Systematic Review

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Whole Genome Sequencing of ESBL Producing *Klebsiella pneumoniae*: Systematic Literature Review

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Data Collection. Final approval of the version to be published/Supervision Drafting the work or revising it critically for important intellectual content,. [3,4,5,6]Active participation in active methodology

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ABSTRACT

Objective: It was aimed to conduct a thorough and systematic examination of the available literature referring to the importance of incorporating Whole genome sequencing in interpreting and assessing the genetic structure of ESBL producing Klebsiella pneumoniae.

Methodology: This systematic literature search was conducted across multiple databases, mainly including PubMed, Scopus and Web of Science focusing on antimicrobial resistance and genomics.

Results: The review amalgamates an extensive range of research studies, hedging into the genetic determinants, evolutionary patterns, and dissemination mechanisms of Extended spectrum beta lactamase producing Klebsiella pneumoniae from across the globe. Conscientious and careful examination of the relevant studies included in this systematic literature review, together intend to enlighten the thoroughness of comprehension provided by Whole genome sequencing in straightening out the foundations of genetics of ESBL producing Klebsiella pneumoniae. It endeavors to characterize its identified genes responsible for resistance, mutations, mobile genetic elements and the factors associated with dissemination of its resistance traits.

Conclusion: This systematic literature review compiles together and provides not only with a valuable summary of the key factors involved in the understanding of the crucial elements, complex interaction and entangled dynamics of the genetic elements connected with antimicrobial resistance, but also supplements the efforts being carried out globally to combat antimicrobial resistance associated in particular with ESBL producing Klebsiella pneumoniae for effective infection prevention and control.

Keywords: Antimicrobial resistance, ESBL, Klebsiella pneumoniae, Whole genome sequencing (WGS).

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Introduction

One of the "ESKAPE" pathogens, *Klebsiella pneumoniae*,[1] an important opportunistic pathogen, can also be found as a part of the intestinal flora[2] and its capability to offer resistance against different classes of antibiotics, underlies the increased virulence and the associated severity of the disease.[2] Detection of multidrug resistance, is of crucial importance, particularly in countries with excessive use of antibiotics and deficient infection control measures.[3] Recently, published global priority list of antibiotic resistant bacteria by WHO, where ESBL producing *Klebsiella pneumoniae* and others, were included in the Priority 1 group.[4] Research shows that multidrug-resistant *Klebsiella pneumoniae* is mostly an oligoclonal population with the exception of a few epidemic/endemic clones.[5]

Spreading of *Klebsiella pneumoniae* has become a major public health problem especially after the emergence of multi-drug resistant isolates,[6] Most commonly due to extended-spectrum beta-lactamases (ESBLs), enzymes encoded by plasmids and hydrolyze beta lactam ring[2] thus making KP ESBL as one of the critical pathogens that need an urgent need of developing new antibiotics.[7]

The fast advancement of whole-genome sequencing (WGS) allows for a more precise analysis of the population structure of multidrug resistant pathogens.[8] The capacity to identify infected or colonized patients early on and to follow them is critical for effective management and prevention of the spread of multidrug resistant infections in healthcare settings.[8] This becomes much more problematic in the setting of an epidemic, when patient to patient transmissions might be facilitated by extra reservoirs such as healthcare personnel and the environment and when many cities / institutions are affected.

During the last decades, the selective pressure exerted by misuse of antibiotics has given rise to highly resistant bacterial species, with limited treatment options,[9] and Whole genome sequencing (WGS) is a powerful approach for investigating transmission of AMR in HAIs to effectively detect and contain transmission of AMR pathogens.[10]

Methodology

The systematic literature review was carried out using electronic databases such as PubMed, Scopus, Web of Science, Google scholar and journals in the field of Microbiology, infectious diseases, antimicrobial resistance, and genomics. The search strategy utilized combination MESH words related to "ESBL producing *Klebsiella pneumoniae*," and "whole genome sequencing

All the original articles, reviews and meta analyses focusing on the utilization of WGS in understanding the resistance mechanisms involved in the production of ESBL producing *Klebsiella pneumoniae* strains, were included. On the contrary all the studies lacking detailed information on WGS data, publications other than those in English and those unrelated were excluded.

PubMed, Scopus and Web of Science focusing on genomics and antimicrobial resistance were mainly used in this systematic search including the relevant articles published within the designated period i.e. from 2019-2025.

Data extraction involved systematically restoring and assembling the retrieved information from selected articles which were found relevant. Essential components for data collection surrounded attributes mainly including source of infections, period of study, and geographical location. WGS methodologies adopted were those that identified mutations, resistance genes and mobile genetic elements associated with extended spectrum beta lactamase resistance in *Klebsiella pneumoniae*. Methods used for data analysis necessitated the phenomenological synthesis of the data extracted identifying common characteristics, patterns followed and trends seen across studies.

Results

After removal of the duplicate and other irrelevant studies a total of 753 studies were identified during the process, a total of 18 met the criteria and were finally included in the study (Figure 1) including the articles published from 2019 to 2025. Main characteristics of how the studies were selected to be included in this systematic literature review are summarized in Table 1.

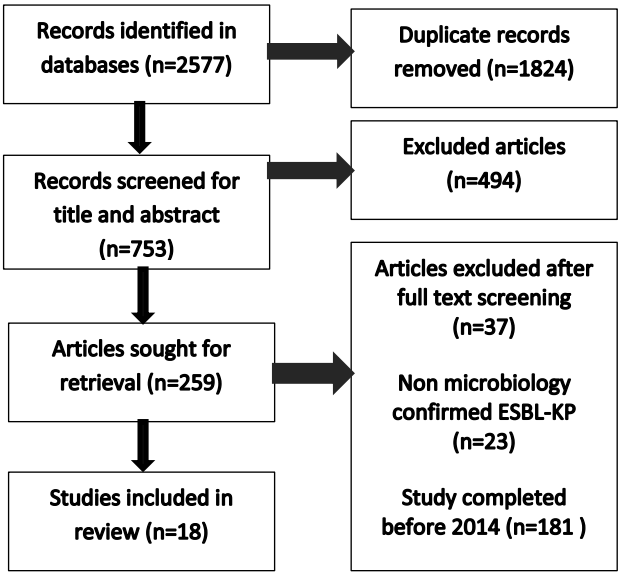

Figure 1. Study selection flow chart.

Discussion

The merger of findings from diverse literature reviews, underscores the crucial role of Whole Genome Sequencing (WGS) in comprehensively understanding ESBL producing *Klebsiella pneumoniae*. The diverse genomic landscape observed within KP ESBL populations, as revealed by these studies, illuminates the intricate evolutionary trajectories and the mosaic nature

Table I: Characteristics and Results of the studies included.

First author and year	Country	Source of infection	Sample size	Results	References
Sumbana JJ, 2023	Mozambique	Blood, pus and cerebrospinal fluid (CSF).	35	*bla* CTX-M-15, *bla* SHV, *bla* TEM-1	11
Mejía-Limones I, 2024	Guayaquil, Ecuador	Blood, urine and peritoneal fluid	14	*bla* SHV-*145*, *bla* TEM-1, *bla* SHV-*101 bla* SHV-11, *bla* CTX-M-12, *bla* KPC-2, *bla* SHV-110, *bla* SHV-106,	12
Flores-Valdez M, 2021	Mexico	Blood	50	*bla* SHV, *bla* TEM *and bla* CTX-M	13
Founou RC, 2019	KwaZulu-Natal, South Africa	Rectal swabs and clinical samples	09	*bla* CTX-M-15 , *bla* TEM-1b, *bla* SHV-1	14
Pustam A, 2024	Trinidad, West Indies	--	10	*bla* CTX-M-15, *bla*TEM-1B, *bla* SHV-28	15
Chen C, 2024.	China	Sputum and broncho alveolar lavage fluid	02	*bla* TEM-1B and *bla* CTX-M-3	16
Sheng J, 2023	Armenia	--	01	*bla* CTX-M-15 *and bla* SHV-27	17
Byarugaba DK, 2023	Uganda	Pus, urine, sputum, wound, blood, high vaginal swabs, endocervical swabs and medical device	69	*bla* CTX-M-15	18
Hetsa BA, 2024	South Africa	Blood	10	ST25, ST101, ST985, ST17, ST15, ST152. *bla* CTX-M-15, *bla* TEM-1B, *bla* SHV	19
de Sales RO, 2022	Asia, North America, Europe, South America, Oceania, Africa and Central America	--	957	ST 16 *bla* SHV-1, *bla* CTX-M-15 and *bla* TEM-1	20
Jin M, 2023	Beijing, China	Blood, ascites, abscess drainage, biliary tract fluid, pleural fluid, and broncho-alveolar lavage aspirate	203	CTX-M14, 15, 3, 27, 65, 9 SHV-1,101,106,107, 109, 11,110, ,134,172,,155,182,187,190,2,207,208, 215, 217,223, 26, 27, 33, 37, 62, 7580. TEM-181	21
Fostervold A, 2022	Norway	Blood, urine	201	ST14, ST15 and ST627 CTX-M-15;SHV-5 CTX-M-15 CTX-M-1 *bla*TEM-3, *bla* SHV	22
Wyres KL, 2019	UK, USA, Nepal, Thailand, Italy, Columbia, Australia Camcodia, Norway, Netherlands, Iran	Blood, urine, respiratory, rectal, catheter and tissue	95	ST307, *bla* CTX-M-15	23
Abdelwahab R, 2021	Egypt	Stool	01	KPE 16, *bla* SHV-40, *bla*TEM-1B and *bla* CTX-M-15)	24
Wang M, 2022	China, Turkey, Nepal, Switzerland, Lebanon, USA, United Kingdom, Thailand, Italy Turkey, Croatia, Slovakia, Netherlands, Portugal, USA: Ohio, Nigeria Hungary, Belgium, Japan, France	Secreta rectum, Sputum, swab, urine, sputum Lower Respiratory Tract Secretion, Blood, Tracheal aspiration, wound Drainage of fluid, feces, Wound Secretion	73	ST15, *bla* CTX-M-15	25
Sabença C, 2025	Portugal	Blood stream infections (BSIs)	14	*bla* CTX-M-**15,** *bla*TEM-1, *bla* SHV-28, *bla* SHV-26	26
Rahmani A, 2023	Algeria	Urinary tract infections, hemoculture and pus	04	*bla* TEM, *bla* SHV, *bla* CTX-M, aac(6')-Ib-cr,	27
Adamu S, 2025	Malaysia	Urine, blood, sputum, pus, gastric and tracheal aspi rates	06	*bla* CTX-M-15_23, *bla* CTX-M-55, blaSHV-1_22, *bla* SHV11_18, *bla* SHV-11, *bla* SHV-1_1.1, *bla* SHV-11_3, *bla* SHV-11_19, *bla* TEM-1_1, *bla* TEM-1_5	28

of resistance mechanisms. This diversity poses significant challenges in controlling and treating infections within healthcare settings. The identification of specific resistance determinants, including those located on mobile genetic elements, emphasizes the critical importance of WGS in pinpointing genetic factors driving resistance emergence and dissemination.

Elucidation of the mechanisms of acquired AMR genes and genes associated with virulence and the genomic diversity among the MDR and XDR isolates would help better understand their dissemination patterns in the regions. This is because of the continuous evolutionary mechanisms required to survive in harsh environments, and they have been spreading globally since long.[24.]

Available evidence of the high prevalence of antimicrobial resistance, particularly in the developing countries, like Pakistan, stresses upon the conduction of studies on the genomic characterization of diverse antimicrobial resistance determinants and genetic back ground of ESBL producing Klebsiella pneumoniae in healthcare setting.

Conclusion

In conclusion, Whole Genome Sequencing (WGS) stands as a pivotal tool in deciphering the intricate complexities of extended spectrum beta lactamase producing Klebsiella pneumoniae. WGS not only identifies specific genetic elements driving resistance but also provides nuanced understandings of how resistance evolves. Despite its promise in tailoring infection control and therapeutic approaches, the integration of WGS insights into clinical practice necessitates ongoing refinement and adaptability to effectively address the associated challenges.

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