Plasmid-Mediated Fluoroquinolone Resistance in 
Pseudomonas aeruginosa and Acinetobacter baumannii

Geetha P. Venkataramana1 Aishwarya K.V. Lalitha1 Shanthi Mariappan1 Uma Sekar1

1 Department of Microbiology, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, Tamil Nadu, India

Abstract

Introduction Pseudomonas aeruginosa and Acinetobacter baumannii are important pathogens in health care-associated infections. Fluoroquinolone resistance has emerged in these pathogens. In this study, we aimed to determine the occurrence of plasmid-mediated quinolone resistance (PMQR) determinants (qnrA, qnrB, qnrS, aac(6')-Ib-cr, oqxAB, and qepA) by polymerase chain reaction (PCR) and the transmissibility of plasmid-borne resistance determinants in clinical isolates of P. aeruginosa and A. baumannii.

Materials and Methods The study included P. aeruginosa (85) and A. baumannii (45) which were nonduplicate, clinically significant, and ciprofloxacin resistant. Antibiotic susceptibility testing was done by disk diffusion method for other antimicrobial agents, namely amikacin, ceftazidime, piperacillin/tazobactam, ofloxacin, levofloxacin, and imipenem. Minimum inhibitory concentration of ciprofloxacin was determined. Efflux pump activity was evaluated using carbonyl-cyanide m-chlorophenylhydrazone (CCCP). The presence of PMQR genes was screened by PCR amplification. Transferability of PMQR genes was determined by conjugation experiment, and plasmid-based replicon typing was performed.

Results Resistance to other classes of antimicrobial agents was as follows: ceftazidime (86.9%), piperacillin/tazobactam (73.8%), imipenem (69.2%), and amikacin (63.8%). The minimal inhibitory concentration (MIC)50 and MIC90 for ciprofloxacin were 64 and greater than or equal to 256 µg/mL, respectively. There was a reduction in MIC for 37 (28.4%) isolates with CCCP. In P. aeruginosa, 12 (14.1%) isolates harbored qnrB, 12 (14.1%) qnrS, 9 (10.5%) both qnrB and qnrS, 66 (77.6%) aac(6')-Ib-cr, and 3 (3.5%) oqxAB gene. In A. baumannii, qnrB was detected in 2 (4.4%), 1 (2.2%) harbored both the qnrA and qnrS, 1 isolate harbored qnrB and qnrS, 21 (46.6%) aac(6')-Ib-cr, and 1 (2.2%) isolate harbored oqxAB gene. Notably, qepA gene was not detected in any of the study isolates. Conjugation experiments revealed that 12 (9.2%) were transferable. Of the transconjugants, seven (58.3%) belonged to IncFII type plasmid replicon, followed by four (33.3%) IncA/C and one (8.3%) IncFIC type.

Conclusion The plasmid-mediated resistance aac(6')-Ib-cr gene is primarily responsible for mediating fluoroquinolone resistance in clinical isolates of P. aeruginosa and A. baumannii. The predominant plasmid type is IncFII.
Introduction

Fluoroquinolones are synthetic antimicrobial agents with a broad spectrum of activity. They are effective against a wide range of gram-negative and gram-positive pathogenic bacteria. Over the past few years, fueled by their wide use, resistance to fluoroquinolones has raised globally. An important resistance mechanism to fluoroquinolones is described by mutations in the quinolone resistance-determining regions of gyrase and topoisomerase encoding genes. Another well-known fluoroquinolone resistance mechanism is the decreased intracellular drug accumulation by upregulation of efflux pumps or decreased expression of outer membrane porin. The emergence of plasmid-mediated quinolone resistance (PMQR) has been reported since 1998. These are horizontally transferable and are referred to as “PMQR.” The three PMQR genes include: (1) the qnr, (2) aac(6’)-Ib-cr (aminoglycoside acetyltransferase), and (3) oqxAB and qepA (efflux pumps).

The plasmid qnr genes (qnrA, qnrB, and qnrS) encode for proteins of the pentapeptide repeat family that protect DNA gyrase and topoisomerase intraviruses from fluoroquinolone inhibition. The aac(6’)-Ib-cr is a bifunctional variant of aminoglycoside acetyltransferase capable of modifying the fluoroquinolones that have an amino nitrogen on the C7 of piperazinyl ring, such as ciprofloxacin and norfloxacin, thereby reducing their activity. Other fluoroquinolones lacking an unsubstituted piperazinyl nitrogen are not affected. The plasmid-mediated qepA efflux pump belongs to the major facilitator superfamily that decreases susceptibility to hydrophilic fluoroquinolones, especially ciprofloxacin. The oqxAB encodes for efflux pumps belonging to the resistance nodulation division family and is a multidrug efflux pump.

Acinetobacter baumannii and Pseudomonas aeruginosa are well recognized representatives of nonfermenting gram-negative pathogens which are responsible for healthcare-acquired infections. In both species, resistance to fluoroquinolones has been a recognized problem due to their ready ability to acquire resistance determinants. Most studies on prevalence of PMQR genes are focused on Enterobacteriaceae. Data on the prevalence of PMQR genes among clinical isolates of P. aeruginosa and A. baumannii are scarce.

The presence of fluoroquinolone resistance genes on plasmid enables their spread to other bacterial species by horizontal gene transfer. The identification of related plasmids associated with specific resistance genes helps track the spread of resistant plasmids. Hence, polymerase chain reaction (PCR)-based replicon typing (PBRT) has been adopted worldwide as the method for plasmid identification and typing.

In this study, we aimed to determine the occurrence of PMQR determinants (qnrA, qnrB, qnrS, aac(6’)-Ib-cr, oqxAB, and qepA) by PCR and the transmissibility of these plasmid-borne resistance determinants in clinical isolates of P. aeruginosa and A. baumannii.

Materials and Methods

Bacterial Isolates

The study included P. aeruginosa (85) and A. baumannii (45) which were nonduplicate, clinically significant and ciprofloxacin resistant (as determined by disc diffusion test) and obtained from clinical specimens of hospitalized patients at university teaching hospital in South India. They were collected over a period of 1 year from July 2014 to June 2015. They were obtained from clinical specimens such as urine (5), exudative samples (66), respiratory secretions (47), and blood stream (12). The isolates were identified up to species level by automated system (VITEK2 GN-card; BioMerieux, Brussels, Belgium) and/or standard biochemical tests.

Antimicrobial Susceptibility Testing

Antibiotic susceptibility testing was done by Kirby–Bauer disc diffusion method for the following antimicrobials: cefazidime (30 µg), piperacillin/tazobactam (30 µg), imipenem (10 µg), amikacin (30 µg), levofloxacin (5 µg), and ofloxacin (5 µg) (Himedia Laboratories, India). The minimal inhibitory concentration (MIC) of ciprofloxacin was determined by agar dilution technique according to CLSI 2017 guidelines.

AtCC Escherichia coli 25922 was used as control for both disc diffusion method and MIC determination.

Phenotypic Detection of Efflux Pump Activity

To detect the presence of efflux pump mechanism, carbonylcyanide m-chlorophenylhydrazone (CCCP), the efflux pump inhibitor was added to each Muller–Hinton (MH) agar plate containing 0.125 to 256 µg/mL of ciprofloxacin. The fixed concentration of CCCP in the MH agar was 20 µg/mL. The MIC with CCCP incorporated was determined in twofold serial dilutions as for the antibiotic (CLSI 2017). A plate without antibiotic and containing only CCCP inhibitor was used as control. The criteria for the presence of efflux pump activity was based on a fourfold decrease in MIC of ciprofloxacin on addition of CCCP.

Polymerase Chain Reaction

The DNA of the study isolates was extracted by the boiling method. The amplification of qnr genes (qnrA, qnrB, and qnrS) was performed by multiplex PCR using the cyclic profile: initial denaturation at 94°C for 7 minutes; denaturation at 94°C for 50 seconds, annealing at 53°C for 40 seconds, and elongation at 72°C for 60 seconds, repeated for 35 cycles, and a final extension at 72°C for 5 minutes. The PCR conditions for acc(6’)-Ib-cr were: initial denaturation at 94°C for 7 minutes, denaturation at 94°C for 50 seconds, annealing at 55°C for 40 seconds, and elongation at 72°C for 60 seconds, repeated for 35 cycles, and a final extension at 72°C for 5 minutes. The PCR cyclic parameters for oqxAB were as follows: initial denaturation at 95°C for 15 minutes; 30 cycles of 94°C for 30 seconds, 63°C for 90 seconds, and 72°C for 90 seconds, followed by a final extension at 72°C for 10 minutes. The PCR conditions used for qepA were as follows: initial denaturation at 96°C for 1 minute, followed by 30 cycles of amplification at 96°C for 1 minute, annealing...
at 60°C for 1 minute, extension at 72°C for 1 minute, and the final extension step was at 72°C for 5 minutes. The primers used is given in Table 1.16–18 The PCR by-product was examined by electrophoresis in agarose gel containing ethidium bromide and visualized by gel documentation system.

DNA Sequencing
The PCR positive amplicons were sequenced at SciGenome Labs Pvt. Ltd., India and analyzed with BLAST tools (www.ncbi.nlm.nih.gov). The assigned GenBank accession number for the submitted sequences are: (1) MH709266 (qnrA); (2) KY130487 (qnrB); (3) KY130488 (qnrS); (4) MH709269 (acc(6′)-Ib-cr), and (5) MN273774 (oqxAB).

Conjugation
Conjugation experiments were performed for all PMQR positive isolates. Escherichia coli J53 Azir strain was used as the recipient and PMQR positive isolates as donor. The donor and recipient cells (0.5 mL each) in logarithmic phase were added to 3 mL of LB broth and incubated at 37°C overnight. Transconjugants were selected by plating on MacConkey agar plates containing sodium azide (100 µg/mL) and ciprofloxacin (0.5 µg/mL).19 The transfer of PMQR genes in transconjugants was confirmed by PCR.

Incompatibility Grouping of Plasmid Encoding Resistance for PMQR Genes
Plasmid Inc group for the transconjugants was determined by PBRT. Five sets of multiplex PCR ([H11, H12, I1]; [X, I/M, N]; [FIA, FIB, W]; [YP FIC]; [A/C, T, Flk]) and three simplex PCR (FrepB, K/B, B/O) were performed.13 The primers employed is depicted in Table 2.13

Results

Antimicrobial Susceptibility Testing
All the study isolates were resistant to other fluoroquinolones—levofloxacin and ofloxacin. Resistance to other classes of antimicrobial agents was as follows: ceftazidime (86.9%), piperacillin/tazobactam (73.8%), imipenem (69.2%), and amikacin (63.8%). The MIC of ciprofloxacin ranged from 4 to greater than or equal to 256 µg/mL. The MIC<sub>50</sub> and MIC<sub>90</sub> values were 64 and greater than or equal to 256 µg/mL, respectively.

Detection of Efflux Pump Activity
Among 130 isolates, twofold reduction was evident in 46 (35.8%) and fourfold or more reduction was observed in 37 (28.4%). Fourfold was evident in 11 (12.9%), 8-fold in 5 (5.8%), 16-fold in 7 (8.2%), 32-fold in 3 (3.5%), and 128 fold in 2 (2.3%) among P. aeruginosa. In A. baumannii, 4-fold reduction was observed in one (2.2%) isolate, 8-fold in three (6.6%), 16-fold in two (4.4%), and 64-fold in three (6.6%), respectively (Table 3).

Polymerase Chain Reaction
Among P. aeruginosa, qnr genes were detected in 36 (27.6%) isolates, of which 12 (14.1%) isolated harbored qnrB, 12 (14.1%) carried qnrS gene, and 9 (10.5%) isolates harbored both qnrB and qnrS genes. Among A. baumannii, qnrB was detected in two (4.4%) isolates and only one (2.2%) harbored both the qnrA and qnrS; 77.6% (66) of P. aeruginosa and 46.6% (21) of A. baumannii isolates harbored acc(6′)-Ib-cr gene; 3.5% (3) of P. aeruginosa and 2.2% (1) of A. baumannii isolates harbored oqxAB gene. qepA gene was not detected in any of the study isolates. The PMQR genes encountered is depicted in Table 4.

PMQR Gene Transfer and Distribution of Plasmid Replicons
In P. aeruginosa, 9.2% (12/130) were transferred successfully. All the 12 transconjugants were positive only for acc(6′)-Ib-cr gene. In A. baumannii, none of them was transferable.

The plasmid incompatibility types of the transconjugants were recognized by PBRT. Of the 12 transconjugants, 7 (58.3%) belonged to IncFII type plasmid replicon, 4 (33.3%) were IncA/C, and 1 (8.3%) IncFIC type.

Table 1 Primers used in this study

| PMQR gene | Primers                                                                 | Product size | Reference |
|-----------|-------------------------------------------------------------------------|-------------|-----------|
| qnrA      | 5′-TCAGCAAGAGGATTCTCA-3′; 5′-GCCGACACTATA CTCCC-3′                       | 516         | 16        |
| qnrB      | 5′-GATCGTGAAAGGACAGAAGG-3′; 5′-ACAGAT CCTGTAAGTCTGG-3′                   | 469         | 16        |
| qnrS      | 5′-ACGCACATCCGTCAACTGCAA-3′; 5′-TAAATGGCCACTCTGATGAC-3′                  | 417         | 16        |
| acc(6′)-Ib-cr | 5′-TTGAAAGCCGCGAGCGGAM-3′; 5′-ACACGGCTGGACCATA-3′                        | 260         | 17        |
| oqxAB     | 5′-CCGCAAGCGATAATTAAGTGC-3′; 5′-GCGAGGTGTTTGATAGTGGA-3′                  | 313         | 18        |
| qepA      | 5′-GCC GTT CCA CCA CGG GTT AG-3; 5′-CTT CCT GCC CGA GTA TCG TG-3          | 218         | 18        |

Abbreviation: PMQR, plasmid-mediated quinolone resistance.
Effect of CCCP on the ciprofloxacin MIC

| Organism (n = 130) | Fold reduction in MIC + CCCP (µg/mL) |
|-------------------|-------------------------------------|
|                   | 0   | 2    | 4    | 8    | 16   | 32   | 64   | 128  |
| Pseudomonas aeruginosa (n = 85) | 21  | 36   | 11   | 5    | 7    | 3    | 0    | 2    |
| Acinetobacter baumannii (n = 45) | 26  | 10   | 1    | 3    | 2    | 0    | 3    | 0    |

Abbreviations: CCCP, carbonyl-cyanide m-chlorophenylhydrazone; MIC, minimal inhibitory concentration.
In Brazil, a low prevalence of \( \text{aac}(6'\text{-})\text{-Ib-cr} \) gene (2.6%) was found in \( P. \text{aeruginosa} \). Studies from Turkey and Egypt reported a high prevalence 56.4 and 79.5% in \( P. \text{aeruginosa} \), respectively. This is similar to the findings of the present study (66.9%).\(^9\)\(^,\)\(^10\) In this study, only four (3%) isolates harbored \( \text{oqxAB} \). Notably, \( \text{qepA} \) gene was not encountered. \( \text{oqxAB} \) and \( \text{qepA} \) genes were not identified in many other studies too.\(^3\)\(^9\)\(^10\)

Conjugation experiments demonstrated that in 14.1% (12/85) of \( P. \text{aeruginosa} \), PMQR determinants were successfully transferred and all the transconjugants harbored the \( \text{aac}(6'\text{-})\text{-Ib-cr} \) gene. In \( A. \text{baumannii} \), none of them was transferable. Jiang et al in their study documented that in 33.3% of nonfermenting gram negative bacteria (NFGNB), the transconjugants harbored the same PMQR determinants as their donors.\(^4\)\(^2\) In this study, more than one half of PMQR determinants, 59.2% were non-conjugative, and this suggests that these genes may be of chromosomal location. Among the PMQR genes, high incidence of \( \text{aac}(6'\text{-})\text{-Ib-cr} \) (66.9%) was encountered and when conjugated, the transferability rate was 100% for this gene. This emphasizes that \( \text{aac}(6'\text{-})\text{-Ib-cr} \) gene plays a major role in mediating fluoroquinolone resistance. In the present study, of the 12 transconjugants, 33.3% belonged to IncA/C type plasmid replicon. In Nigeria, IncFII is the predominant plasmid type followed by IncFIC type.\(^7\)

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Conflict of Interest
None declared.

References
1. Wang M, Tran JH, Jacoby GA, Zhang Y, Wang F, Hooper DC. Plasmid-mediated quinolone resistance in clinical isolates of \( \text{Escherichia coli} \) from Shanghai, China. Antimicrob Agents Chemother 2003;47(07):2242–2248
2. Bonomo RA, Szabo D. Mechanisms of multidrug resistance in \( \text{Acinetobacter} \) species and \( P. \text{aeruginosa} \). Clin Infect Dis 2006;43(2, Suppl 2):S49–S56
3. Hooper DC, Jacoby GA. Mechanisms of drug resistance: quinolone resistance. Ann N Y Acad Sci 2015;1354(01):12–31
4. Martínez-Martínez L, Pascual A, Jacoby GA. Quinolone resistance from a transferable plasmid. Lancet 1998;351(9105):797–799
5. Robicsek A, Jacoby GA, Hooper DC. The worldwide emergence of plasmid-mediated quinolone resistance. Lancet Infect Dis 2006;6(10):629–640
6. Yamane K, Wachino J, Suzuki S, et al. New plasmid-mediated fluoroquinolone efflux pump, \( \text{QepA} \), found in an \( \text{Escherichia coli} \) clinical isolate. Antimicrob Agents Chemother 2007;51(09):3354–3360
7. Jacoby GA, Strahilevitz J, Hooper DC. Plasmid-mediated quinolone resistance. Microbiol Spectr 2014;2(05):10
8. Rodríguez-Martínez JM, Díaz de Alba P, Briales A, et al. Contribution of \( \text{OqxAB} \) efflux pumps to quinolone resistance in extended-

### Table 4 Distribution of PMQR genes

| PMQR genes                  | Pseudomonas aeruginosa (n = 85) | Acinetobacter baumannii (n = 45) | Total prevalence (n = 130) |
|-----------------------------|--------------------------------|----------------------------------|---------------------------|
| \( \text{aac}(6'\text{-})\text{-Ib-cr} \) | 31 (36.4%)                   | 17 (37.7%)                       | 48 (36.9%)                |
| \( \text{oqxAB} \)          | 1 (1.1%)                      | 1 (2.2%)                         | 2 (1.5%)                  |
| \( \text{qnrB} + \text{aac}(6'\text{-})\text{-Ib-cr} \) | 12 (14.1%)                   | 2 (4.4%)                         | 14 (10.7%)                |
| \( \text{qnrS} + \text{aac}(6'\text{-})\text{-Ib-cr} \) | 12 (14.1%)                   | 0                               | 12 (9.2%)                 |
| \( \text{qnrA} + \text{qnrS} + \text{aac}(6'\text{-})\text{-Ib-cr} \) | 0                             | 1 (2.2%)                         | 1 (0.7%)                  |
| \( \text{qnrB} + \text{qnrS} + \text{aac}(6'\text{-})\text{-Ib-cr} \) | 9 (10.5%)                    | 1 (2.2%)                         | 10 (7.6%)                 |
| \( \text{qnrB} + \text{qnrS} + \text{oqxAB} + \text{aac}(6'\text{-})\text{-Ib-cr} \) | 1 (1.1%)                      | 0                               | 1 (0.7%)                  |
| \( \text{oqxAB} + \text{aac}(6'\text{-})\text{-Ib-cr} \) | 1 (1.1%)                      | 0                               | 1 (0.7%)                  |
| **Total**                  | **67 (78.8%)**                | **22 (48.8%)**                   | **89 (68.5%)**            |

Abbreviation: PMQR, plasmid-mediated quinolone resistance.
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spectrum-β-lactamase-producing Klebsiella pneumoniae. J Anti-

Rodríguez-Martínez JM, Cano ME, Velasco C, Martínez-Martínez

L, Pascual A. Plasmid-mediated quinolone resistance: an update. J

Infect Chemother 2011;17(02):149–182

Yang H, Chen H, Yang Q, Chen M, Wang H. High prevalence of

plasmid-mediated quinolone resistance genes qnr and aac(6′)-Ib-
cr in clinical isolates of Enterobacteriaceae from nine teaching

hospitals in China. Antimicrob Agents Chemother 2008;52(12):

4268–4273

Zhu YL, Yang H-F, Liu YY, et al. Detection of plasmid-mediated

quinolone resistance gene. Int J Antimicrob Agents 2010;36(05):

476–481

Infect Dev Ctries 2016;10(06):600

40

Diagn Microbiol Infect Dis 2013;75(03):327–329

14

Clinical and Laboratory Standards Institute. Performance Stan-

ards for Antimicrobial Susceptibility Testing. M100. 27th ed.

Wayne (PA): Clinical and Laboratory Standards Institute; 2017

15

Ardebili A, Talebi M, Azimi L, Rastegar Lari A. Effect of efflux pump

inhibitor carbonyl cyanide 3-chlorophenylhydrazone on the

minimum inhibitory concentration of ciprofloxacin in Acinetobacter

baumannii clinical isolates. Jundishapur J Microbiol 2014;7(01):

e6891

16

Robicsek A, Strahilevitz J, Sahm DF, Jacoby GA, Hooper DC. qnr

prevalence in cefazidime-resistant Enterobacteriaceae isolates from

the United States. Antimicrob Agents Chemother 2006;50

(08):2872–2874

17

Wareham DW, Umoren I, Khanna P, Gordon NC. Allele-specific

polymerase chain reaction (PCR) for rapid detection of the aac

(6′)-Ib-cr quinolone resistance gene. Int J Antimicrob Agents

2010;36(05):476–477

18

Saleh MA, Balboula MM. Plasmid mediated quinolone resistance

determinants among nosocomial clinical Pseudomonas aerugi-
nosa isolates. Int J Curr Microbiol Appl Sci 2017;6(01):42–50

19

Wang M, Tran JH, Jacoby GA, Zhang Y, Wang F, Hooper DC.

Plasmid-mediated quinolone resistance in clinical isolates of

Escherichia coli from Shanghai, China. Antimicrob Agents Chem-

other 2003;47(07):2242–2248

20

Pham TDM, Ziora ZM, Blakovich MAT. Quinolone antibiotics.

MedChemComm 2019;10(10):1719–1739

21

Navon-Venezia S, Ben-Ami R, Carmeli Y. Update on Pseudomonas

aeruginosa and Acinetobacter baumannii infections in the health-
care setting. Curr Opin Infect Dis 2005;18(04):306–313

22

Zaki MES, Abou ElKheir N, Mofreh M. Molecular study of quinol-
one resistance determining regions of gyrA gene and parC genes

in clinical isolates of Acinetobacter baumannii resistant to fluoro-
quino酮. Open Microbiol J 2018;12:116–122

23

Chen H, Pillay B, Pillay D. Analysis of the mechanisms of

fluoroquinolone resistance in urinary tract pathogens. J Anti-

microb Chemother 2006;58(06):1274–1278

24

Osei Sekyere J, Amoako DG. Genomic and phenotypic characteri-
sation of fluoroquinolone resistance mechanisms in Enterobacte-

riaceae in Durban, South Africa. PLoS One 2017;12(06):

e0178888

25

Nikaido H, Pagès JM. Broad-spectrum efflux pumps and their role

in multidrug resistance of Gram-negative bacteria. FEMS Micro-
bioi Rev 2012;36(02):340–363

26

Talebi-Taher M, Majdpour A, Golamı A, Rasouli-Kough S, Adabi

M. Role of efflux pump inhibitor in decreasing antibiotic cross-

resistance of Pseudomonas aeruginosa in a burn hospital in Iran.

J Infect Dev Ctries 2016;10(06):600–604

27

Al Rashed N, Joji RM, Saeed NK, Bindayna KM. Detection of overexpression of efflux pump expression in fluoroquinolone-

resistant Pseudomonas aeruginosa isolates. Int J Appl Basic Med

Res 2020;10(01):37–42

28

Helmy OM, Kashef MT. Different phenotypic and molecular

characteristics associated with multidrug resistance in Gram-

negative clinical isolates from Egypt. Infect Drug Resist 2017;

10:479–498

29

Gomaa FM, Tawakol WM, El-Azm FI. Phenotypic and genotypic
detection of some antimicrobial resistance mechanisms among

multidrug-resistant Acinetobacter baumannii isolated from immu-

nocompromised patients in Egypt. J Med Microbiol 2014;23(04):

99–111

30

El-Badawy MF, Alrobaian MM, Shohayeb MM, Abdelwahab SF.

Investigation of six plasmid-mediated quinolone resistance genes

among clinical isolates of Pseudomonas: a genotypic study in

Saudi Arabia. Infect Drug Resist 2019;12:915–923

31

Rafiq K, Ahmad K, Ahmad N, Gohar M, Shehzad MA, Saeed MQ.

Determination of Qnr allele frequencies in fluoroquinolone resist-
tant Pseudomonas aeruginosa isolated from burned wounds. J Pak

Med Assoc 2019;68(02):250–252

32

Yang X, Xing B, Liang C, Ye Z, Zhang Y. Prevalence and fluoroquin-

olone resistance of Pseudomonas aeruginosa in a hospital in South

China. Int J Clin Exp Med 2015;8(01):1386–1390

33

Nazik H, Ongen B, Kuvat N. Investigation of plasmid-mediated

quinolone resistance among isolates obtained in a Turkish inten-
sive care unit. Jpn J Infect Dis 2008;61(04):310–312

34

Coban AY, Tanriverdi Çayçi Y, Yildırım T, Erturan Z, Durupınar B,

Bozdoğan B. Investigation of plasmid-mediated quinolone resist-

ance in Pseudomonas aeruginosa strains isolated from cystic fibrosis

patients [in Turkish]. Mikrobiyol Bul 2011;45(04):602–608

35

Hamed SM, Elkhatabt WF, El-Mahallawy HA, Helmy MM, Ashour

MS, Aboshaab KMA. Multiple mechanisms contributing to cip-

rofloxacin resistance among Gram negative bacteria causing

infections to cancer patients. Sci Rep 2018;8(01):12268

36

Touati A, Brasme L, Benallaloua S, Charout A, Madoux J, De Champs

C. First report of qnrB-producing Enterobacter cloacae and qnrA-

producing Acinetobacter baumannii recovered from Algerian hos-

pitals. Diagn Microbiol Infect Dis 2008;60(03):287–290

37

Araujo BF, Ferreira ML, Campos PA, et al. Clinical and molecular
epidemiology of multidrug-resistant P. aeruginosa carrying aac

(6′)-Ib-cr, qnrS1 and blaSM genes in Brazil. PLoS One 2016;11

(05):e0155914

38

Çayci YT, Coban AY, Gunaydin M. Investigation of plasmid-medi-

ated quinolone resistance in Pseudomonas aeruginosa clinical isolates.

Indian J Med Microbiol 2014;32(03):285–289

39

Jafari M, Fallah F, Borhan RS, et al. The first report of CMY, aac

(6′)-lb and 16S rRNA methylase genes among Pseudomonas aerugi-
nosa isolates from Iran. Arch Pediatr Infect Dis 2013;1(03):

109–112

40

Xue-qing Z, Dan-ping L, Chun-quan X, et al. Detection of plasmid-

mediated quinolone resistance determinants in clinical non-

fermentative bacteria and ciprofloxacin sensitive Enterobacter-

iaceae strains. Dis Surveill 2014;29(02):130–135

41

Michalska AD, Sacha PT, Ojdana D, Wieczorek A, Tryniszeswska E.

Prevalence of resistance to aminoglycosides and fluoroquinolone-

s among Pseudomonas aeruginosa strains in a University Hospital

in Northeastern Poland. Braz J Microbiol 2015;46(04):

1455–1458

42

Jiang X, Yu T, Jiang X, Zhang W, Zhang L, Ma J. Emergence of

plasmid-mediated quinolone resistance genes in clinical isolates of

Acinetobacter baumannii and Pseudomonas aeruginosa in Henan,

China. Diagn Microbiol Infect Dis 2014;79(03):381–383

43

Ogbolu DO, Daini OA, Ogunledun A, Terry Alli OA, Webber MA.

Dissemination of IncF plasmids carrying beta-lactamase genes in

Gram-negative bacteria from Nigerian hospitals. J Infect Dev

Ctries 2013;7(05):382–390

44

Elena A, Quinteros M, Di Conza J, Gutkind G, Cejas D, Radice MA.

Full characterization of an IncR plasmid harboring qnrS1
recovered from a VIM-11-producing *Pseudomonas aeruginosa*. Rev Argent Microbiol 2020;52(04):298–304

45 Ogbolu DO, Alli AO, Anorue MC, Daini OA, Oluwadun A. Distribution of plasmid-mediated quinolone resistance in Gram-negative bacteria from a tertiary hospital in Nigeria. Indian J Pathol Microbiol 2016;59(03):322–326

46 Castanheira M, Mendes RE, Jones RN. Update on *Acinetobacter* species: mechanisms of antimicrobial resistance and contemporary in vitro activity of minocycline and other treatment options. Clin Infect Dis 2014;59(6, suppl 6):S367–S373