

Supplementary Online Content

Lin IF, Wu YY, Huang YH, et al: Clinical Clinical characteristics and beta-lactamase genes of carbapenem-nonsusceptible *Klebsiella pneumoniae* strains which remains susceptible to beta-lactams of narrower spectra. E-Da Med J 2023;10:12-23. doi:10.6966/EDMJ.202312_10(4).0002.

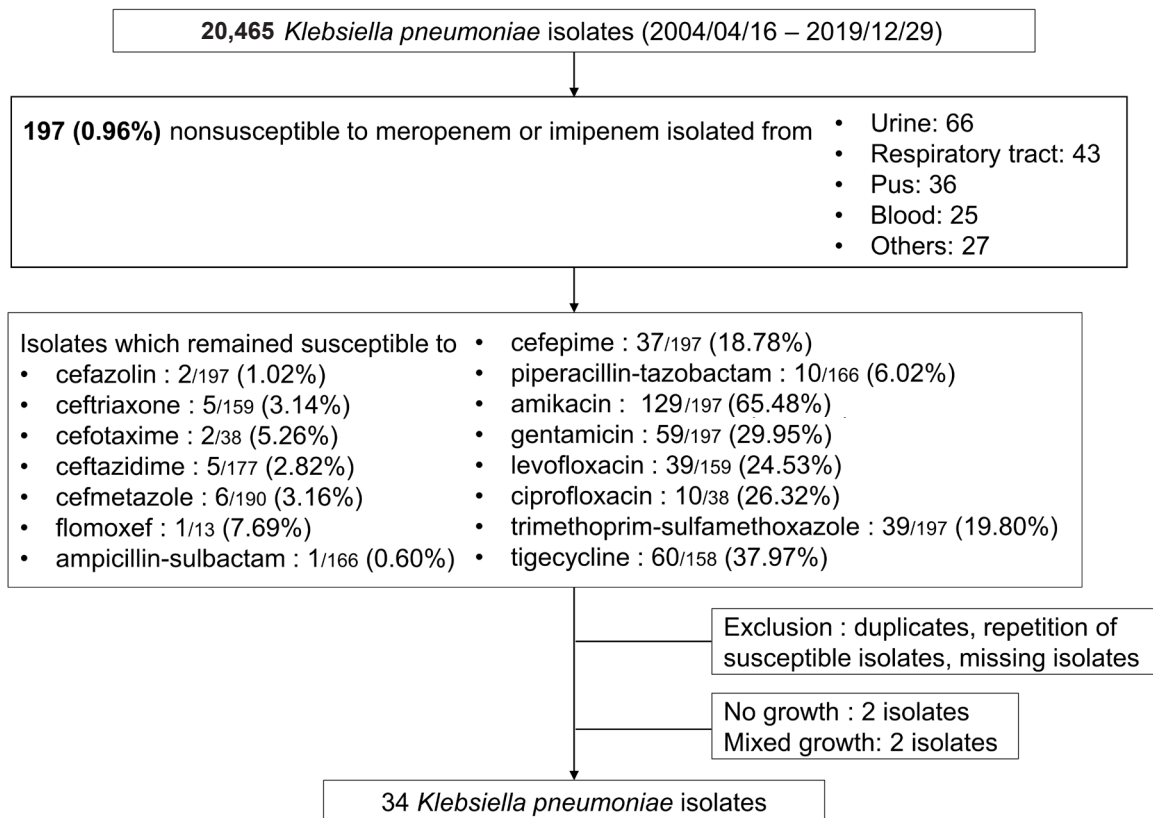
eFig. 1 Flow diagram of this study.

eFig. 2 Increasing prevalence of carbapenem nonsusceptibility among *Klebsiella pneumoniae*.

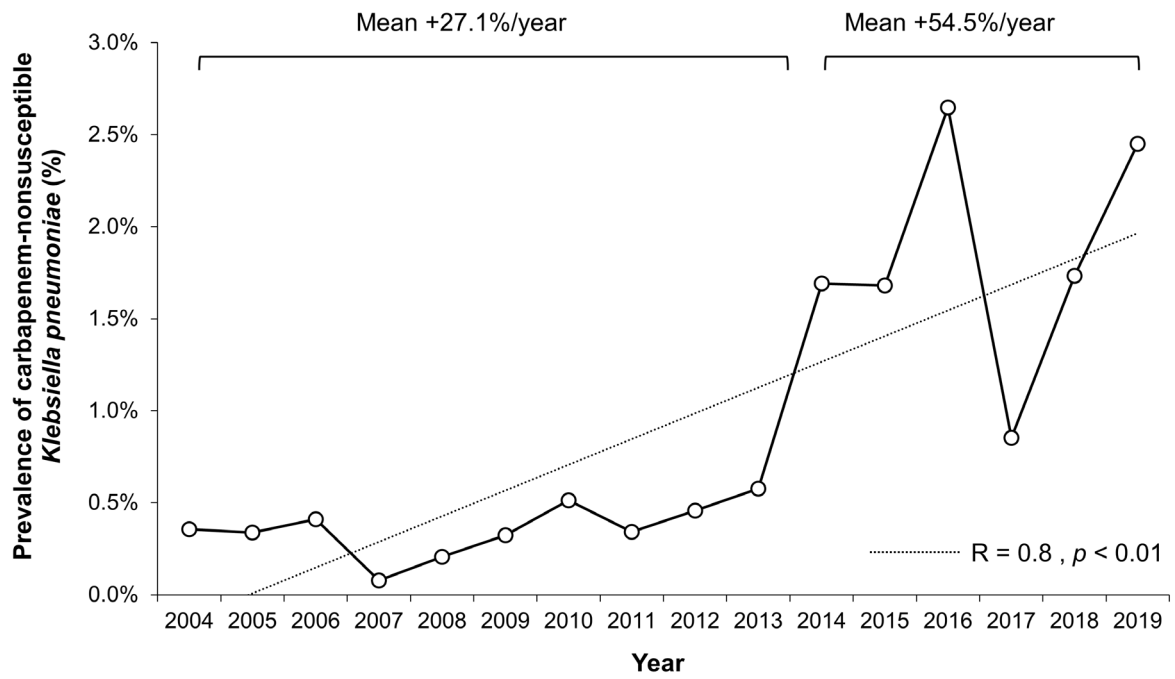
eTable 1. PCR primer sequences used for amplification of genes encoding ESBLs, AmpC β -lactamases, and carbapenemases.

eTable 2. Antibiograms, treatment outcomes and β -lactamase genes of nine isolates which were identified as susceptible to meropenem in customized broth microdilution assays. In every column of antibiotics, the left panels are minim inhibitory concentrations (MICs) obtained by automated antimicrobial susceptibility testing at the time of isolation, and the right panels are MICs obtained by customized broth microdilution assays at the time of this study.

This supplementary material has been provided by the authors to give readers additional information about their work.



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eTable 1. PCR primer sequences used for amplification of genes encoding ESBLs, AmpC β -lactamases, and carbapenemases.

| Target gene | Primer name | Sequence (5' – 3') | Reference |
|--|-------------|-------------------------------|----------------------------------|
| Genes encoding ESBLs | | | |
| SHV | bla-SHV.SE | ATGCGTTATATTCGCCTGTG | Monstein HJ et al. ²¹ |
| | bla-SHV.AS | TGCTTTGTTATTCGGGCCAA | |
| TEM | TEM-164.SE | TCGCCGCATACACTATTCTCAGAATGA | Monstein HJ et al. ²¹ |
| | TEM-165.AS | ACGCTCACCGGCTCCAGATTTAT | |
| CTX-M | CTX-M-U1 | ATGTGCAGYACCAGTAARGTKATGGC | Monstein HJ et al. ²¹ |
| | CTX-M-U2 | TGGGTRAARTARGTSACCAGAAYCAGCGG | |
| Genes encoding AmpC β-lactamases | | | |
| CMY | CMY-F | CAAGTTTGATTTCCTTGGACTCT | Chiu SK et al. ⁴ |
| | CMY-R | CTCATCGTCAGTTATTGCAGCT | |
| DHA-1 | DHA-1-F | CTGATGAAAAAATCGTTATC | Chiu SK et al. ⁴ |
| | DHA-1-R | ATCCAGTGCACCTCAAATA | |
| Genes encoding class A carbapenemases | | | |
| GES | GES-F | GCTTCATTACGCCTATT | Hong SS et al. ²² |
| | GES-MR | CGATGCTAGAAACCGCTC | |
| IMI/NMCA | IMI(NMC)-F1 | TGCGGTTCGATTGGAGATAAA | Hong SS et al. ²² |
| | IMI(NMC)-R1 | CGATTCTTGAAGCTTCTGCG | |
| SME | SME-F1 | ACTTTGATGGGAGGATTGGC | Hong SS et al. ²² |
| | SME-R1 | ACGAATTCGAGCATCACCAG | |
| KPC | KPCF2 | GTATCGCCGTCTAGTTCTGC | Hong SS et al. ²² |
| | KPCFR | GGTCGTGTTCCCTTTAGCC | |
| Genes encoding class B metalloenzymes | | | |
| IMP-1 | IMP-1-F | TGAGCAAGTTATCTGTATTC | Chiu SK et al. ⁴ |
| | IMP-1-R | TTAGTTGCTTGGTTTTGATG | |
| IMP-2 | IMP-2-F | GGCAGTCGCCCTAAAACAAA | Chiu SK et al. ⁴ |
| | IMP-2-R | TAGTTACTTGGCTGTGATGG | |
| NDM | NDM-F | TCTCGACAATGCCGGGTTT | Chiu SK et al. ⁴ |
| | NDM-R | GAGATTGCCGAGCGACTT | |
| Genes encoding class D oxacillinases | | | |
| OXA-48-type | OXA-48-F | TTGGTGGCATCGATTATCGG | Chiu SK et al. ⁴ |
| | OXA-48-R | GAGCACTTCTTTTGTGATGGC | |

eTable 2. Antibigrams, treatment outcomes and β -lactamase genes of nine isolates which were identified as susceptible to meropenem in customized broth microdilution assays. In every column of antibiotics, the left panels are minim inhibitory concentrations (MICs) obtained by automated antimicrobial susceptibility testing at the time of isolation, and the right panels are MICs obtained by customized broth microdilution assays at the time of this study.

| Site of isolation | Cefazolin | | Ceftriaxone | | Ceftazidime | | Cefepime | | Piperacillin-tazobactam | | Meropenem | | Treatment | Outcome | Gene of β -lactamase |
|-------------------|----------------|--------|-----------------|------------|-------------|----------|----------------|----------|-------------------------|------------|-----------------|------------|---------------------------------|----------|---|
| Blood | ≤ 4 | 2 | $\leq 2^*$ | ≤ 0.5 | ≤ 2 | ≤ 1 | ≤ 2 | ≤ 4 | 8/4 | $\leq 8/4$ | $> 8^\dagger$ | ≤ 0.5 | Amp-sulb | Death | <i>bla_{SHV}</i> |
| Urine | R [§] | > 16 | R ^{*§} | 8 | R | > 16 | R [§] | ≤ 4 | S [§] | $\leq 8/4$ | I ^{†§} | ≤ 0.5 | Ciprofloxacin | Survival | <i>bla_{SHV}, bla_{DHA-1}</i> |
| Blood | ≤ 4 | 2 | 4 | ≤ 0.5 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 4 | 8 | $\leq 8/4$ | 2 | ≤ 0.5 | Pip-tazo \rightarrow Imipenem | Survival | <i>bla_{SHV}</i> |
| Blood | ≥ 64 | > 16 | ≥ 64 | > 32 | ≥ 64 | > 16 | ≤ 1 | ≤ 4 | ≥ 128 | $> 128/4$ | 4 | ≤ 0.5 | Pip-tazo | Death | <i>bla_{SHV}, bla_{DHA-1}</i> |
| Urine | ≥ 64 | > 16 | ≥ 64 | 1 | ≥ 64 | 8 | 4 | ≤ 4 | ≥ 128 | $\leq 8/4$ | 4 | ≤ 0.5 | Cefazolin | Survival | <i>bla_{TEM}, bla_{DHA-1}</i> |
| Urine | ≥ 64 | > 16 | ≥ 64 | 16 | ≥ 64 | > 16 | 8 | ≤ 4 | ≥ 128 | 64/4 | 2 | ≤ 0.5 | Cefazolin | Survival | <i>bla_{TEM}, bla_{DHA-1}, bla_{CMY}</i> |
| Urine | ≥ 64 | > 16 | 4 | 4 | ≥ 64 | > 16 | ≤ 1 | ≤ 4 | 64 | $\leq 8/4$ | 2 | ≤ 0.5 | Cefmetazole | Survival | <i>bla_{TEM}, bla_{DHA-1}</i> |
| Urine | ≥ 64 | > 16 | 2 | 1 | 16 | 8 | ≤ 1 | ≤ 4 | 16 | $\leq 8/4$ | I [§] | ≤ 0.5 | Cefmetazole | Survival | <i>bla_{SHV}, bla_{DHA-1}</i> |
| Urine | ≥ 64 | > 16 | ≥ 64 | > 32 | 16 | > 16 | ≥ 64 | > 32 | ≥ 128 | $> 8/4$ | 4 | ≤ 0.5 | Ceftriaxone | Survival | <i>bla_{SHV}, bla_{TEM}, bla_{CTX-M}, bla_{DHA-1}</i> |

* MIC of cefotaxime.

† MIC of imipenem.

§ The antimicrobial susceptibility was determined by disk diffusion method.

Amp-sulb: ampicillin-sulbactam; Pip-tazo: piperacillin-tazobactam.