

RESEARCH

Open Access



The distribution characteristics of global *blaOXA*-carrying *Klebsiella pneumoniae*

Lingning Meng^{1†}, Ziyao Liu^{2†}, Chang Liu¹, Chuchu Li³, Han Shen^{1*} and Xiaoli Cao^{1*}

Abstract

Objective To analyze the distribution of *blaOXA* among global *Klebsiella pneumoniae* and the characteristics of *blaOXA*-carrying *K. pneumoniae*.

Materials and Methods The genomes of global *K. pneumoniae* were downloaded from NCBI by Aspera software. After quality check, the distribution of *blaOXA* among the qualified genomes was investigated by annotation with the resistant determinant database. The phylogenetic tree was constructed for the *blaOXA* variants based on the single nucleotide polymorphism (SNP) to explore the evolutionary relationship between these variants. The MLST (multi-locus sequence type) website and blastn tools were utilized to determine the sequence types (STs) of these *blaOXA*-carrying strains, and sample resource, isolation country, date and host were extracted by perl program for analyzing the characteristics of these strains.

Results A total of 12,356 *K. pneumoniae* genomes were downloaded and 11,429 ones were qualified. Among them, 4386 strains were found to carry 5610 *blaOXA* variants which belonged to 27 varieties of *blaOXAs*, *blaOXA-1* ($n = 2891$, 51.5%) and *blaOXA-9* ($n = 969$, 17.3%) were the most prevalent *blaOXA* variants, followed by *blaOXA-48* ($n = 800$, 14.3%) and *blaOXA-232* ($n = 480$, 8.6%). The phylogenetic tree displayed 8 clades, three of them were composed of carbapenem-hydrolyzing oxacillinase (CHO). Totally, 300 distinct STs were identified among 4386 strains with ST11 ($n = 477$, 10.9%) being the most predominant one followed by ST258 ($n = 410$, 9.4%). *Homo sapiens* (2696/4386, 61.5%) was the main host for *blaOXA*-carrying *K. pneumoniae* isolates. The *blaOXA-9*-carrying *K. pneumoniae* strains were mostly found in the United States and *blaOXA-48*-carrying *K. pneumoniae* strains were mainly distributed in Europe and Asia.

Conclusion Among the global *K. pneumoniae*, numerous *blaOXA* variants were identified with *blaOXA-1*, *blaOXA-9*, *blaOXA-48* and *blaOXA-232* being the most prevalent ones, indicating that *blaOXA* rapidly evolved under the selective pressure of antimicrobial agents. ST11 and ST258 were the main clones for *blaOXA*-carrying *K. pneumoniae*.

Keywords *Klebsiella pneumoniae*, OXA, Sequence Type, Phylogeny, ST11

[†]Lingning Meng and Ziyao Liu have contributed equally to this work and share first authorship.

*Correspondence:

Han Shen
shenhan10366@sina.com
Xiaoli Cao
cao-xiao-li@163.com

Full list of author information is available at the end of the article



Introduction

Klebsiella pneumoniae belonging to *Klebsiella spp.* is one of the important species of *Enterobacteriales*. As one of the most common opportunistic pathogens, it is also a major cause of hospital associated infections, ranking in the top three causative agents in most hospital settings [1]. As we know that extended β -lactams and carbapenem are high-efficiency broad-spectrum antibiotics with high sensitivity to *Enterobacteriales* and are commonly used to treat *K. pneumoniae* infections. Therefore, with the antimicrobial agents being extensively used in clinical therapy, extended-spectrum β -lactam (ESBL)-producing and carbapenem-resistant *K. pneumoniae* (CRKp) have rapidly developed and disseminated, leading to subsequently increased morbidity and mortality. Thus, they were taken as a critical public health threat by The World Health Organization (WHO) [2].

It has been well known that *bla*CTX-M, *bla*TEM, *bla*SHV and *bla*OXA were the most frequent ESBLs, *bla*KPC, *bla*NDM and *bla*OXA-48 were the most common carbapenem-hydrolyzing β -lactamase (CH β LS) encoding genes widely prevalent in *K. pneumoniae* worldwide [3, 4]. In recent years, carbapenem-hydrolyzing oxacillinase, especially *bla*OXA-48-carrying *K. pneumoniae* has been increasingly reported worldwide, with Europe and Asia being a hot spot for outbreaks of infection [5, 6], which endangers public health. However, information on the characterization of *bla*OXA-carrying *K. pneumoniae* is little. Unfortunately, the spread of *bla*OXA-48 gene in Iran, as an endemic country, has not been investigated and only one study has been investigated. Iran, Spain, Greece and China are countries with high prevalence of *bla*OXA-48 gene [7]. So, in this study, we intended to know the changing epidemic characteristics and trends of *bla*OXA genes in *K. pneumoniae* which is helpful for the formulation of infection control measures.

Oxacillinases or OXA β -lactamase was first recognized in the 1960s, displaying hydrolytic activity against penicillins and oxacillin. Afterwards, certain OXA β -lactamases were found to inactivate the cephalosporins and carbapenems. To date, more than 940 types of OXA β -lactamases have been found, showing heterogeneous substrate profiles. OXA β -lactamases were divided into the 4 groups by Poirel and colleagues in 2010 [8]. Group I include OXA-1, OXA-2, and OXA-101 subgroups, belonging to acquired narrow-spectrum class D β -lactamases without significant activity toward cephalosporins or the carbapenems. Group II is the acquired extended spectrum class D β -lactamases hydrolyzing certain extended-spectrum cephalosporins (especially ceftriaxone and cefepime), which often originates from point mutations of narrow-spectrum

class D β -lactamases. However, structurally, certain extended-spectrum OXA enzymes are not related to the narrow-spectrum group I OXA-lactamases. Group III owns the ability to weakly hydrolyze carbapenems, but do not significantly hydrolyze the extend-spectrum cephalosporins. It is named carbapenem-hydrolyzing class D β -lactamases and composed of 2 subgroups. One subgroup named the OXA-23-like enzymes, responsible for carbapenem resistance among *Acinetobacter spp.*, the other subgroup is named the OXA-48-like enzymes, mainly found among the *Enterobacteriales*, especially in *K. pneumoniae*. Group IV forms parts of the chromosomes of various non-fermenting Gram-negative bacteria, which includes the OXA-51-like subgroup in the *Acinetobacter baumannii* complex.

Molecular studies displayed a frequent distribution of *bla*OXA including *bla*OXA-1, *bla*OXA-2, *bla*OXA-48 etc. among *K. pneumoniae* [9]. Among the *bla*OXA-48-like CH β LS group, *bla*OXA-48, *bla*OXA-181, *bla*OXA-232, *bla*OXA-204, *bla*OXA-162, and *bla*OXA-244 are the most common enzymes identified, and some of them showed an epidemic state, for example, it has been reported that *bla*OXA-48 is endemic in Europe and Asia [5, 6]. The *bla*OXA-162 and *bla*OXA-244 (derivatives of *bla*OXA-48) were present in Europe [10]. The *bla*OXA-181 and *bla*OXA-232 were endemic in the Indian subcontinent and certain sub-Saharan African countries [11, 12]. Additionally, clonal dissemination of certain high-risk clones such as *K. pneumoniae* ST147, ST307, ST15, and ST14 play roles in the global dispersion of *bla*OXA-48-like CH β LS [12]. In recent years, detection of *bla*OXA-48 and clonal dissemination of *bla*OXA-48-carrying carbapenem-resistant Enterobacteriaceae (CRE) has been reported in China [13]. However, the distribution of *bla*OXA among global *K. pneumoniae* is unknown and the information available is quite limited.

In this study, we firstly analyzed the distribution and phylogeny of *bla*OXA among global *K. pneumoniae* isolates. For the *bla*OXA-carrying strains, we further investigated the sequence type (ST) and the characteristics.

Materials and Methods

The acquisition and quality check of *K. pneumoniae* genomes

Aspera software was applied to download the *K. pneumoniae* genomes deposited in GenBank (<https://www.ibm.com/aspera/connect/>). A total of 12,356 complete genomes of *K. pneumoniae* strains were accessible. After the genome quality check by CheckM and Quest software, 11,429 qualified genomes were finally analyzed in this study.

Standardized genome annotations

All the 11,429 genomes were annotated by prokaryotic genome rapid annotation software Prokka to analyze the *blaOXA* genotype, thus to avoid differences in genomic predictions with different annotation methods and to get the strains carrying *blaOXA*.

Phylogenetic tree of *blaOXA* variants

Multiple sequence alignment for nucleotide sequences of the *blaOXA* gene was performed using Muscle [14], and then the GTRCAT replacement model was selected through the RaxML software [15]. In addition, 500 bootstrapping samples were set up to construct the preliminary phylogenetic tree, which was further imported into iTOL software to obtain the final one by setting bootstrap value being with less than 50 for the branches being deleted to obtain the final evolutionary tree [16].

Analysis of sequence types (STs)

Seven housekeeping gene sequences (*gapA*, *infB*, *mdh*, *pgi*, *phoE*, *rpoB*, and *tonB*) and typing profile files of *K. pneumoniae* strains were obtained from MLST website (<https://pubmlst.org>). All the nucleotide sequences of 4386 *blaOXA*-carrying strains were analyzed using blastn tools in batches using housekeeping gene sequences as the database (parameters: value = 1e-5; identity = 100%; coverage = 100%).

Investigation of antimicrobial resistance genes among *blaOXA*-carrying *K. pneumoniae*

The distribution of other resistance genes including CHβLs encoding genes, aminoglycoside and

fluoroquinolone resistance genes was investigated by blastn tools. All the nucleotide sequences of *blaOXA*-carrying strains were analyzed with the sequence of antimicrobial resistant genes as database using blastn, and then the results were filtered (parameters: identity >= 90%; coverage >= 90%; value = 1e-5).

Acquisition of strain meta information

Strain meta information such as isolation source, country, and date, etc. was extracted in batches from the downloaded gbk file by using perl script. Meanwhile, the corresponding cds, genes, contig quantity and genome length information of the genomes were also obtained from the prokka annotation file. All the information in addition to STs were integrated in an excel to facilitate the further analysis.

Results

OXA distribution among global *K. pneumoniae* strains

Among the 11,429 *K. pneumoniae* strains, 4386 ones carried a total of 5610 *blaOXA* variants which belonged to 27 genotypes of *blaOXAs*. The predominant was *blaOXA-1* (n = 2891, 51.5%), followed by *blaOXA-9* (n = 969, 17.3%), *blaOXA-48* (n = 800, 14.3%), *blaOXA-232* (n = 480, 8.6%), *blaOXA-10* (n = 158, 2.8%), *blaOXA-181* (n = 146, 2.6%), and *blaOXA-2* (n = 108, 1.9%) (Fig. 1A). Variants including *blaOXA-244* (n = 12, 0.2%), *blaOXA-245* (n = 11, 0.2%), *blaOXA-162* (n = 5, 0.1%), *blaOXA-4* (n = 5, 0.1%), *blaOXA-926* (n = 4, 0.1%), *blaOXA-204* (n = 3, 0.1%), *blaOXA-534* (n = 3, 0.1%), *blaOXA-58* (n = 2, 0.03%), and *blaOXA-320* (n = 2, 0.03%) were few. Whereas, the following variant was only detected in single strain

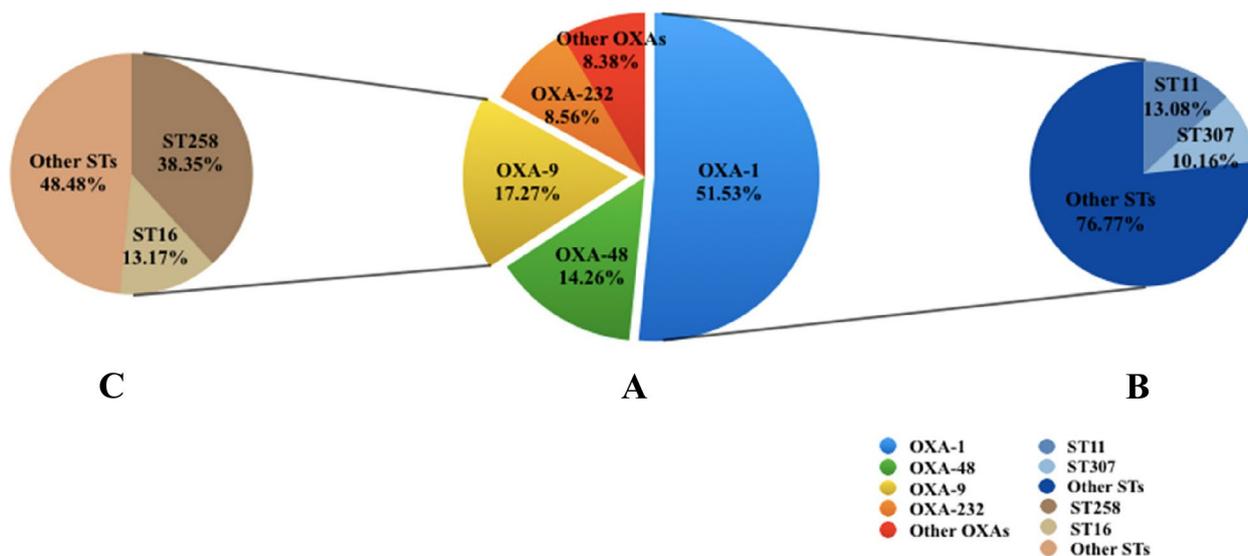


Fig. 1 Distribution of *K. pneumoniae* *blaOXA* variants and sequence types

which were *blaOXA-21*, *blaOXA-392*, *blaOXA-517*, *blaOXA-519*, *blaOXA-663*, *blaOXA-796*, *blaOXA-827*, *blaOXA-427*, *blaOXA-544*, *blaOXA-436* and *blaOXA-17*.

Phylogenetic relationship of *blaOXA* variants among global *K. pneumoniae*

The phylogenetic tree showed that *blaOXA* variants could be divided into 8 clades (Fig. 2). Among them, clade A was composed of 10 variants and all of them belonged to carbapenem-hydrolyzing class D β-lactamase (Group III, *blaOXA-48-like* subgroup). Clade B belonged to Group IV (*blaOXA-51-like* subgroup). Clade C belonged to Group II with the activity of acquired extended spectrum class D β-lactamases, amongst them, *blaOXA-10-type* oxacillinase, with weak carbapenemases being previously found [17]. Natural variant of *blaOXA-10* was reported to own increased carbapenemase activity and high-level expression of *blaOXA-10* and *blaOXA-10* derivative *blaOXA-663* can confer carbapenem resistance when expressed at sufficiently high levels in the OmpK36 deficiency

background [18], indicating that clade C may own the potential to develop to be group III. In clade D, *blaOXA-544* derived from *blaOXA-2* family, as well as *blaOXA-21* all belonged to Group 1, acquired narrow-spectrum oxacillinase without significant activity toward cephalosporins or the carbapenems [19]. The *blaOXA* variants within Clade H may belong to Group I considering the activity of *blaOXA-1* and *blaOXA-4*, although the hydrolyzing activity of *blaOXA-534*, *blaOXA-329*, *blaOXA-320* and *blaOXA-796* remained unknown. Clade E, F and G were composed of single *blaOXA* variant, where, *blaOXA-9* and *blaOXA-926* were narrow-spectrum oxacillinase [20], *blaOXA-427* was a new plasmid-borne carbapenem-hydrolyzing class D β-lactamase in *Enterobacteriaceae* [21]. Overall, a relatively independent evolutionary relationship between carbapenem-hydrolyzing oxacillinase *blaOXA* and non-carbapenem-hydrolyzing oxacillinase *blaOXA* were observed. However, several *blaOXA* within Group I and II may develop carbapenem-hydrolyzing activity under the selective pressure of antimicrobial agents.

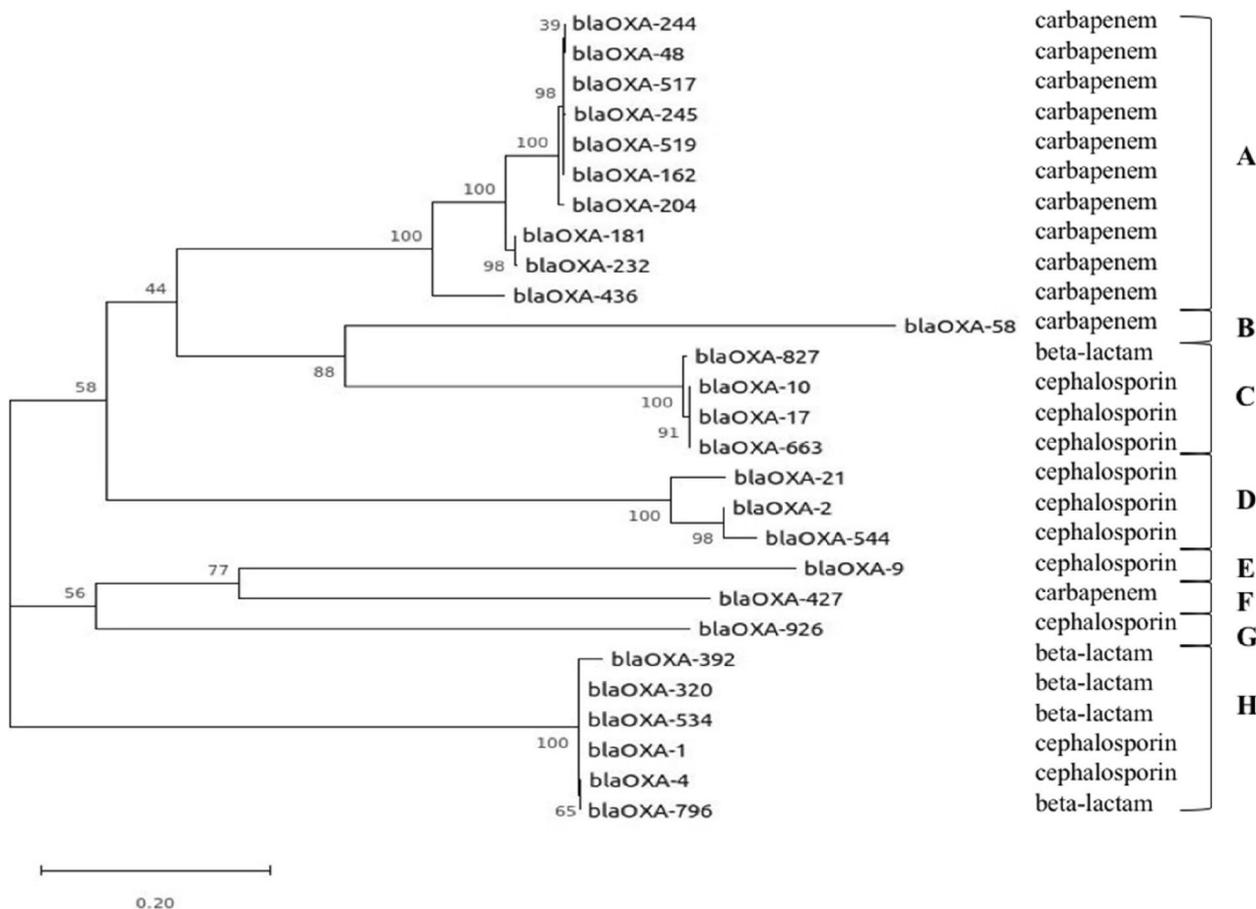


Fig. 2 Phylogenetic tree based on SNP sequence of global *blaOXA* variants

The sequence types of *bla*OXA-carrying *K. pneumoniae*

A total of 300 different STs were identified among the 4386 *bla*OXA-carrying *K. pneumoniae* strains. The predominant type was ST11 ($n=477$, 10.9%), followed by ST258 ($n=410$, 9.4%), ST15 ($n=367$, 8.4%), ST307 ($n=300$, 6.8%), ST147 ($n=292$, 6.7%), ST16 ($n=266$, 6.1%) and other STs (Figure S1). In addition, 94 strains were novel or unknown STs (Table S1).

For strains producing different *bla*OXA variants, 2845 *bla*OXA-1-carrying *K. pneumoniae* strains were assigned into 209 STs. Amongst them, ST11 ($n=372$, 13.1%) was the predominant one, followed by ST307 ($n=287$, 10.2%) (Fig. 1B). Meanwhile, 957 *bla*OXA-9-carrying *K. pneumoniae* strains belonged to 74 STs, with ST258 being accounting for the majority (367/957 38.4%), followed by ST16 (126/957 13.2%) (Fig. 1C). The most extensively studied *bla*OXA-48-carrying *K. pneumoniae* were assigned into 91 STs, with ST11 (136/794, 17.1%) and ST101 (103/794, 13.0%) being the leading STs.

Additionally, the predominant *bla*OXA variant of 477 ST11 strains was *bla*OXA-1 ($n=378$, 79.2%) and the main *bla*OXA variant of 410 ST258 strains was *bla*OXA-9 ($n=370$, 90.2%). The distribution of *bla*OXA-1 in ST11 (378/477, 79.2%) was significantly higher than that in ST258 (24/410, 5.9%), the difference was statistically significant ($p=0.000$). Meanwhile, the prevalence of *bla*OXA-9 in ST258 (370/410, 90.2%) was obviously higher than that in ST11 (48/477, 10.1%), the difference was also statistically significant ($p=0.000$).

Distribution characteristics of *bla*OXA among global *K. pneumoniae*

The *bla*OXA-9 was the earliest *bla*OXA variants in the genome submitted in USA in 2001 albeit *bla*OXA-1 was the first reported one. Since the first identification of *bla*OXA-48-carrying *K. pneumoniae* isolates in 2001, the number of *bla*OXA-carrying *K. pneumoniae* isolates collected from all the specimen types had basically shown an increasing trend till 2014 and had been stable since then (Fig. 3). The predominant *bla*OXA-1, *bla*OXA-9 and *bla*OXA-48 variants showed the same trend, which should be of concern.

The main host of *bla*OXA-carrying *K. pneumoniae* isolates was homo sapiens (2696/4386, 61.5%), followed by water-related host (60/4386, 1.4%), animal-related host (45/4386, 1.0%) and plant-related host (20/4386, 0.5%). The isolates of homo sapiens were mainly derived from blood, respiratory, alimentary tract, and urinary tract infections (Table 1).

The most predominant *bla*OXA-1-carrying *K. pneumoniae* strains were distributed widely around the world except Northern America, which was relatively rare. The *bla*OXA-9-carrying *K. pneumoniae* strains were mostly found in Northern America rather than other regions, especially, ST258 was mainly distributed in this area. The most studied *bla*OXA-48-carrying *K. pneumoniae* strains were mainly distributed in Europe and Asia. The *bla*OXA-232-carrying *K. pneumoniae* strains and *bla*OXA-181-carrying *K. pneumoniae* strains were almost found in Asian countries (Fig. 4).

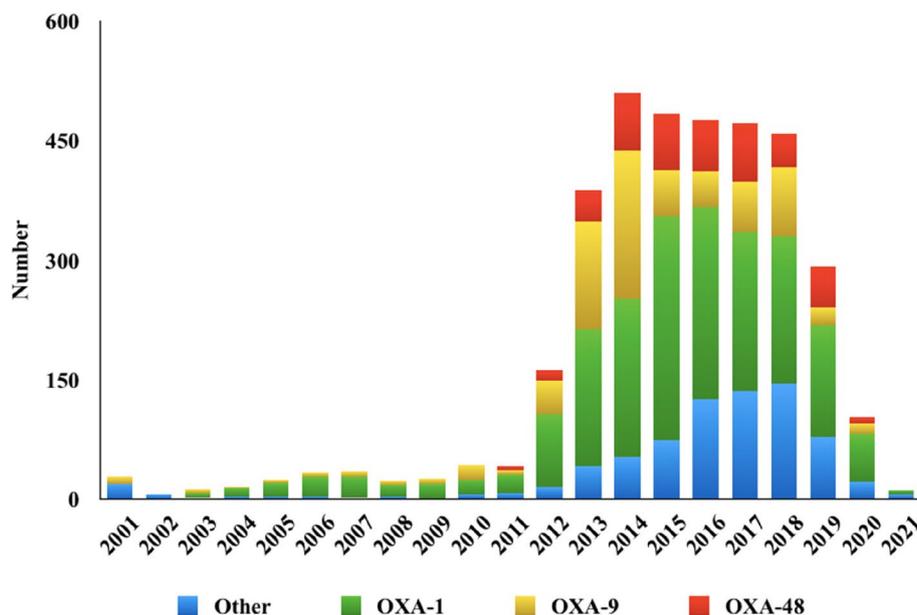


Fig. 3 The number of global *K. pneumoniae* *bla*OXA variants detected from 2001 to 2021

Table 1 Source distribution and ratio of global *blaOXA*-carrying *K. pneumoniae* strains in homo sapiens

Specimen type	Strains Number	Ratio (%)
Blood	572	21.2
Urine	464	17.2
Sputum	204	7.6
Rectum	184	6.8
Faeces	136	5.0
Endotracheal aspirate	87	3.2
Wound	69	2.6
Ascitic fluid	36	1.3
Pus	28	1.0
Cerebrospinal fluid	10	0.4
Blank	763	28.3
Others	143	5.4
Total	2696	100

The distribution of antimicrobial resistance determinants among global *blaOXA*-carrying *K. pneumoniae*

Among the 4386 *blaOXA*-carrying *K. pneumoniae* strains, *blaKPC* ($n=985$, 22.5%) and *blaNDM* ($n=732$, 16.7%) were the main *blaCHβLs* with *blaVIM* ($n=135$, 3.1%) and *blaIMP* ($n=28$, 0.6%) also being identified. Although *aph* ($n=5645$, 128.7%), *aad* ($n=2927$, 66.7%)

and *aac* ($n=2742$, 62.5%) were the predominant aminoglycoside resistance genes, *rmt* ($n=347$, 7.9%), *armA* ($n=332$, 7.6%), and *ant* (2')-1a ($n=99$, 2.3%) were also found. *qnr* ($n=2340$, 53.4%), *oqxAB* ($n=4131$, 94.2%), *aac(6')-Ib-cr* ($n=49$, 1.1%) and *qepA* ($n=12$, 0.3%) were the fluoroquinolone resistance genes.

In detail, the *blaNDM-1* ($n=618$, 84.1%) and *blaKPC-3* ($n=586$, 59.6%) were the most common subtypes of *blaKPC* and *blaNDM* respectively. Moreover, *rmtF1* and *rmtB1* were the main variants of *rmt* gene. *qnrB1* and *qnrS1* were the major subtypes of *qnr* gene (Fig. 5).

Discussion

Current evidence suggests that compared to other Gram-negative opportunists, *K. pneumoniae* has a wider ecological distribution, significantly greater antimicrobial resistance gene diversity and a higher plasmid burden [22]. In recent years, with the carbapenem being frequently used in clinical treatment. Carbapenem-hydrolyzing oxacillinase has been increasingly found, with the outbreaks of infection being reported in Mediterranean and China [2, 5, 6]. As we know that carbapenem-hydrolyzing oxacillinase was commonly prevalent in *Enterobacterale*, especially in *K. pneumoniae* [22]. So the analysis of the distribution of *blaOXA* among the global *K. pneumoniae* based on the genomes could help us to

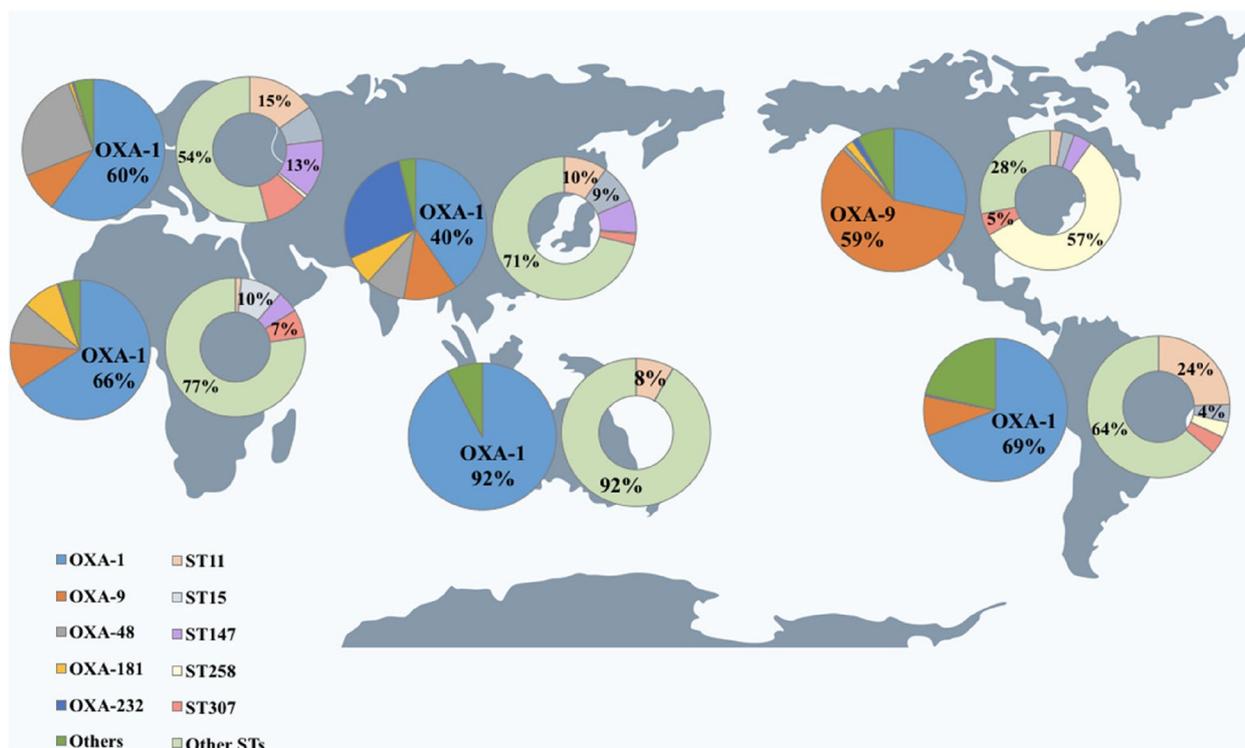


Fig. 4 Global distribution of *blaOXA* variants and sequence types of *blaOXA*-carrying *K. pneumoniae* strains

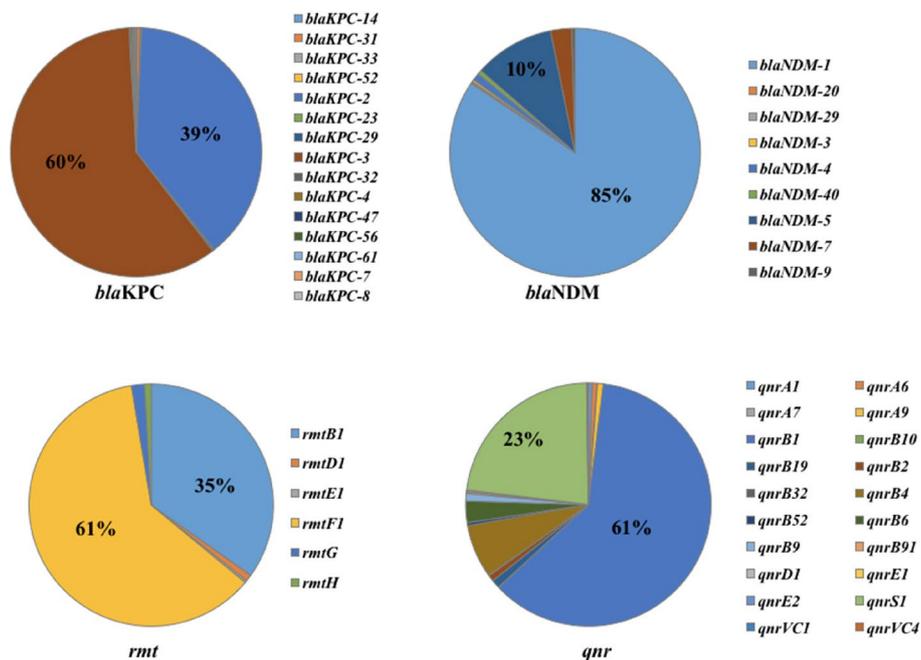


Fig. 5 Subtypes of antimicrobial resistance genes among global *blaOXA*-carrying *K. pneumoniae* strains

fully illustrate the characteristics of *blaOXA*-carrying *K. pneumoniae*, which is quite useful for formulation and implementation of infection control measures.

In this study, we found that there was a rapid increase in global *blaOXA*-carrying *K. pneumoniae* strains since the first *blaOXA* was identified [23]. Overall, *blaOXA-1* variants were widely distributed around the world. The *blaOXA-9* variants were mostly prevalent in Northern America. Whereas, *blaOXA-48* variants were mainly reported in Europe and Asia which was in accordance with previous studies [5, 6]. Notably, as the *blaCHβ*Ls, albeit *blaOXA-48*, *blaOXA-232* and *blaOXA-181* were not the most prevalent ones in our study, the emergence of them in different parts of the world has been reported and such genes were found to be most likely underreported due to problems with the laboratory detection of these enzymes [10]. Moreover, we found an increasing trend and wider distribution of the *blaOXA-48* CHβLs, which is consistent with the previous reports [13], indicating an escalating threat of CRKp.

The phylogenetic tree showed a diversity of *blaOXA* variants identified within *K. pneumoniae*. Functionally, all the *blaOXA*-variants could be divided into carbapenem-hydrolyzing oxacillinase and non-carbapenem-hydrolyzing one. Within the 29 *blaOXA* variants, 12 out of them have been identified to be *blaCHβ*Ls, albeit the detailed hydrolyzing activities of 5 variants remained unknown, the increasing diversity and activity towards

carbapenem of these *blaOXA*-variants remind us of the continual change trend under the selective pressure of antimicrobial agents.

Diverse STs identified in our study indicated genetic diversity for *blaOXA*-carrying *K. pneumoniae* and a broad host for *blaOXA* variants. Of great concern, high-risk epidemic clones ST11 and ST258 were the predominant STs in our study which have also been the most common host for *blaCHβ*Ls [24]. As we know that the prevalence of ST11 is high in the continent of Europe, in Greece and Spain, as well as in China [2, 24], and the ST11 clone was reported not only to be the dominant host for *blaKPC* and *blaNDM* [25, 26], but also associated with *blaOXA-48-like* genes (e.g., *blaOXA-163*, *blaOXA-181*) [27, 28]. Although *blaOXA-1* was the main variant among ST11 clones, the frequent occurrence of *blaOXA-48* within global high-risk clone ST11 in our study indicates us that there may be a consistent distribution of *blaOXA-blaCHβ*Ls within *K. pneumoniae*. Additionally, albeit multiple *blaOXA* variants were detected in the ST11 strains, a simultaneous occurrence of *blaOXA-48* and *blaOXA-1* was frequently found, further suggesting the compatibility between these 2 variants within ST11 clone. It has been well known that ST258 clones was the predominant host for *blaKPC* in European and American countries [24], Fortunately, *blaOXA-9* was the main variant within ST258 clone in our study, without other *blaOXA* variants concurrence, which was consistent with the

previous study [29, 30], probably indicating a better fitness between *blaOXA-9* and ST258 clones.

Of great concern, more than half of the *blaOXA*-carrying *K. pneumoniae* carried *blaCHβLs*. The frequent occurrence of *blaNDM-1* was mainly among *blaOXA-1* producing *K. pneumoniae*, and high prevalence of *blaKPC-3* was predominantly within *blaOXA-1* and *blaOXA-9* carrying one, which may indicate a better fitness between *blaOXA-1* and *blaNDM-1*, and an association between *blaOXA-1/ blaOXA-9* with *blaKPC-3*. Moreover, almost all the *blaOXA*-carrying *K. pneumoniae* carried at least a fluoroquinolone resistance gene, especially *oqxAB*, suggesting that these genes may play an important role in the fluoroquinolone resistance of *K. pneumoniae*. Additionally, albeit *rmt* and *armA* were not the mainly prevalent aminoglycoside resistance gene, such genes frequently should attract our attention based on the conferred resistance to clinically important amikacin.

There are several limitations. First, part of strain information uploaded to GenBank was incomplete, this may result in statistical bias. Second, some *blaOXA*-variants within *K. pneumoniae* have never been reported and the detailed activity remained unknown, since we could just get the genome without the exact strain, so it is hard for us to further analyze the hydrolyzing activity.

In summary, *blaOXA-1* and *blaOXA-9* were the main *blaOXA* among global *K. pneumoniae* with ST11 and ST258 being the predominant STs. *blaOXA* evolved rapidly towards *blaCHβLs* under the selective pressure of antimicrobial agents with *blaOXA-48* and *blaOXA-232* group being increasingly found.

Abbreviations

CRE	Carbapenem-resistant Enterobacteriaceae
ESBLs	Extended-spectrum β-lactamases
CHβLs	Carbapenem-hydrolyzing β-lactamase
KPC	<i>Klebsiella pneumoniae</i> Carbapenemase
NDM	New Delhi metallo-beta-lactamase
ESBLs	Extended-spectrum β-lactamases
MLST	Multi-locus sequence typing
STs	Sequence types
ARGs	Antibiotics resistance genes

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-023-08156-5>.

Additional file 1: FigureS1. The main sequence types of *blaOXA*-carrying *K. pneumoniae*.

Additional file 2: TableS1. The sequence types of *blaOXA*-carrying *K. pneumoniae*.

Additional file 3: TableS2. The accession number and the web link to datasets for the provided name of all the strains in this study.

Acknowledgements

We are very grateful to Tianshe Li for providing technical help on data sorting and bioinformatic analysis.

Authors' contributions

MLN performed the Bioinformatics analysis and writing; LZ Y sorted the data and help with the writing; LCC interpreted the data regarding the resistant determinants and STs. LC performed statistical analysis. SH and CXL designed the work and were a major contributor in revising the manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (81902124 and 82002205).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from GenBank and the accession number and web link to datasets for the provided name of these strains were shown in table S2.xlsx.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Laboratory Medicine, Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Zhongshan Road 321, Gulou, Jiangsu Province, Nanjing, People's Republic of China. ²The Precision Medicine Centre of Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China. ³Department of Acute Infectious Disease Control and Prevention, Jiangsu, Provincial Center for Disease Control and Prevention, Nanjing, China.

Received: 28 November 2022 Accepted: 14 March 2023

Published online: 29 March 2023

References

- Shrestha R, Luterbach CL, Dai W, et al. Characteristics of community-acquired carbapenem-resistant Enterobacteriales. *J Antimicrob Chemother.* 2022;77(10):2763–71.
- Hu Y, Liu C, Shen Z, et al. Prevalence, risk factors and molecular epidemiology of carbapenem-resistant *Klebsiella pneumoniae* in patients from Zhejiang, China, 2008–2018. *Emerg Microbes Infect.* 2020;9(1):1771–9.
- Medrzycka-Dabrowska W, Lange S, Zorena K, et al. Carbapenem-resistant *Klebsiella pneumoniae* Infections in ICU COVID-19 patients—a scoping review. *J Clin Med.* 2021;10(10):1–13.
- Suay-Garcia B, Perez-Gracia MT. Present and future of Carbapenem-Resistant Enterobacteriaceae (CRE) Infections. *Antibiotics (Basel).* 2019;8(3):1–16.
- Mairi A, Pantel A, Ousalem F, et al. OXA-48-producing Enterobacteriales in different ecological niches in Algeria: clonal expansion, plasmid characteristics and virulence traits. *J Antimicrob Chemother.* 2019;74(7):1848–55.
- Touati A, Mairi A. Epidemiology of carbapenemase-producing Enterobacteriales in the Middle East: a systematic review. *Expert Rev Anti Infect Ther.* 2020;18(3):241–50.
- Azimi L, Nordmann P, Lari AR, et al. First report of OXA-48-producing *Klebsiella pneumoniae* strains in Iran. *GMS Hyg Infect Control.* 2014;9(1):Doc07.

8. Poirel L, Naas T, Nordmann P. Diversity, epidemiology, and genetics of class D beta-lactamases. *Antimicrob Agents Chemother*. 2010;54(1):24–38.
9. Mehrbakhsh P, Basharkhah Y, Bahkshi A, et al. Prevalence of OXA-type class D beta-lactamases among clinical isolates of *Klebsiella pneumoniae* in multiple centers of Tehran. *Iran Infect Disord Drug Targets*. 2021;21(4):558–63.
10. Pitout JDD, Peirano G, Kock MM, et al. The global ascendancy of OXA-48-type carbapenemases. *Clin Microbiol Rev* 2019;33(1):1–48.
11. Naha S, Sands K, Mukherjee S, et al. OXA-181-Like Carbapenemases in *Klebsiella pneumoniae* ST14, ST15, ST23, ST48, and ST231 from septicemic neonates: coexistence with NDM-5, resistome, transmissibility, and genome diversity. *mSphere*. 2021;6(1):e1156–20.
12. Shankar C, Mathur P, Venkatesan M, et al. Rapidly disseminating blaOXA-232 carrying *Klebsiella pneumoniae* belonging to ST231 in India: multiple and varied mobile genetic elements. *BMC Microbiol*. 2019;19(1):137.
13. Chen Y, Fang L, Yang Y, et al. Emergence of carbapenem-resistant *Klebsiella pneumoniae* harbouring bla OXA-48-like genes in China. *J Med Microbiol*. 2021;70(3):1–5.
14. Edgar RC. MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic Acids Res*. 2004;32(5):1792–7.
15. Kozlov AM, Darriba D, Flouri T, et al. RAxML-NG: a fast, scalable and user-friendly tool for maximum likelihood phylogenetic inference. *Bioinformatics*. 2019;35(21):4453–5.
16. Letunic I, Bork P. Interactive Tree Of Life (iTOL) v4: recent updates and new developments. *Nucleic Acids Res*. 2019;47(W1):W256–9.
17. Kotsakis SD, Flach CF, Razavi M, et al. Characterization of the first OXA-10 natural variant with increased carbapenemase activity. *Antimicrob Agents Chemother*. 2019;63(1):1–18.
18. Ma P, Laibinis HH, Ernst CM, et al. Carbapenem resistance caused by high-level expression of OXA-663 beta-Lactamase in an OmpK36-Deficient *Klebsiella pneumoniae* clinical isolate. *Antimicrob Agents Chemother*. 2018;62(11):1–12.
19. Laudy AE, Rog P, Smolinska-Krol K, et al. Prevalence of ESBL-producing *Pseudomonas aeruginosa* isolates in Warsaw, Poland, detected by various phenotypic and genotypic methods. *PLoS ONE*. 2017;12(6): e0180121.
20. Liu L, Feng Y, Wei L, et al. KPC-2-Producing Carbapenem-resistant *Klebsiella pneumoniae* of the uncommon ST29 type carrying OXA-926, a novel narrow-spectrum OXA beta-Lactamase. *Front Microbiol*. 2021;12: 701513.
21. Bogaerts P, Naas T, Saegeman V, et al. OXA-427, a new plasmid-borne carbapenem-hydrolysing class D beta-lactamase in Enterobacteriaceae. *J Antimicrob Chemother*. 2017;72(9):2469–77.
22. Wyres KL, Holt KE. *Klebsiella pneumoniae* as a key trafficker of drug resistance genes from environmental to clinically important bacteria. *Curr Opin Microbiol*. 2018;45:131–9.
23. Poirel L, Heritier C, Tolun V, et al. Emergence of oxacillinase-mediated resistance to imipenem in *Klebsiella pneumoniae*. *Antimicrob Agents Chemother*. 2004;48(1):15–22.
24. Spadar A, Perdigao J, Campino S, et al. Large-scale genomic analysis of global *Klebsiella pneumoniae* plasmids reveals multiple simultaneous clusters of carbapenem-resistant hypervirulent strains. *Genome Med*. 2023;15(1):3.
25. Li Z, Ding Z, Yang J, et al. Carbapenem-resistant *Klebsiella pneumoniae* in Southwest China: molecular characteristics and risk factors caused by KPC and NDM producers. *Infect Drug Resist*. 2021;14:3145–58.
26. Chen R, Liu Z, Xu P, et al. Deciphering the epidemiological characteristics and molecular features of bla KPC-2- or bla NDM-1-Positive *Klebsiella pneumoniae* Isolates in a newly established hospital. *Front Microbiol*. 2021;12: 741093.
27. Abdelaziz MO, Bonura C, Aleo A, et al. NDM-1- and OXA-163-producing *Klebsiella pneumoniae* isolates in Cairo, Egypt, 2012. *J Glob Antimicrob Resist*. 2013;1(4):213–5.
28. Tao G, Tan H, Ma J, et al. Resistance phenotype and molecular epidemiology of carbapenem-resistant *Klebsiella pneumoniae* Isolated from Nanjing children's hospital in Jiangsu Province. *China Infect Drug Resist*. 2022;15:5435–47.
29. Lee Y, Kim BS, Chun J, et al. Clonality and Resistome analysis of KPC-producing *Klebsiella pneumoniae* strain isolated in Korea using whole genome sequencing. *Biomed Res Int*. 2014;2014: 352862.
30. Kocsis E, Lo Cascio G, Piccoli M, et al. KPC-3 carbapenemase harbored in FIK plasmid from *Klebsiella pneumoniae* ST512 and *Escherichia coli* ST43 in the same patient. *Microb Drug Resist*. 2014;20(5):377–82.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

