Review Article

Klebsiella pneumonia and Its Antibiotic Resistance: A Bibliometric Analysis

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The rapid development of antibiotic resistance in K. pneumonia has led to a major concern. In order to analyze the hotspots and develop trends in this field through visual analysis, this study used CiteSpace software to summarize the available data in the literature to provide insights. A total of 9366 research articles were retrieved from the Web of Science Core Collection, and the number of published papers is increasing year by year. The country with the most articles was the USA, followed by China and India. The institution with the highest number of publications was LERU. The author with the highest number of articles was Li. The journal with the highest citation rate was Antimicrobial Agents and Chemotherapy. In addition, based on keyword co-occurrence analysis and cited literature prominence analysis by CiteSpace, the current research focus in the field was therapy, CRKP, and resistance genes. This paper provides a new quantitative visualization way for the development of the field in the recent ten years. The results show global trends that researchers can use to determine future directions.

1. Introduction

Klebsiella pneumonia, belonging to the family Enterobacteriaceae, is a natural inhabitant of the gastrointestinal tract microbiome of healthy humans and animals [1]. It has a variety of antibiotic resistance mechanisms and is a common pathogen causing hospital-acquired surgical wound infections, digestive tract infections, and community-onset infections, which can cause outbreaks of nosocomial infection [2]. The global drug resistance rate of K. pneumonia has reached as high as 70%, and the infection-related fatality rate has also reached 40%~70% [3]. In recent years, multiple-drug resistance (MDR) K. pneumonia and carbapenem-resistant Klebsiella pneumonia (CRKP) have emerged as a major global public health problem.

In this study, we reviewed the literature on antibiotic resistance of K. pneumonia by bibliometrics [4]. This study is aimed at analyzing the trend of antibiotic resistance research of K. pneumonia in recent 10 years. According to data from the Web of Science Core Collection (WoSCC), the CiteSpace5.8.R3 software system was employed to display the detailed analysis based on visualization of the cooperative network of the countries, coauthors, and co-occurring keywords [5]. The method and results of this paper may provide potential prospects for the study of antibiotic resistance of K. pneumonia in the future.

2. Data Collection and Methodology

The data from 2012 to 2021 (10 years) were from WoSCC on April 13, 2022, to reduce bias incurred by database updating. Search terms were used as follows: “((((((TS=(Antibiotic resistance)) OR TS=(Antibiotic resistant)) OR TS=(Antimicrobial Resistance)) OR TS=(Antimicrobial Resistant)) OR TS=(Drug Resistance)) OR TS=(Drug Resistant)) AND (TS=(Klebsiella pneumonia)) OR TS=(K. pneumonia))
AND (EDN==("WOS.SCI") AND DT==("ARTICLE" OR "REVIEW") AND LA==("ENGLISH"))) in Advanced Search. In addition to data collection, the CiteSpace 5.8.R3 (64-bit) software system was also used to show the detailed data analysis. All records such as titles, abstracts, and references are exported to CiteSpace for subsequent analysis.

3. Results and Discussion

3.1. Publication Characteristics. The Web of Science Core Collection (WoSCC) database shows 9366 publications that use our search terms, with 8398 articles and 968 reviews. In general, the number of papers published in recent years shows an upward trend, which indicates that the number of papers published in antibiotic resistance research in *K. pneumonia* is receiving more and more attention from researchers. Especially in the past three years, the number of publications has increased sharply, accounting for almost half of the total number of publications. Therefore, the analysis period of this study is from 2012 to 2021, and the research period is divided into one year.

3.2. Countries/Regions and Institutions Co-Operation Analysis. The distribution of studies on antibiotic resistance research in *K. pneumonia* in different countries can be understood by analyzing the country information according to the affiliation of the authors. Many institutions or universities from different countries around the world have contributed to this research field. Research papers from 178 countries have been published, and we have listed the top 10 most productive and influential countries and institutions in *K. pneumonia* antibiotic resistance research field, based on the total publications, citations, and *H*-index during 2012–2021 (Figure 1). As shown in Table 1, the USA and China ranked first and second, with 1,908 and 1,416 publications, accounting for 20.37% and 15.12% of the total, respectively, ahead of India (664 publications and 7.09%), which ranked third. In regard to institutions (Table 2), League of European Research Universities (LERU) is the most

Table 1: Top 10 most productive and influential countries.

| Rank | Countries/regions | Publications | Citations | Average citation per item | H-index |
|------|------------------|--------------|-----------|--------------------------|---------|
| 1    | USA              | 1908         | 65125     | 34.13                    | 109     |
| 2    | China            | 1416         | 24047     | 16.98                    | 58      |
| 3    | India            | 664          | 12636     | 19.03                    | 50      |
| 4    | Italy            | 550          | 16284     | 29.61                    | 58      |
| 5    | UK               | 530          | 21504     | 40.57                    | 64      |
| 6    | France           | 511          | 17375     | 34                       | 61      |
| 7    | Brazil           | 424          | 6720      | 15.85                    | 38      |
| 8    | Spain            | 397          | 11076     | 27.9                     | 49      |
| 9    | Australia        | 366          | 14155     | 38.67                    | 60      |
| 10   | Germany          | 360          | 9481      | 26.34                    | 50      |

Figure 1: (a) Publication volume and growth trends in each year on antibiotic resistance research of *K. pneumonia* from 2012 to 2021. (b) Publication volume and growth trends of the top 10 countries/regions on antibiotic resistance research of *K. pneumonia* from 2012 to 2021. Bar chart reflects number of publications per year.
productive institution in the field of “antibiotic resistance research in K. pneumonia” contributing 521 papers and 18990 total citations. Udice French Research Universities (UFRU) and Egyptian Knowledge Bank (EKB) are ranked second and third in terms of the number of papers.

Besides the total number of publications, the H-index, which represents the cited influence of papers, was given in the tables, too. Sometimes, a high total number of publications or citation number alone does not ensure a high H-index. Therefore, some scientists prefer to use the H-index to rank top countries (institutions), because this bibliometric indicator can more fully evaluate the impact of research [4].

In our case, in terms of “most productive countries,” the USA topped the H-index by a wide margin. However, in regard to prolific institutions, LERU is the most prolific institution with an H-index value of 65. We also analyzed the results using the CiteSpace 5.8.R3 to visually show the most productive countries (institutions) and their connections to each other (Figures 2 and 3). Meanwhile, to highlight the attention of core countries (regions) and relevant academic institutions in this field, the VOSviewer 1.6.18 and Scimago Graphica 1.0.17 software were used for analysis [6].

### Table 2: Top 10 most productive and influential institutions.

| Rank | Institutions                                      | Publications | Citations   | Average citation per item | H-index |
|------|--------------------------------------------------|--------------|-------------|---------------------------|---------|
| 1    | League of European Research Universities (LERU)  | 521          | 18990       | 36.45                     | 65      |
| 2    | Udice French Research Universities (UFRU)        | 261          | 12201       | 46.75                     | 51      |
| 3    | Egyptian Knowledge Bank (EKB)                    | 225          | 3633        | 16.15                     | 30      |
| 4    | Institut National de la Sante et de la Recherche Medicale (INSERM) | 218          | 8951        | 41.06                     | 41      |
| 5    | Zhejiang University                              | 197          | 7449        | 37.81                     | 34      |
| 6    | Assistance Publique Hopitaux Paris               | 171          | 8307        | 48.58                     | 42      |
| 7    | Universite de Paris                              | 145          | 4532        | 31.26                     | 33      |
| 8    | US Department of Veterans Affairs                | 143          | 7162        | 50.08                     | 44      |
| 9    | Veterans Health Administration (VHA)             | 142          | 7059        | 49.71                     | 44      |
| 10   | Monash University                                | 133          | 3825        | 28.76                     | 33      |

**Figure 2: The cooperation network of productive countries.**

3.3. *Authors’ Coanalysis.* Among the top 10 authors with publications, four are from China, three from the USA, two from Australia, and one from France, respectively, as shown in Table 3. Li of Monash University, Australia, tops
the list with 87 publications. Bonomo from the USA and Wang from China ranked second and third, with 84 and 81 publications, respectively. On $H$-index, Bonomo (34) and Paterson (29) rank the top two, showing the absolute advantages and influence of these authors on antibiotic resistance research in K. pneumonia.

Generating a productive author collaboration network is shown in Figure 4. The size of the circle indicates the number of papers the author has published, and the lines between the circles indicate the connections between the authors. The group of primary core authors is the most representative and provides centralized information. From the centrality analysis, Paterson (0.25) ranked the highest followed by Hsueh (0.15), Badal (0.09), and Bonomo (0.09), which reflect their emphasis on this field.

3.4. Journal Analysis. From 2012 to 2021, a total of 1301 journals worldwide published academic papers on antibiotic resistance research in K. pneumonia. Among them, the number of publications of the top 10 journals is more than 140, accounting for 28.25% of the total number of publications, as shown in Table 4. Antimicrobial Agents and Chemotherapy ranked first in terms of published research with 426 articles, accounting for 4.54% of total articles, followed by Frontiers in Microbiology and Journal of Antimicrobial Chemotherapy, and 364 and 303 papers were published, respectively.
respectively, accounting for 3.88% and 3.23% of the total publications. These top two journals also ranked first and second in average citation per article and $H$-index, respectively. Among the 10 journals, one is in Q1 subregion, and eight are in Q2 subregion with impact factors ranging from 3.0 to 5.7, among which, Journal of Antimicrobial Chemotherapy has the highest impact factor.

### 3.5. Keyword Analysis

#### 3.5.1. Coword Analysis.

Through keyword coword analysis, research topics and hotspots can be analyzed, and the transition of research frontiers in a certain knowledge field can be monitored [7]. We used Citespace software to identify keywords from selected papers. At this stage, keywords with

| Number | Freq. | Keyword            |
|--------|-------|--------------------|
| 1      | 4345  | Klebsiella pneumonia |
| 2      | 4105  | Antibiotic resistance |
| 3      | 2791  | Escherichia coli |
| 4      | 1526  | Enterobacteriaceae |
| 5      | 1295  | Infection          |
| 6      | 1107  | Epidemiology       |
| 7      | 995   | Pseudomonas aeruginosa |
| 8      | 895   | Prevalence         |
| 9      | 886   | Risk factor        |
| 10     | 864   | Emergence          |

**Table 5:** Top 10 high-frequency keywords related to antibiotic resistance research in *K. pneumonia.*

Figure 4: Collaborative network of productive authors.
similar meanings were combined, such as “antibiotic resistance,” “antimicrobial resistance,” and “drug resistance.” Table 5 shows the top 10 keywords for frequency and centrality in this field over the past 10 years. We also developed networks for the analysis in Figure 5. It can be seen that the top five keywords of co-occurrence were *Klebsiella pneumonia*, antibiotic resistance, *Escherichia coli*, Enterobacteriaceae, and infection. In order of centrality, the top five keywords were biological activity (0.17), synergy (0.14), penetration (0.14), antimicrobial peptide (0.12), and high prevalence (0.12). Centrality refers to the ratio of the shortest path that passes through a certain point and connects the two points to the total number of shortest path lines between the two points, which is used to describe the importance of a node. The larger the value is, the more influential the node is in the key position in the network [8].

3.5.2. Clustering Analysis. Keyword clustering analysis can cluster similar points together and identify clusters that represent relevant research areas. We use CiteSpace to summarize the clustering of the keyword timeline map. Cluster size is the number of terms contained in each cluster. CiteSpace gives cluster ID 0 to the largest cluster, cluster ID 1 to the second largest, and so on. As shown in Figure 6, the main research directions can be classified as follows: #0 whole genome sequencing, #1 antibacterial activity, #2 polymyxin b, #3 identification, #4 combination therapy, #5 virulence, #6 drug resistance, #7 United States, #8 bactericidal activity, #9 mortality, #10 sequence, #11 liver abscess, #12 mgbr, #13 Escherichia coli, and # 14 carbapenem resistance: these clusters can summarize the development of antibiotic resistance research in *K. pneumonia* and reveal the current research hotspots.

3.6. Keyword and Reference Burst Detection. Keyword burst detection refers to a significant increase in the frequency of keywords in a short period of time. If we understand the studies with high attention in this period, we can judge the hot topics and frontiers of research in the field accordingly. Keyword burst detection of antibiotic resistance research in 10 years in *K. pneumonia* is shown in Figure 7(a). Sorted by emergence time, it can be seen that the research frontier is whole genome sequencing, activation, phage therapy, gut microbiota, and care associated infection. To some extent, this result represents the trend of the future research. According to Figure 7(b), it can be seen that in the past 10 years that the research hotspot changes and advances the process of antibiotic resistance research in *K. pneumonia*. Depending on the burst strength, the first 1 papers are reviewed from two high-level journals: Lancet Infections Diseases and Clinical Microbiology Reviews [9–12].
Figure 6: (a) Clustered networks of keywords in research papers via CiteSpace. The top 15 largest clusters are shown. (b) Timeline view of the top 15 largest clusters. The horizontal axis represents the evolution time, and #0–#14 represent keywords.
The article with the strongest burst strength was published in *Lancet Infect Dis* in 2010, which reported a new antibiotic resistance mechanism of a new type of carbapenem resistance gene designated *bla*NDM-1 [13]. Another three papers show that the heat continues to this day. Two of them are reviews about *K. pneumonia* [14–17]. Another article was published in *PNAS* in 2015 which sequenced the genomes of 300 diverse *K. pneumonia* and performed a pan-genome-wide association study (PGWAS) to look for associations between gene profiles associated with virulence and antibiotic resistance and the differing disease outcomes seen for *K. pneumonia* [18].
4. Conclusion

This paper provides a visual and comprehensive literature review of antibiotic resistance research in K. pneumonia. We examined the characteristics of publications, collaboration between countries, institutions, and authors, and co-occurrence analysis of journals and keywords. In the past 10 years, there have been 9366 journal articles related to this field, and the number of publications increased rapidly, which showed that scientists are paying increasing attention to this area. Antibiotic resistance in K. pneumonia has emerged as a significant threat to global public health problems [19].

We find several interesting keywords with high co-occurrence frequency through co-word analysis. According to recent research, carbapenem-resistant Klebsiella pneumonia (CRKP) has been paid much attention. Carbapenems have strong antibacterial activity and a wide antibacterial spectrum. Carbapenems are the preferred drugs for the treatment of serious Enterobacteriaceae bacterial infections [20]. However, the emergence and prevalence of CRKP pose a serious threat to patients with low immune function and have become an independent risk factor leading to the death of patients with nosocomial infections [21].

Drug efflux, biofilm formation, enzymatic inactivation of the drug, alteration of drug targets, and reduced permeability due to porin loss or modification are the major mechanisms conferring antibiotic resistance to K. pneumonia [22]. For combating antibiotic resistance in K. pneumonia infections, several therapies are currently being developed. Phage therapy, phytotherapy, photodynamic therapy, antimicrobial peptides, and nanoantibiotics are the potential of some alternatives.

Phages have low natural toxicity and high strain specificity. Due to the specificity of phages, their action is limited to the site of infection and can prevent the destruction of the inherent microbiome [23]. This reduces the development cost of phage therapy compared to antibiotics [24].

Additionally, we highlight the highly cited papers and reveal the research hotspots on antibiotic resistance research in K. pneumonia. This paper uses CiteSpace software to perform bibliometrics and visualization analysis on antibiotic resistance research in K. pneumonia data from the Web of Science database. This work presents direct and specific ways to describe existing information in different perspectives to the reader and can provide reference and reference for the relevant scientific research workers in the topic selection and development direction of the research.

Data Availability

All data generated or analyzed during this study are included in this published article. Other data may be requested through the corresponding author.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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