

Bibliometric Analysis of Research on ESBL-Producing *Escherichia coli* in Healthcare Settings

Baslan Fatih Hakimi^{1*}, Brian Eka Rachman^{2*}, Riski Nabila³

¹Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

²Division of Tropical Medicine and Infectious Diseases, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

³Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

(*) Correspondent: brian.eka@fk.unair.ac.id

ABSTRAK

Penelitian ini memetakan lanskap penelitian global mengenai ESBL-producing *E. coli* di lingkungan pelayanan kesehatan serta menelaah tren luaran ilmiah, kontributor utama, dan fokus tematik. Artikel yang terindeks di Scopus hingga tahun 2025 dianalisis menggunakan Bibliometrix (R) dan VOSviewer untuk mengevaluasi pertumbuhan publikasi, produktivitas negara dan institusi, penulis terkemuka, jurnal inti, jaringan kolaborasi, serta pola kata kunci. Sebanyak 4.032 dokumen teridentifikasi, menunjukkan peningkatan yang signifikan sejak pertengahan tahun 2000-an, terutama setelah 2010. Amerika Serikat, Tiongkok, serta beberapa negara di Eropa dan Asia muncul sebagai kontributor dominan. Analisis kata kunci dan jaringan menunjukkan adanya pergeseran tematik dari studi awal yang berfokus pada enzim menuju klon berisiko tinggi, ko-produksi karbapenemase, strategi terapi, serta transmisi terkait pendekatan One Health. Secara keseluruhan, bidang ini tampak telah matang namun terus berkembang, mencerminkan tren global resistensi antimikroba yang lebih luas.

Kata kunci: ESBL-producing *Escherichia coli*; infeksi terkait pelayanan kesehatan; resistensi antimikroba; analisis bibliometrik; Scopus.

ABSTRACT

This study mapped the global research landscape on ESBL-producing *E. coli* in healthcare settings and examined trends in scientific output, major contributors, and thematic focus. Articles indexed in Scopus up to 2025 were analyzed using Bibliometrix (R) and VOSviewer to evaluate publication growth, country and institutional productivity, leading authors, core journals, collaboration networks, and keyword patterns. A total of 4,032 documents were identified, showing substantial expansion since the mid-2000s, especially after 2010. The United States, China, and several European and Asian countries emerged as dominant contributors. Keyword and network analyses revealed a thematic shift from early enzyme-focused studies toward high-risk clones, carbapenemase co-production, therapeutic strategies, and one health-related transmission. Overall, the field appears mature yet continuously evolving, reflecting broader global antimicrobial resistance trends.

Keywords: ESBL-producing *Escherichia coli*; healthcare-associated infections; antimicrobial resistance; bibliometric analysis; scopus

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Introduction

Extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*) is a major public health concern because of its ability to resist a wide range of beta-lactam antibiotics, including penicillins and cephalosporins.¹ *E. coli* is a Gram-negative bacterium that normally resides in the human intestinal tract as a harmless commensal, but pathogenic strains of Enterobacteriaceae can cause a wide spectrum of infections, ranging from urinary tract infections to life-threatening sepsis.^{1,2} ESBL production arises from the acquisition of genes encoding enzymes that hydrolyze beta-lactam antibiotics, including advanced-generation cephalosporins, thereby rendering these drugs ineffective and complicating treatment.^{3,4} The global prevalence of ESBL-producing *E. coli* is increasing, particularly in hospital settings with high antibiotic use, and hospital-acquired infections caused by ESBL-producing *E. coli* are now reported worldwide.¹ In Asia, the prevalence is notably high; for example, a Chinese study estimated that 38.9–55.8% of *E. coli* isolates from hospitalized patients were ESBL producers, while 2016 data from Myanmar reported a prevalence of 49.1%.^{5,6} Factors such as high population density, substantial infectious disease burden, and widespread antibiotic availability make Southeast Asia one of the regions at greatest risk for antimicrobial resistance.⁶

Despite the growing body of antimicrobial resistance (AMR) bibliometric studies, previous analyses have generally focused on broader AMR trends, specific pathogens such as MRSA, or resistance in food-producing animals and environmental settings, rather than providing a dedicated and comprehensive evaluation of ESBL-producing *Escherichia coli* in healthcare environments. Many prior studies also relied on limited timeframes, single analytical indicators, or did not integrate collaboration networks, thematic evolution, and institutional productivity into a unified framework. Consequently, the specific research landscape of ESBL-producing *E. coli* in healthcare settings remains insufficiently characterized. This study addresses these gaps by offering a focused and up-to-date bibliometric assessment using Scopus-indexed data up to 2025, integrating productivity analysis, citation impact, collaboration structures, keyword co-occurrence mapping, and temporal thematic evolution. By synthesizing these dimensions, this research provides a more comprehensive understanding of the development, structure, and future direction of ESBL-producing *E. coli* research within healthcare systems.

Bibliometric analysis is a structured, quantitative method for examining scientific literature to identify publication patterns, research trends, collaboration structures, and the overall impact of work within a specific field. It typically involves systematic data retrieval from major databases (e.g., Scopus, Web of Science, PubMed), followed by data cleaning, standardization, and analysis using techniques such as citation analysis, co-authorship and co-occurrence networks, keyword mapping, and temporal trend analysis.⁷

Although ESBL-producing *E. coli* represents a pressing clinical and public health threat, its global research landscape has not been systematically characterized using bibliometric methods, leaving evidence on research output, collaboration patterns, and emerging themes fragmented. This study therefore conducts a comprehensive bibliometric analysis of Scopus-indexed publications on ESBL-producing *E. coli* in healthcare settings, assessing temporal publication trends, leading countries and institutions, influential authors and journals, co-authorship networks, keyword co-occurrence, and thematic evolution, and demonstrating that ESBL-producing *E. coli* has become a substantial healthcare burden, particularly among hospitalized populations.

Research Method

Data Source and Literature Search Strategy:

Scopus was selected as the primary database for this study due to its extensive coverage of over 4,000 academic journals and its widespread use among researchers. Relevant articles were retrieved and exported from Scopus on June 23, 2025. The search was conducted using the following keywords: (“healthcare-acquired infection”) AND (“*Escherichia coli*”) AND (“ESBL-producing *E. coli*”). Only studies published in English were considered for inclusion. The complete records and cited references of the selected publications were downloaded in Excel format for further analysis.

Software For Bibliometric Analysis:

This study used R software (version 4.5.0) and VOSviewer as the primary tools for conducting the bibliometric analysis. These programs were employed to construct scientific mapping visualizations and to detect patterns, relationships, and emerging trends within the research field. The Bibliometrix package in R (version 4.0.0) was specifically used to quantify and compare collaboration frequencies between countries, providing insight into international research partnerships. VOSviewer, in turn, was applied to assess publication output, citation counts, and the distribution of author keywords, thereby highlighting influential articles, topics, and contributors.⁸

Using VOSviewer's integrated clustering algorithm, co-occurrence networks of frequently used terms were generated and displayed as visual maps, allowing the main thematic clusters of the literature to be identified.⁹ Furthermore, VOSviewer was also used to analyze and visualize collaboration structures at multiple levels, including countries, institutions, and individual authors. Finally, to better understand how scientific output has evolved over time, the increase in annual publication numbers was modeled using an exponential growth function developed in Microsoft Excel.¹⁰

Results

As shown in Figure 1, 4032 articles on ESBL-producing *E. coli* were included in this study. Figure 2 displays the annual scientific production related to ESBL-producing *E. coli*. Initially, between 1989 and 2006, the number of articles published each year remained low, indicating limited research on the topic during this period. Starting around 2006, there was a sharp increase in publications, peaking around 2015-2022. This surge suggests growing research interest, possibly due to advances in the field, greater funding, or a heightened awareness of the subject. The graph shows an exceptional rise in articles around 2022, which could signify a breakthrough or significant external factors driving research output. However, after this peak, there is a dramatic decline in the number of articles in 2023. This drop could reflect data issues, a shift in research focus, or changes in funding and global priorities. Overall, the figure highlights a rapid increase in research output in recent years, with a notable drop at the end, signaling either a disruption in publication trends or a shift in research priorities.

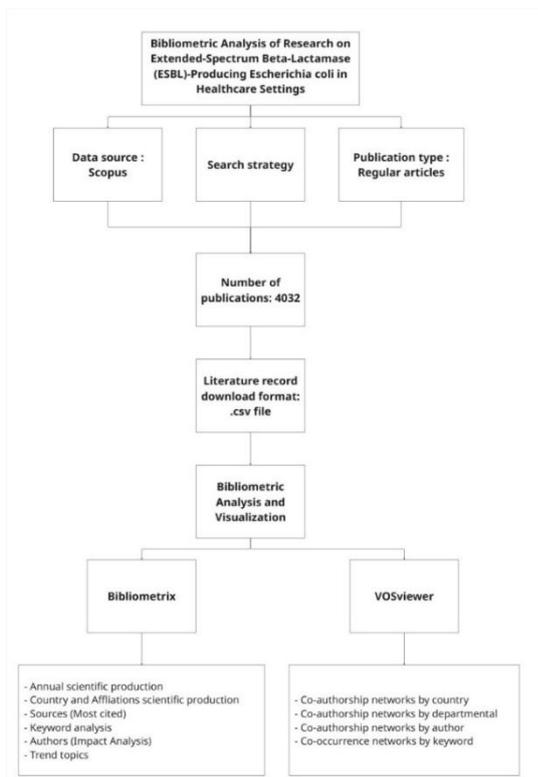


Figure 1. Flow-chart of the study

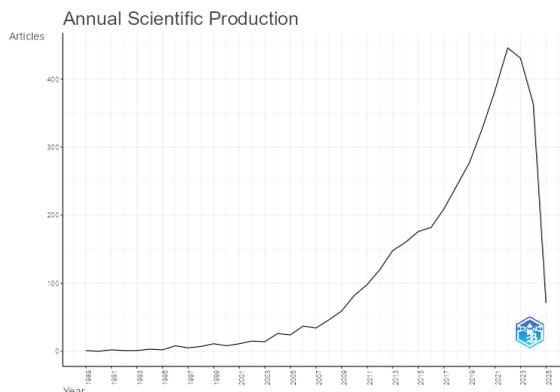


Figure 2. Annual Scientific Production

Analysis of countries publication

Figure 3 highlights the global distribution of research on ESBL-producing *E. coli*. The USA (3,244 publications) and China (3,023) are the top contributors, followed by France, Spain, Japan, India, Germany, the UK, Italy, and South Korea. Together, these countries form the core of worldwide efforts to address this AMR problem, reflecting strong research capacity and sustained focus on ESBL-related issues in healthcare settings. Figure S1A (Supplementary Figure link: <https://tinyurl.com/ya2nrfdn>) visualizes international co-authorship networks. Node size represents publication volume and links

indicate collaboration strength. The United States appears as the main hub, with dense connections to Europe, Asia, and South America. Countries such as France, China, Japan, Brazil, Spain, and Italy form prominent regional clusters, underscoring a broad but asymmetrical global collaboration structure. Figure S1B (Supplementary Figure link: <https://tinyurl.com/ya2nrfdn>) presents a time-overlay view of these collaborations (2017–2021). The USA, France, China, and Japan remain central throughout, while ties with Brazil, Spain, Italy, and other countries intensify over time. Earlier years (2017–2018) show sparser networks, whereas 2019–2021 display a denser, more interconnected map, reflecting a rapidly growing global focus on ESBL-producing *E. coli* research across Europe, Asia, and the Americas.

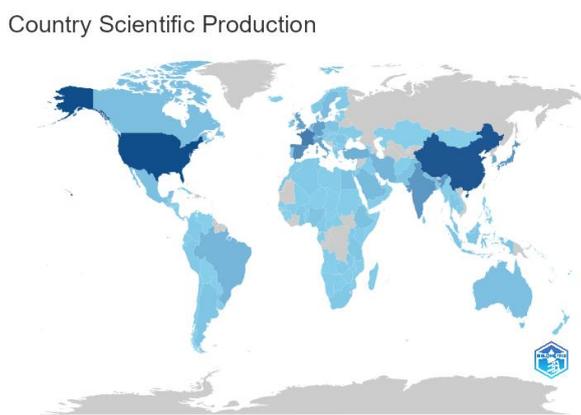


Figure 3. Countries contribution to the ESBL-producing *E. coli*

Analysis of affiliations publication

As part of our investigation, we visualized the number of publications from various affiliations on ESBL-producing *E. coli* in Table 1. JIM Laboratories leads with 130 publications, followed by Tribhuvan University with 101. Other significant contributors include Zhejiang University (98), University of California (94), and Hospital Universitario Virgen Macarena (85). University of Manitoba (85) and University Hospital Basel (83) also show strong involvement. Sichuan University (80), Christian Medical College (78), and University of Oxford (78) contribute to the field, though at slightly lower levels. This chart highlights the global distribution of research, with a few universities leading the way in advancing knowledge on ESBL-producing *E. coli*.

Table 1. Affiliations With Most Publication

No.	Affiliation	Articles
1.	JMI LABORATORIES	130
2.	TRIBHUVAN UNIVERSITY	101
3.	ZHEJIANG UNIVERSITY	98
4.	UNIVERSITY OF CALIFORNIA	94
5.	HOSPITAL UNIVERSITARIO VIRGEN MACARENA	85
6.	UNIVERSITY OF MANITOBA	85
7.	UNIVERSITY HOSPITAL BASEL	83
8.	SICHUAN UNIVERSITY	80
9.	CHRISTIAN MEDICAL COLLEGE	78
10.	UNIVERSITY OF OXFORD	78

Whereas, in Figure S2 (Supplementary Figure link: <https://tinyurl.com/ya2nrfdn>) shows the co-authorship network of affiliations is presented, illustrating collaboration patterns between different departments involved in ESBL-producing *E. coli* research. It shows two primary clusters: one associated with the Department of Pediatrics and the other with the Department of Internal Medicine. The red cluster represents the Department of Pediatrics, showing connections between various pediatric institutions, indicating active collaboration within this field. The green cluster represents the Department of Internal Medicine, with strong links between internal medicine departments, reflecting a focus on the clinical and medical aspects of ESBL-producing *E. coli*. The lines connecting the two clusters suggest some co-authorship between the pediatrics and internal medicine departments, although the collaboration is relatively limited compared to intra-departmental connections.

Author Impact Analysis

Table 2 summarizes the top 10 authors in ESBL-producing *E. coli* research, based on publication count and H-index. NORDMANN P ranks first with 43 articles and an H-index of 25, indicating both high productivity and strong citation impact. WOODFORD N (31 articles; H-index 24), RODRÍGUEZ-BAÑO J and JONES RN (30 articles; H-indices 23 and 22), together with LIVERMORE DM, PASCUAL A, and POIREL L (29 articles each; H-indices 20–22), represent core contributors to the field. SADER HS, DOI Y (28 publications each), and CANTÓN R (26 publications) also show substantial influence. Collectively, these authors have played a central role in shaping current understanding of ESBL-producing *E. coli* through both volume and impact of their work.

Researchers' collaborative relationships are visualized in Supplementary Figure S3 (Supplementary Figure link: <https://tinyurl.com/ya2nrfdn>). Each node represents an author (node size = number of publications), while colors indicate collaboration clusters and edges represent co-authorship strength. Central nodes—such as NORDMANN P, WOODFORD N, and BONOMO R.A.—form dense clusters, reflecting frequent collaboration and leadership in the network. Smaller peripheral clusters (e.g., involving KO WEN-CHIEN and JEAN SHIO-SHIN) suggest more specialized or regionally focused teams. Overall, this network highlights the global and collaborative nature of ESBL-producing *E. coli* research and the pivotal role of a relatively small group of highly connected authors.

Table 2. Author Impact Analysis

No.	Author	Articles	H-index
1.	NORDMANN P	43	25
2.	WOODFORD N	31	24
3.	RODRÍGUEZ-BAÑO J	30	23
4.	JONES RN	30	22
5.	LIVERMORE DM	29	22
6.	PASCUAL A	29	21
7.	POIREL L	29	20
8.	SADER HS	28	19
9.	DOI Y	28	18
10.	CANTÓN R	26	17

Most cited publications

The influence of articles within this field can be assessed by examining their citation counts. In Table S1 (Supplementary Table link: <https://tinyurl.com/yvr6yvf5>), we summarize the 10 most frequently cited publications. Among them, a 2001 study titled “Extended-Spectrum β -Lactamase–Producing *Escherichia coli* and *Klebsiella pneumoniae*: Risk Factors for Infection and Impact of Resistance on Outcomes” included 33 patients with infections caused by ESBL-producing *E. coli* or *K. pneumoniae*; 25 (75.8%) cases were attributed to *K. pneumoniae* and 8 (24.2%) to *E. coli*. Reported infection sites were the urinary tract in 17 patients (51.5%), wounds in 5 (15.2%), central venous catheters in 4 (12.1%), bloodstream in 3 (9.1%), respiratory tract in 3 (9.1%), and abdomen in 1 (3.0%) (Lautenbach et al., 2001). Another highly cited article published in 2021 demonstrated that, in the United States, the incidence of ESBL-producing Enterobacterales isolated from clinical cultures rose by approximately 53% between 2012 and 2017 (Tamma et al., 2022). Together, these influential articles illustrate how ESBL-producing *E. coli* has emerged as a critical public health concern, reinforcing the importance of ongoing research to guide prevention, diagnosis, and management strategies.

Analysis of keywords

Figure S4A (Supplementary Figure; link: <https://tinyurl.com/ya2nrfdn>) shows the keyword co-occurrence network, where node size reflects frequency and edge thickness indicates how often terms appear together. Central keywords such as *Escherichia coli*, *Enterobacteriaceae*, carbapenemase, infection, colonization, risk factors, prevalence, and virulence form the core, emphasizing the main focus on epidemiology, clinical outcomes, and resistance mechanisms. Surrounding clusters include resistance genes and plasmids, key antimicrobials (e.g., ceftazidime–avibactam, fosfomicin, piperacillin–tazobactam), and clinical conditions (surgical site infection, bacteremia, community-onset and nosocomial infection), illustrating how the field connects microbiology, clinical epidemiology, and therapy. Figure S4B (Supplementary Figure; link: <https://tinyurl.com/ya2nrfdn>) displays the network as a temporal overlay, with colors indicating the average publication year. Core concepts (e.g., *E. coli*, *Enterobacteriaceae*, carbapenemase, infection, colonization) appear in intermediate colors, suggesting sustained interest over time, whereas peripheral keywords related to novel drugs, emerging resistance determinants, and community or fecal carriage appear in warmer colors, indicating more recent attention. This pattern reflects a shift from foundational ESBL/Enterobacterales epidemiology toward advanced treatment options, detailed resistance mechanisms, and community transmission. Figure 4 illustrates topic evolution over time: older antimicrobials (trovafloxacin, cefaloridine, cefodizime, monobactam) show brief, earlier peaks, mainly in the late 1990s–mid 2000s, while methodological and clinical concepts (e.g., isoelectric focusing, RT-PCR, dilution, *Enterobacter* infection, *Bacteroides vulgatus*) display longer, higher-frequency trajectories into the late 2000s and 2010s. Overall, the timeline suggests a transition from short-lived interest in specific older drugs toward more durable methodological and clinically oriented themes that continue to shape ESBL-related research.

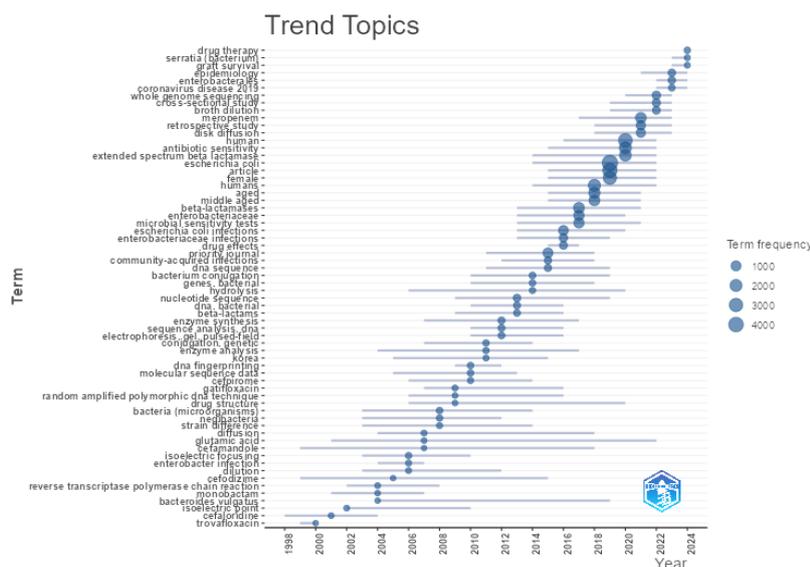


Figure 4. Trend Topics

Discussion

This bibliometric analysis shows that research on ESBL-producing *E. coli* in healthcare settings has expanded sharply over the past two decades, mirroring global AMR trends.^{11,12} Annual publication output rises steeply after 2010, in line with earlier estimates of high annual growth in AMR-related fields ($\approx 20\%$ per year).¹¹ This acceleration reflects epidemiological realities: by the 2010s, ESBL-producing organisms had become a major public health challenge in both hospital and community settings.^{13,14} The rapid global dissemination of CTX-M-type β -lactamases transformed *E. coli* into the principal ESBL reservoir,^{15,16} with CTX-M enzymes—almost absent in the 1990s—now the most widespread ESBL variants, supplanting TEM and SHV in both healthcare and community isolates.¹⁷ This shift, repeatedly documented in molecular epidemiology studies,¹⁸ is mirrored in our thematic patterns, which move from early enzyme-focused work toward transmission, high-risk clones, and complex resistance profiles.

Research output is dominated by high-income countries, particularly the United States and Western Europe, with strong and growing contributions from Asia. The U.S. is the most prolific contributor in our dataset, in line with prior AMR bibliometrics showing U.S. leadership in uropathogen-AMR and MRSA bacteremia research.^{19,20} China ranks second and has expanded rapidly, a recurrent finding in AMR studies—including food-animal and polymyxin-resistance research—where Chinese output is increasing faster than that of many Western nations.^{19,21,22} Western European countries (e.g. the UK, Germany, France) also rank among the top producers,²² reflecting both local disease burden (e.g. $>5,000$ ESBL *E. coli* bacteremias annually in the UK)²³ and substantial AMR investment. Similar to WHO-priority-pathogen analyses,¹⁹ we also found substantial contributions from India and Iran, consistent with high ESBL prevalence and strong academic centers. Nevertheless, countries in Africa and parts of Asia with high ESBL *E. coli* incidence remain under-represented in the literature,²⁴ highlighting the “10/90 gap,” where most research is produced in wealthier settings despite a global one-health problem.²⁵ Emerging contributions from China, India, Brazil and increased cross-national projects suggest this imbalance is beginning to narrow.^{19,22}

Co-authorship patterns indicate moderate but increasing international collaboration. Many prolific authors are based in North America, Europe, and East Asia and cluster within regional networks, consistent with other AMR bibliometrics where North America and Europe form the core of global research collaboration.²⁶ For example, Wang et al. showed that international cooperation in thrombosis research is concentrated in these regions,²⁶ and Sweileh et al. reported “inadequate” cross-regional collaboration in environmental AMR research.²⁷ We observe similar structures: cross-country collaborations are frequent among high-output countries but many groups still publish largely within domestic or regional consortia. Germany is a notable exception, showing a strong inclination toward international collaboration in infectious-disease bibliometrics²² and in our ESBL network. Increasing numbers of large multicenter studies and surveillance networks (e.g. GLASS, transatlantic AMR initiatives)^{20,27} underscore the need for coordinated global responses and are often highly cited.²⁰ The rise of China in this field also appears linked to partnerships with Western institutions,¹⁸ illustrating how networking can accelerate output and impact. The mean of ≈ 5 –6 authors per article in our dataset is similar to that reported for uropathogen-AMR literature (mean 5.3),¹⁹ indicating that multidisciplinary, multi-institution teams are now standard. A small subset of well-known antibiotic-resistance experts (including authors from Japan and Europe) act as “knowledge hubs,” as seen in co-authorship and co-citation networks,¹⁹ which likely helps shape research agendas but also highlights the underrepresentation of investigators from some high-burden low-income settings.

The ESBL-producing *E. coli* literature is spread across nearly 200 journals, yet a relatively small group of high-impact titles accounts for much of the influential work, consistent with Bradford's law.²² Journals such as *Antimicrobial Agents and Chemotherapy*, *Journal of Antimicrobial Chemotherapy*, *Clinical Infectious Diseases*, *PLOS ONE*, and *Applied and Environmental Microbiology* appear repeatedly as key outlets in AMR bibliometric surveys and in our dataset,^{27,28} and many are Q1 journals.²⁸ This concentration suggests that publication in top-tier venues has been crucial for shaping discourse around ESBL-producing *E. coli*. Within this corpus, landmark works include highly cited early reviews—such as Bradford's 2001 *Clinical Microbiology Reviews* article on ESBLs²⁹ and Rossolini et al.'s 2008 synthesis of CTX-M dissemination³⁰—which remain central references and anchor much of the later literature. More focused clinical studies, although less cited overall, have produced important paradigm shifts. The citation “bursts” following these trials illustrate how practice-changing evidence can quickly reshape both clinical management and research priorities.

Conclusion and Suggestion

This bibliometric analysis shows that research on ESBL-producing *E. coli* in healthcare settings has grown rapidly, is dominated by high-income countries and a small group of influential institutions and authors, and has shifted thematically from enzyme-focused work toward high-risk clones, carbapenemase co-production, advanced therapies, and One Health perspectives. Despite increasingly dense international collaboration, many high-burden low- and middle-income regions remain underrepresented, and clinical, microbiological, and genomic data are still not consistently integrated. Future efforts should strengthen research capacity and output in under-studied high-burden settings, promote multicenter and international consortia, expand One Health-oriented and outcome-focused studies, and align research priorities with antimicrobial stewardship and infection-prevention policies to more effectively address

the growing clinical and public health threat of ESBL-producing *E. coli* in healthcare environments.

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