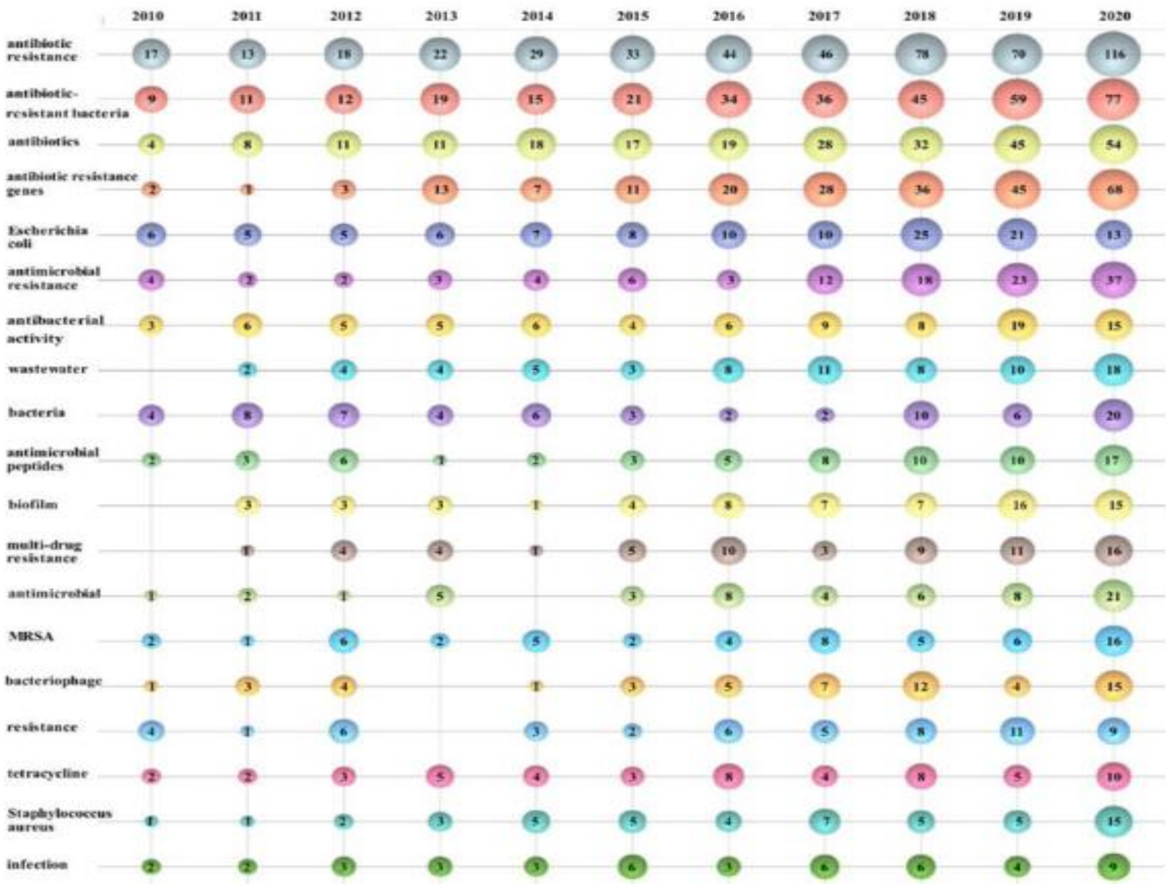

Figure 1.5: Bubble chart of the top 30 author keywords by year.

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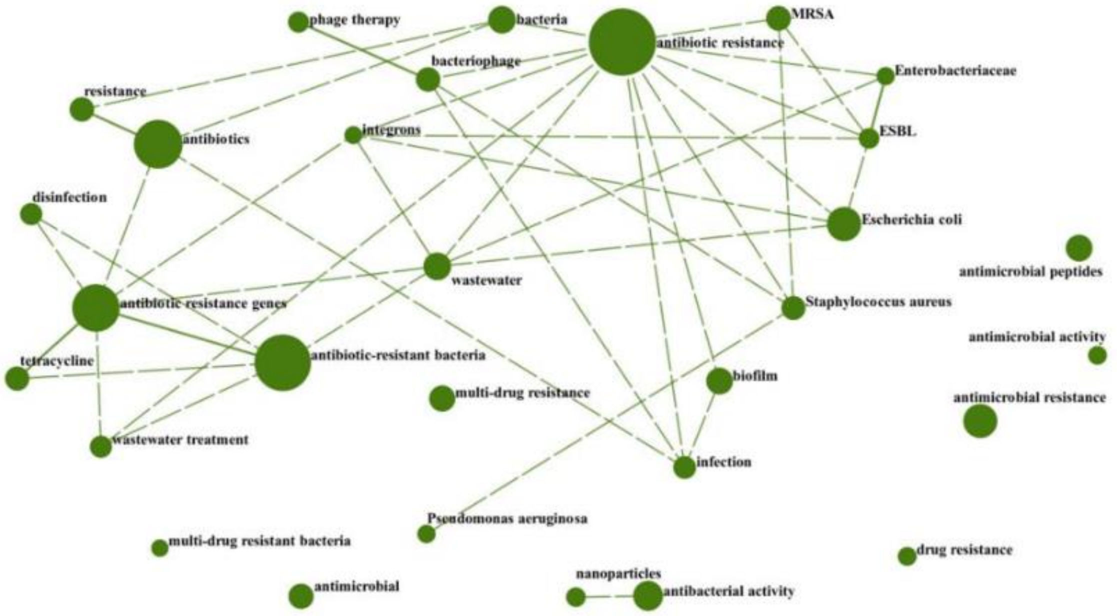

Figure 1.6: Cross-correlation graph of the top 30 author keywords.

The cross-correlation plot shows that two keywords occurred in one paper at the same time. Through the cooccurrence analysis of author keywords, the cross-connection between each author keywords can be better revealed. We designed a cross-correlation plot of the leading 30 author keywords by DDA (Figure 1.6). The size of the circle reflects how frequently the author keywords appear in total articles; the line connecting the two circles indicates that the two author keywordsappear in the same article. The dashed line indicates a correlation between the two author keywords ranging from 0.25 to 0.5, and the solid line means 0.5–0.75. Undoubtedly, the author keywords with the highest frequency also correspond to the largest circles. We can also clearly discover that the author keywords appearing at the same time as "Antibiotic resistance" are the most, indicating that their research scope is wider. Among them, "Antibiotic-resistant bacteria" and "Antibiotic resistance genes," "Resistance" and "Antibiotics," "Phage therapy" and "Bacteriophage," "Enterobacteriaceae" and "ESBL", and "Antibiotic resistance genes" and "Tetracycline" are five pairs of closely related keywords, indicating that those two keywords had a high frequency of appearing simultaneously in an article.

4. DISCUSSION

It is well known that the goal of studying antibiotic resistant is to resist ABR by understanding the mechanisms of the generation, evolution as well as transmission of the antibiotic resistance, such as the implement of sewage treatment processes; to find effective methods to reduce the harm caused by antibiotic resistant bacteria to global humankind and ecosystem, such as the research and development of new antibiotics, antibiotic substitutes, adjuvants.

According to the author keywords bubble chart (Figure 1.5), cross-correlation graph (Figure 1.6) and ESI highly cited papers, it can be found that the research on antibiotic resistance has been the first place and plays a leading role in this field for the last decade. The scope of research mainly includes the existence of antibiotic resistance in the aquatic systems, sewage treatment processes, and negative effects [28]. This may be related to the early abuse of antibiotics in many countries, such as China, USA, India, Italy, and so on. It is undeniable that those studies play a significant role in the understanding of antibiotic resistance. However, some studies have pointed out that MRSA existed long before the antibiotics were used [29]. Mutations in microbial metabolism can also lead to antibiotic resistance. This just goes to show that our understanding of antibiotic resistance is not thorough enough. Further research on the induction factors and relevant mechanisms that lead to antibiotic resistance is required in the future. According to the ESI hot papers (Figure 1.2 and 1.3), nanomaterials have been the hottest topic in this field in the last 2 years, which is closely related to their superior antibacterial properties. However, according to the author keywords bubble chart (Figure 1.5) and cross-correlation graph (Figure 1.6), it can be found that the research on antimicrobial peptides and bacteriophages has gradually increased in the last decade but

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has not received enough attention. Peptide-based antibiotics have been found to be effective against MDRB because bacterial resistance responds slowly to the action mode of peptide natural products [30]. Encrypted peptide kills bacteria by targeting the cell membranes of pathogenic bacteria and is not susceptible to selective resistance [31]. At present, research has found candidate peptide antibiotics in human intestinal flora using machine learning, which breaks through the path dependence on the traditional antibiotic discovery. Bacteriophages have been found in human intestines either, which are in a harmonious symbiotic relationship with intestinal flora, rather than an antagonistic mode. Bacteriophage related therapies are in the concern once more [32]. In addition, there has been also some progress in the relationship between intestinal flora and antibiotic resistance, the effect of antibiotics on intestinal flora, the effect of vaccines on antibiotic resistance and antibiotic-resistant bacterial inhibitors. However, these studies are not thorough enough [33-36]. Therefore, it is necessary to pay attention to the diversification of research and strengthen the research on antibiotic substitutes, human intestinal flora and adjuvants in the future.

Antibiotic resistance imposes a heavy burden on human beings. A study on the worldwide burden of antibiotic resistance found that the mortality in the whole age interval caused by antibiotic resistance is the highest in the Africa. Pseudomonas aeruginosa, MRSA and other MDRB have caused a large number of deaths [37]. This suggests that low-resource settings bear the heaviest burden, which is consistent with the statistical analysis of this study in the leading countries or regions (Table 1.0), leading institutions (Table 1.1) and leading authors (Table 1.3).

Although countries in Africa have made some contributions in this field, the relevant research is not sufficient and is not in the leading position; the understanding of antibiotic resistant bacteria is not enough. According to the author keywords bubble chart, it can be found that MRSA, Pseudomonas aeruginosa and other MDRB have received more attention in recent 2 years [38]. The extremely strong resistance not only causes great losses to humans, but also threatens the existing antibiotics. Studies have shown that the COVID-19 pandemic has led to overuse of antibiotics in many areas, which will aggravate the antibiotic resistance. Therefore, every country needs to establish strict antibiotic prescription guidelines to regulate antibiotic use. However, one study has shown that reducing antibiotic prescriptions cannot stop the spread of antibiotic resistant [39].

There is a gap between antibiotic stewardship in the paper and in practice [40]. Even treatments that match susceptibility of pathogens may result in resistance, because the development of antibiotic resistance is essentially driven by rapid re-infection of different strains of the patient with prescription resistance, and they suggest that the personalized antibiotic treatment suggestions can be given by predicting the patient's past infection or history using the machine learning, thus reducing the emergence of ABR. However, ABR can circulate and transfer between humans and animals. Therefore, it is not enough to reduce the propagation of antibiotic resistance by simply managing the use of antibiotic in human beings. There is no boundary among environment, animal and human beings. The control of antibiotic resistance requires simultaneous communication and cooperation of these three fields, rather than the separation of them [41].

5. CONCLUSION

This study provides an overview of the state of research in the field of Antibiotic Resistance, highlighting the global threat caused by ABR and the interdisciplinary nature of the research field. While progress has been made in the development of novel antibiotics, such as bacteriocins, phage therapy, nanomaterials, human intestinal flora and machine learning, there is still a need for further research. The study also identifies certain limitations, such as the exclusion of articles without author keywords. However, the analysis will hopefully benefit researchers, enabling them to better understand current research trends and hotspots in the field.

Abbreviations

ABR: Antibiotic Resistance

SPSS: Statistical Package for Social Sciences

WHO: World Health Organization

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Competing interests

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