RESEARCH ARTICLE

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Genomic Resistome of Multidrug-Resistant *Klebsiella pneumoniae* Bloodstream Infections in Iraqi Cancer Patients

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Abstract

Background: Multidrug-resistant (MDR) *Klebsiella pneumoniae* is an important cause of bloodstream infection (BSI) in cancer patients, particularly those with haematological malignancies, where delayed or inappropriate therapy is associated with high mortality. Genomic data on resistance mechanisms in oncology settings in Iraq remain limited. This study aimed to characterise, using whole-genome sequencing, the antibiotic resistance determinants of MDR K. pneumoniae bloodstream isolates from cancer patients and to explore their potential implications for empirical treatment strategies in this high-risk population. **Methods:** This genomic substudy was nested within a prospective multi-centre cohort of cancer patients with bloodstream infection at oncology hospitals in Baghdad. Adult patients with haematological malignancies and solid tumours with monomicrobial MDR K. pneumoniae infection were included. Identification and antimicrobial susceptibility testing were performed using the VITEK 2 system and interpreted according to Clinical and Laboratory Standards Institute standards. MDR was defined as non-susceptibility to at least three antibiotic classes. Whole-genome sequencing was performed using an Illumina platform. Resistance genes were identified using curated databases and grouped into β-lactamase/carbapenemase, non-β-lactam, and efflux/regulatory categories. Clinical data (age, sex, and malignancy type) were extracted from medical records. **Results:** Thirty-five MDR K. pneumoniae bloodstream isolates were analysed, with most infections occurring in patients with haematological malignancies (30/35, 85.7%). Detected resistance genes included CTX-M-type extended-spectrum β-lactamases (including CTX-M-15), SHV and TEM enzymes, and OXA-48-like carbapenemases (OXA-48 and OXA-232). Non-β-lactam resistance determinants (aadA, EreA, Mph(A), Mrx, sul1, sulI) and efflux-related genes were also identified. **Conclusions:** MDR K. pneumoniae bloodstream infections in this cohort were predominantly observed in patients with haematological malignancies. Whole-genome sequencing identified multiple resistance determinants. These findings provide genomic insights that may help explain resistance patterns in this setting and support the need for strengthened infection prevention and locally tailored antimicrobial stewardship strategies.

Keywords: *Klebsiella pneumoniae*, multidrug resistance, whole-genome sequencing, bloodstream infection

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Introduction

Multidrug-resistant (MDR) *Klebsiella pneumoniae* bloodstream infections (BSIs) are a major cause of healthcare-associated infections worldwide and contributes substantially to the global burden of antimicrobial resistance (AMR), particularly in vulnerable populations such as immunocompromised and oncology patients [1, 2]. Recent global surveillance reports continue to highlight the high burden of *Klebsiella pneumoniae* infections among immunocompromised and oncology populations, with increasing rates of antimicrobial resistance reported in 2024–2025. In the 2024 World Health Organization (WHO) bacterial priority pathogens

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list, carbapenem-resistant K. pneumoniae is classified as a critical priority pathogen due to its rapid dissemination, limited therapeutic options, and association with severe clinical outcomes [1]. Multidrug-resistant (MDR) K. pneumoniae commonly harbours resistance determinants across multiple major antibiotic classes, compounding the clinical challenge in bloodstream infection (BSI), defined as the presence of viable bacteria in the bloodstream confirmed by positive blood cultures [2, 3].

In patients with haematological malignancies and solid tumours, BSIs caused by K. pneumoniae are of particular concern due to prolonged neutropenia, intensive chemotherapy, and frequent invasive procedures. Cohort studies have shown that carbapenem-resistant K. pneumoniae (CRKP) BSIs in this population are associated with high early mortality, often exceeding 40–50%, as well as prolonged hospitalisation and increased healthcare costs [4-8]. Delayed or inappropriate initial therapy has been identified as an independent predictor of mortality, underscoring the importance of understanding local resistance patterns to guide empirical and targeted treatment [5, 6].

The MDR phenotype in K. pneumoniae is driven by a combination of plasmid-encoded and chromosomal mechanisms. Extended-spectrum β-lactamases (ESBLs), including common families such as CTX-M, SHV, and TEM, are widely disseminated and confer resistance to third-generation cephalosporins [3]. Regional data from Iraq and neighbouring countries report a high prevalence of ESBL-producing K. pneumoniae, with bla_CTX-M, bla_SHV, and bla_TEM among the most frequently detected genes [9]. In parallel, carbapenem resistance is increasingly reported to be mediated by OXA-48-like and NDM metallo-β-lactamases in Middle Eastern healthcare settings, including Iraqi tertiary hospitals, often carried on mobile genetic elements that facilitate rapid spread [9, 10]. These β-lactamase genes frequently coexist with additional resistance determinants and efflux systems, contributing to complex multidrug-resistant phenotypes [4, 9 ,10].

Whole-genome sequencing (WGS) has emerged as a powerful tool for characterising the resistome of MDR K. pneumoniae, enabling simultaneous identification of β-lactamases, carbapenemases, non-β-lactam resistance genes, and efflux-associated mechanisms [2, 3]. Studies using WGS have demonstrated that bloodstream isolates often harbour diverse combinations of resistance determinants, reflecting substantial genomic plasticity and adaptation under antimicrobial pressure [2, 3, 11, 12]. These findings highlight the importance of context-specific genomic surveillance in high-risk populations such as cancer patients.

Despite the growing recognition of MDR K. pneumoniae as a critical pathogen in oncology care, genomic data from cancer patients in low- and middle-income settings, including Iraq, remain limited. Most existing studies have focused on phenotypic susceptibility profiles or a restricted set of resistance genes, with limited insight into the broader resistome of bloodstream isolates from oncology settings [9, 10]. Most genomic studies from the Middle East have focused on general hospital or mixed patient populations, with limited emphasis on oncology-specific cohorts, where risk factors, antimicrobial exposure, and clinical trajectories may differ substantially.

To address this specific gap in oncology-focused genomic data from the region, the present study uses whole-genome sequencing to characterise the resistome of MDR K. pneumoniae bloodstream isolates in cancer patients and to evaluate their implications for antimicrobial therapy and stewardship in this high-risk population. While other ESKAPE pathogens also contribute to antimicrobial resistance in oncology settings, this study focused specifically on *Klebsiella pneumoniae* due to its high prevalence and clinical significance in bloodstream infections within the study centres.

Materials and Methods

Study design and setting

This study was a nested substudy within a prospective, multi-centre observational investigation of bacterial bloodstream infections among cancer patients in Iraq. The parent study was conducted at three tertiary oncology centres in Baghdad including Oncology Teaching Hospital Baghdad , Alamal National Hospital for Cancer Treatment, and Medical Complex city that specialise in the management of solid and haematological malignancies. Laboratory procedures across all sites were standardised through shared protocols aligned with Clinical and Laboratory Standards Institute (CLSI) guidance for antimicrobial susceptibility testing, with regular cross-site calibration and adherence monitoring [13, 14].

Study population and period

The source population comprised all patients with a confirmed diagnosis of cancer who underwent blood culture testing at the three participating centres between 1 January 2024 and 1 March 2025. A bloodstream infection (BSI) episode was defined as the first positive blood culture yielding a clinically significant pathogen for each patient during the study period. For patients with multiple positive cultures, only the first episode was included to avoid duplication and to reflect the initial resistance phenotype.

The present analysis included adult patients with monomicrobial BSI due to *Klebsiella pneumoniae* in whom the index isolate fulfilled the definition of multidrug resistance and whole-genome sequencing (WGS) data were available. All included cases therefore shared a common clinical and microbiological profile, comprising adult cancer patients with monomicrobial bloodstream infection due to multidrug-resistant *Klebsiella pneumoniae*, ensuring a clinically homogeneous high-risk cohort for genomic analysis.

Inclusion and exclusion criteria

During the study period, all cancer patients with positive blood cultures at the participating centres were screened. Isolates identified as *Klebsiella pneumoniae* were evaluated for antimicrobial susceptibility, and those meeting the multidrug-resistant (MDR) definition were considered eligible. Inclusion criteria comprised adult

patients with histologically or clinically confirmed solid tumours or haematological malignancies, at any stage, with at least one positive blood culture yielding K. pneumoniae. Only non-duplicate bloodstream isolates (first episode per patient) were included.

Exclusion criteria included polymicrobial cultures, isolates considered contaminants by treating clinicians and microbiology teams, and cases with incomplete clinical or microbiological data precluding confirmation of MDR status or whole-genome sequencing analysis. After applying these criteria, a total of 35 MDR K. pneumoniae bloodstream isolates were included in the final analysis.

Sampling strategy and sample size

The parent cohort used convenience sampling and included all eligible cancer patients with positive blood cultures during the study period. A total of cancer patients with positive blood cultures were screened, yielding K. pneumoniae bloodstream isolates, of which were classified as multidrug-resistant. All MDR K. pneumoniae isolates with successful sequencing (n = 35) were included in this substudy.

Microbiological procedures

Blood culture processing and organism identification

Blood cultures were obtained as part of routine clinical care and processed according to standard microbiological protocols at each site. Positive cultures were subcultured onto appropriate media, and isolates were identified using conventional biochemical methods and the automated VITEK 2 system (bioMérieux, France) [15].

Antimicrobial susceptibility testing and MDR definition

Antimicrobial susceptibility testing (AST) was performed using the VITEK 2 system and interpreted according to CLSI M100 standards [13]. Multidrug resistance was defined as non-susceptibility to at least one agent in three or more antimicrobial classes, in accordance with established international criteria [16]. Only MDR K. pneumoniae isolates were included in the genomic analysis.

Whole-genome sequencing and bioinformatic analysis

Genomic DNA was extracted from overnight bacterial cultures using a standardised commercial extraction kit (e.g., Qiagen DNeasy Blood & Tissue Kit) following manufacturer protocols. DNA concentration and purity were assessed prior to library preparation.

Whole-genome libraries were prepared using the Illumina DNA Prep kit and sequenced on an Illumina platform (e.g., MiSeq/NextSeq) using paired-end reads (e.g., 2 × 150 bp) with a target coverage of ≥30×.

Raw sequencing reads underwent quality control using tools such as FastQC and trimming using Trimmomatic. Reads were assembled using a standard de novo assembly pipeline (e.g., SPAdes).

Antimicrobial resistance genes were identified using curated databases (e.g., ResFinder/CARD; specify database and version if available) with predefined identity and coverage thresholds (e.g., ≥90% identity and ≥60% coverage).

To focus on clinically relevant resistance mechanisms, outputs were filtered to retain genes associated with antimicrobial resistance, including β-lactamases, carbapenemases, non-β-lactam resistance determinants, and efflux-related genes. Identified genes were subsequently grouped into functional categories comprising β-lactamase and carbapenemase genes, non-β-lactam resistance genes, and efflux pump and regulatory systems, which formed the basis of the resistance gene analyses presented in the Results. The analysis was deliberately restricted to antimicrobial resistance determinants to align with the primary objective of characterising resistance mechanisms relevant to the clinical management of bloodstream infections. Virulence factors and plasmid replicon profiling were not systematically analysed, as these were beyond the predefined scope of the genomic investigation.

Clinical data collection

Clinical and demographic data were extracted from medical records using a standardised case-report form. Variables included age, sex, underlying malignancy type (solid vs haematological), cancer subtype, and relevant clinical characteristics at the time of BSI.

Statistical analysis

Descriptive analyses were performed to summarise clinical characteristics and genomic findings. Categorical variables were reported as frequencies and percentages, while continuous variables were summarised using means (standard deviation) or medians (interquartile range), depending on distribution.

Given the absence of a susceptible comparator group, analyses focused on describing the distribution and functional classification of resistance determinants rather than hypothesis testing. Statistical analyses were conducted using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA) [17].

Results

Clinical characteristics of patients with MDR Klebsiella pneumoniae bloodstream infection

A total of 35 patients with multidrug-resistant (MDR) *Klebsiella pneumoniae* bloodstream infections were included in the analysis (Table 1). Most infections occurred in patients with haematological malignancies (30/35, 85.7%). The most frequent subtypes were acute myeloid leukaemia (AML; 11/35, 31.4%), acute lymphoblastic leukaemia (ALL; 8/35, 22.9%) and non-Hodgkin lymphoma (NHL; 6/35, 17.1%). Smaller numbers of cases were observed in myelodysplastic syndromes (MDS; 2/35, 5.7%), chronic myelogenous leukaemia (CML; 2/35, 5.7%) and aplastic anaemia (1/35, 2.9%), which was included as a non-malignant haematological condition managed within the same oncology care pathway. Five patients (5/35, 14.3%) had solid tumours, including breast cancer (4/35, 11.4%) and pancreatic cancer (1/35, 2.9%).

Table 1. Baseline Characteristics of Participants with *Klebsiella pneumonia* -Positive Bloodstream Infections, Stratified by Resistance Status

Resistance Status	Total *Pseudomonas aeruginosa* Isolates (n)	Hematological Cancer n (%)	Solid Cancer n (%)	Main Hematological Subtypes n (%)	Main Solid Cancer Subtypes n (%)
MDR (Resistant)	35	30	5	AML: 11 ALL: 8 NHL: 6 MDS: 2 CML: 2 Aplastic anemia: 1	Breast: 4 Pancreatic: 1

AML, Acute Myeloid Leukemia; ALL, Acute Lymphoblastic Leukemia; NHL, Non-Hodgkin Lymphoma; MDS, Myelodysplastic Syndromes; CML, Chronic myelogenous leukemia

Table 2. β-lactamase and Carbapenemase Genes Detected among Multidrug-Resistant *Klebsiella pneumoniae* Bloodstream Isolates

Gene / gene family	Product (annotation)	Classification
CTX-M family	Class A β-lactamase (EC 3.5.2.6), CTX-M family, extended spectrum	Extended-spectrum β-lactamase (ESBL); antibiotic inactivation enzyme
CTX-M-15	Class A β-lactamase (EC 3.5.2.6), CTX-M family, extended spectrum	Extended-spectrum β-lactamase (ESBL); antibiotic inactivation enzyme; β-lactam resistance gene
SHV family	Class A β-lactamase (EC 3.5.2.6), SHV family	β-lactamase; antibiotic inactivation enzyme
SHV-11	Class A β-lactamase (EC 3.5.2.6), SHV family	β-lactamase; antibiotic inactivation enzyme; β-lactam resistance gene
TEM family	Class A β-lactamase (EC 3.5.2.6), TEM family	β-lactamase; antibiotic inactivation enzyme
TEM-1	Class A β-lactamase (EC 3.5.2.6), TEM family	β-lactamase; antibiotic inactivation enzyme; β-lactam resistance gene
OXA-48 family	Class D β-lactamase (EC 3.5.2.6), OXA-48 family	Carbapenem-hydrolysing class D β-lactamase (CHDL); antibiotic inactivation enzyme
OXA-48	Class D β-lactamase (EC 3.5.2.6), OXA-48 family	Carbapenem-hydrolysing class D β-lactamase (CHDL); antibiotic inactivation enzyme; β-lactam resistance gene
OXA-232	Class D β-lactamase (EC 3.5.2.6), OXA-48 family	Carbapenem-hydrolysing class D β-lactamase (CHDL); antibiotic inactivation enzyme; β-lactam resistance gene

EC, Enzyme Commission number: an internationally standardised numerical classification that groups enzymes according to the specific chemical reactions they catalyse.

Genomic profile of β-lactamase and carbapenemase determinants

Whole-genome sequencing identified multiple β-lactamase genes among MDR *Klebsiella pneumoniae* bloodstream isolates (Table 2). Extended-spectrum β-lactamase (ESBL) genes of the CTX-M family were detected, including CTX-M-15. SHV and TEM family β-lactamases, including SHV-11 and TEM-1, were also identified.

Carbapenemase genes of the OXA-48 family were detected, including OXA-48 and OXA-232.

Non-β-lactam resistance determinants

Non-β-lactam resistance genes were identified among the MDR K. pneumoniae bloodstream isolates (Table 3). Aminoglycoside resistance genes included aadA. Macrolide-associated genes included EreA, Mph(A), and Mrx. Sulfonamide resistance genes included

Table 3. Non-β-lactam Antibiotic Resistance Genes Detected among Multidrug-Resistant *Klebsiella pneumoniae* Bloodstream Isolates

Gene / gene family	Product (annotation)	Classification
aadA	Aminoglycoside 3″-nucleotidyltransferase (EC 2.7.7.-) → ANT(3″)-Ia (AadA family)	Aminoglycoside resistance gene; antibiotic inactivation enzyme
EreA family	Erythromycin esterase (EC 3.1.1.-) → EreA family	Antibiotic inactivation enzyme
Mph(A) family	Macrolide 2′-phosphotransferase → Mph(A) family	Antibiotic inactivation enzyme; macrolide resistance gene
Mrx	Hypothetical protein	Antibiotic inactivation enzyme; macrolide resistance gene
sul1	Dihydropteroate synthase type-2 (EC 2.5.1.15) @ sulfonamide resistance protein	Antibiotic target replacement protein; sulfonamide resistance gene
sulI	Dihydropteroate synthase type-2 (EC 2.5.1.15) @ sulfonamide resistance protein	Drug target (sulfacetamide)

sul1 and sulI.

Efflux pump and regulatory resistance determinants

Multiple efflux pump systems and regulatory genes were identified across isolates (Table 4). Resistance–nodulation–division (RND) transporters included AcrAB-TolC, AcrAD-TolC, AcrEF-TolC, and MdtABC-TolC. Additional efflux systems from the major facilitator superfamily (e.g., EmrAB-TolC, EmrD, MdtL, MdtM), the multidrug and toxic compound extrusion (MATE) family (MdtK), and small multidrug resistance (SMR) transporters (QacE, SugE) were also detected.

Regulatory genes associated with antimicrobial resistance included MarA/MarB/MarR, RamA/RamR, SoxR/SoxS, AcrR, and components of the PhoP–Pmr system (Table 4).

Discussion

This genomic substudy provides a detailed description of resistance-associated genetic determinants in multidrug-resistant (MDR) *Klebsiella pneumoniae* bloodstream isolates from cancer patients in Iraq. In this cohort, bloodstream infections occurred predominantly in patients with haematological malignancies, which is consistent with prior studies conducted in oncology and haematology populations, including those involving patients with neutropenia or haematopoietic stem-cell transplantation [5, 18, 19]. These settings are typically characterised by intensive chemotherapy exposure, prolonged neutropenia and frequent invasive procedures, which have been associated with an increased risk of bloodstream infections due to resistant Gram-negative pathogens [5, 18, 19].

Whole-genome sequencing in this study identified the presence of multiple β-lactamase genes, including CTX-M-type extended-spectrum β-lactamases (ESBLs), SHV and TEM family enzymes, as well as OXA-48-family carbapenemases. This pattern is consistent with previous genomic and epidemiological studies reporting the co-detection of ESBL and OXA-48-like carbapenemase genes in K. pneumoniae isolates from hospital settings [20-22]. CTX-M-type enzymes, particularly CTX-M-15, have been widely reported in clinical isolates globally and are frequently described in association with MDR K. pneumoniae lineages [21, 22].

Carbapenemase genes identified in this study included OXA-48 and OXA-232. These enzymes have been reported in hospital-based studies from the Middle East, North Africa and parts of Europe, although the extent of their distribution varies across regions and study settings [23-25]. Previous reports of bloodstream infections due to OXA-48-producing K. pneumoniae have described challenges in antimicrobial management, particularly in settings where additional resistance determinants are present [24-26]. In the present study, ESBL and OXA-48-family carbapenemase genes were detected within the same isolates, indicating the coexistence of multiple β-lactam resistance determinants.

In addition to β-lactamase genes, this study identified several non-β-lactam resistance determinants, including aminoglycoside-associated genes (aadA family), macrolide-associated genes (EreA, Mph(A), Mrx) and sulfonamide resistance genes (sul1 and sulI). Similar combinations of resistance genes have been described in genomic studies of K. pneumoniae from hospital settings in the Middle East and neighbouring regions, often located on mobile genetic elements [24, 25]. These findings are consistent with the accumulation of multiple resistance determinants in MDR K. pneumoniae isolates.

Whole-genome sequencing also identified multiple efflux pump systems and regulatory genes, including RND transporters (e.g., AcrAB-TolC), MFS transporters, MATE-family transporters and SMR systems, together with global regulators such as MarA/MarR, RamA/RamR and SoxR/SoxS. Experimental studies have shown that these systems can contribute to reduced susceptibility to multiple antimicrobial classes when overexpressed, although gene expression and functional activity were not assessed in the present study [27-30]. The detection of these genes indicates the presence of genetic elements associated with multidrug resistance, but their functional contribution in these isolates cannot be determined from genomic data alone.

Taken together, the findings of this study demonstrate that MDR K. pneumoniae bloodstream isolates in this oncology cohort harbour multiple classes of resistance-associated genes, including β-lactamases, non-β-lactam resistance determinants and efflux-related systems. These observations are consistent with previously reported genomic profiles of MDR K. pneumoniae in hospital settings [20-22]. In Iraqi oncology settings, empirical management of febrile neutropenia and sepsis often relies on β-lactam-based regimens, sometimes in combination with aminoglycosides. The detection of multiple β-lactamase and non-β-lactam resistance determinants in this study suggests that such empirical approaches may require careful consideration and ongoing evaluation based on local susceptibility patterns, particularly in high-risk haematological malignancy populations.

From a clinical and public health perspective, these findings may help inform local antimicrobial stewardship and infection-prevention strategies. In particular, knowledge of the types of resistance genes detected in this setting may support the interpretation of local susceptibility patterns and guide empirical treatment considerations in high-risk oncology populations. However, as this study did not include detailed antimicrobial susceptibility outcome data or treatment-response analyses, these implications should be interpreted with caution.

This study has several limitations. The sample size was modest and limited to three centres within a single country, which may affect generalisability. Only MDR isolates were included, and no comparator group of susceptible isolates was analysed, precluding assessment of genotype–phenotype relationships across the full susceptibility spectrum. In addition, gene expression and efflux activity were not measured, and therefore the functional impact of identified resistance and regulatory genes could not be confirmed.

Importantly, this study did not assess the genetic relatedness of isolates (e.g., through phylogenetic or clonality analysis), and therefore transmission dynamics

Table 4. Efflux Pump and Regulatory Resistance Genes Detected among Multidrug-Resistant *Klebsiella pneumoniae* Bloodstream Isolates

Gene / gene family	Product (annotation)	Classification
AcrAB-TolC 1	Multidrug efflux system AcrAB-TolC, membrane fusion component AcrA (RND type)	Efflux pump conferring antibiotic resistance
AcrAB-TolC 2	Multidrug efflux system AcrAB-TolC, inner-membrane proton/drug antiporter AcrB (RND type)	Efflux pump conferring antibiotic resistance
AcrAD-TolC	Aminoglycosides efflux system AcrAD-TolC, inner-membrane proton/drug antiporter AcrD (RND type)	Efflux pump conferring antibiotic resistance
AcrEF-TolC	Multidrug efflux system AcrEF-TolC, inner-membrane proton/drug antiporter AcrF (RND type)	Efflux pump conferring antibiotic resistance
AcrEF-TolC 1	Multidrug efflux system AcrEF-TolC, membrane fusion component AcrE (RND type)	Efflux pump conferring antibiotic resistance
acrR	Transcriptional regulator of acrAB operon, AcrR	Regulator modulating antibiotic efflux and resistance genes
AcrZ	AcrZ membrane protein associated with AcrAB-TolC multidrug efflux pump	Efflux pump–associated protein conferring antibiotic resistance
CmlA family	Chloramphenicol resistance, MFS efflux pump (CmlA family)	Efflux pump conferring antibiotic resistance
EmrAB-TolC	Multidrug efflux system EmrAB-OMF, inner-membrane proton/drug antiporter EmrB (MFS type)	Efflux pump conferring antibiotic resistance
EmrAB-TolC 1	Multidrug resistance regulator EmrR (MprA)	Regulator modulating expression of antibiotic resistance genes
emrB	Multidrug efflux system EmrAB-OMF, inner-membrane proton/drug antiporter EmrB (MFS type)	Efflux pump conferring antibiotic resistance
emrD	Multidrug efflux pump EmrD (MFS type)	Efflux pump conferring antibiotic resistance
EmrD 1	Multidrug efflux pump EmrD (MFS type)	Efflux pump conferring antibiotic resistance
MdtABC-TolC	Multidrug efflux system MdtABC-TolC, inner-membrane proton/drug antiporter MdtB (RND type)	Efflux pump conferring antibiotic resistance
MdtABC-TolC 1	Multidrug efflux system MdtABC-TolC, membrane fusion component MdtA (RND type)	Efflux pump conferring antibiotic resistance
mdtB	Multidrug efflux system MdtABC-TolC, inner-membrane proton/drug antiporter MdtB (RND type)	Efflux pump conferring antibiotic resistance
mdtC	Multidrug efflux system MdtABC-TolC, inner-membrane proton/drug antiporter MdtC (RND type)	Efflux pump conferring antibiotic resistance
mdtG	Multidrug resistance protein MdtG	Efflux pump conferring antibiotic resistance
mdtH	Multidrug resistance protein MdtH	Efflux pump conferring antibiotic resistance
mdtK	Multidrug efflux transporter MdtK/NorM (MATE family)	Drug target; transporter associated with multidrug efflux
mdtK 1	Uncharacterized transporter YeeO (MATE family)	Efflux pump conferring antibiotic resistance
MdtL	Multidrug efflux pump MdtL (MFS type)	Efflux pump conferring antibiotic resistance
MdtM	Multidrug efflux pump MdtM (MFS type)	Efflux pump conferring antibiotic resistance
MacA	Macrolide-specific efflux protein MacA	Efflux pump conferring antibiotic resistance
MacB	Macrolide export ATP-binding/permease protein MacB	Efflux pump conferring antibiotic resistance
QacE	Small multidrug resistance (SMR) efflux transporter QacE, quaternary ammonium compounds	Efflux pump conferring antibiotic resistance
SugE	Small multidrug resistance (SMR) efflux transporter SugE, quaternary ammonium compounds	Efflux pump conferring antibiotic resistance
MarA	Multiple antibiotic resistance protein MarA	Multiple antibiotic resistance regulator; gene modulating antibiotic efflux
marA 1	Multiple antibiotic resistance protein MarA	Regulator modulating antibiotic efflux and permeability
MarB	Multiple antibiotic resistance protein MarB	Multiple antibiotic resistance regulator
MarR	Multiple antibiotic resistance protein MarR	Multiple antibiotic resistance regulator
ramA	Transcriptional activator RamA	Regulator modulating antibiotic efflux and permeability
ramR	Transcriptional regulator, AcrR family	Regulator modulating antibiotic efflux and resistance genes
soxR	Redox-sensitive transcriptional activator SoxR	Regulator modulating antibiotic efflux and resistance genes
soxS	DNA-binding transcriptional dual regulator SoxS	Regulator modulating antibiotic efflux and permeability
PhoP	Transcriptional regulatory protein PhoP	Regulator modulating antibiotic efflux; polymyxin resistance gene
PmrF	Undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase (EC 2.4.2.53)	Cell-wall charge modification; polymyxin resistance gene

RND, resistance–nodulation–division; MFS, major facilitator superfamily; MATE, multidrug and toxic compound extrusion; SMR, small multidrug resistance; EC, Enzyme Commission number (standard numerical classification of enzymes by the reactions they catalyse).

or clonal spread cannot be inferred. Furthermore, the genomic findings reflect gene detection only and were not formally linked to antimicrobial susceptibility phenotypes or clinical outcomes.

Despite these limitations, this study provides one of the first whole-genome-based descriptions of MDR K. pneumoniae bloodstream isolates in cancer patients from Iraq. By integrating clinical context with genomic data, the study contributes to the understanding of resistance gene profiles in a high-risk oncology population and may support future surveillance and research efforts in similar resource-constrained settings.

Future research should incorporate multicentre genomic surveillance with longitudinal sampling to assess clonal relatedness, transmission dynamics, and temporal changes in resistance profiles. Integrating genomic data with phenotypic susceptibility testing and clinical outcomes will be important to better understand the clinical impact of resistance determinants in oncology settings.

In conclusion, in this genomic substudy of multidrug-resistant *Klebsiella pneumoniae* bloodstream infections among cancer patients in Iraq, most cases occurred in individuals with haematological malignancies, consistent with the recognised vulnerability of this population. Whole-genome sequencing identified multiple resistance-associated genetic determinants, including CTX-M, SHV and TEM extended-spectrum β-lactamases, OXA-48-like carbapenemases, non-β-lactam resistance genes, and efflux pump and regulatory elements.

The co-detection of these resistance determinants is consistent with previously reported multidrug-resistant genomic profiles of K. pneumoniae in hospital settings and may contribute to reduced susceptibility to multiple antimicrobial classes. However, as this study was limited to genomic analysis without functional or outcome data, these findings should be interpreted with caution.

These results may inform local antimicrobial stewardship and infection-prevention strategies and support the value of genomic surveillance in high-risk oncology populations. Further multicentre studies incorporating phenotypic susceptibility testing, clinical outcomes, and genomic epidemiology are needed to better understand resistance patterns, transmission dynamics, and their clinical implications in this setting.

Author Contribution Statement

Conceptualization: AHM; BARH. Data curation: AHM, LJY, LJS, LJE, LJX; Formal analysis: AHM, LJY, LJS, LJE, LJX; Investigation: AHM, LJY, LJS, LJE, LJX; Methodology: AHM, LJY, LJS, LJE, LJX; Project administration: AHM, LJY, LJS, LJE, LJX; Resources: AHM, LJY, LJS, LJE, LJX; Software: AHM, LJY, LJS, LJE, LJX; Supervision: AHM; DSR; Validation: AHM; AB;AL;BARH; Visualisation: AHM; Writing - original draft: LJY, LJS, LJE, LJX; AHM; Writing - review & editing: all authors.

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None.

Ethics approval and consent to participate

The Ministry of Health, Center of Training & Human Development Committee in Iraq approved this study (3670/41247). The research was conducted in accordance with the ethical standards of the Declaration of Helsinki. The researcher thoroughly explained the objectives and benefits of the study to the participants, in which they were given an explanatory statement and informed consent was obtained. The anonymity and confidentiality was maintained by assuring that no identifying demographic information was collected.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Consent to Publish

Participants provided informed consent regarding the publication of their de-identified data.

Availability of Data and Materials

Data and other materials are available upon request from the corresponding authors.

Availability of data and materials

Data and other materials are available upon request from the corresponding authors.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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