Egyptian Journal of Medical Microbiology Volume 33 / No.3 / July 2024 119-124 Online ISSN: 2537-0979

ORIGINAL ARTICLE

Characterization of Aminoglycoside-resistant *Enterobacteriaceae* Isolated from Inanimate Hospital Surfaces in Egypt

[1]Amr H. Fahmy, [2]Khaled A. El-Dogdog, [1]El-Sayed T. Abd-Elsalam, [1]Mohamed G. Salah*
[1]Botany and Microbiology Department, Faculty of Science, Cairo University, 12613 Giza, Egypt
[2]Microbiology Department, Faculty of Agriculture, Ain Shams University

Key words:
Aminoglycoside resistance; Inanimate surface; Enterobacteriaceae prevalence, Nosocomial infection

Corresponding Author:
Mohamed G. Salah
Botany and Microbiology Department, Faculty of Science, Cairo University, 12613 Giza, Egypt
farahat@sci.cu.edu.eg

ABSTRACT

Background: *The emergence of antibiotic resistance is one of the major issues facing global healthcare systems.* ***Objectives:*** *This study aims to determine the prevalence and resistance profiles of Enterobacteriaceae isolated from inanimate surfaces of an Egyptian hospital.* ***Methodology:*** *MALDI-TOF identified Gram-negative bacteria and the antibiotic resistance profile of Enterobacteriaceae isolates was determined by Vitek 2 system.* ***Results:*** *From the inanimate surfaces, 266 isolates of Gram-negative nosocomial bacteria were identified of which 175 (65.79%) belonged to Enterobacteriaceae. The most frequently isolated bacteria were Klebsiella pneumoniae (n=72), followed by Escherichia coli (n=65) while Acinetobacter baumannii (n=54) and Pseudomonas aeruginosa (n=21) were the dominant non-Enterobacteriaceae isolates. Moreover, the Enterobacteriaceae isolates exhibited high degrees of resistance against aminoglycosides, penicillins, and carbapenem. In addition, various aminoglycoside-resistance genes were detected by the polymerase chain reaction (PCR). Results revealed that most Enterobacteriaceae isolates harbours aac(3')-Ib gene (89.1%) followed by aph(3')-Ia (52.5%) and aac(3)-II (50.2%).* ***Conclusion:*** *Our findings demonstrate that inanimate surfaces may be potential reservoirs of resistant Gram-negative bacteria, which directly threaten hospitalized patients.*

INTRODUCTION

The alarming rise in antibiotic-resistant bacteria continues to be a critical challenge for global healthcare systems. Within this context, the decreased susceptibility of *Enterobacteriaceae* to aminoglycosides, particularly amikacin, has emerged as a pressing concern.[1] Amikacin, a crucial aminoglycoside antibiotic, is often employed as a familiar treatment for severe infections caused by multi-drug resistant (MDR) Gram-negative bacteria.[2] However, the efficacy of amikacin is increasingly being compromised by emergence of resistant *Enterobacteriaceae* strains. This resistance is predominantly mediated by certain genes that encode aminoglycoside-modifying enzymes (AMEs) or induce target site modifications.[3] Recent reports highlighted the alarming rise in amikacin resistance among *Enterobacteriaceae* isolates globally.[4] The genetic underpinnings of this resistance are multifaceted, involving several mechanisms. A primary mechanism is mediated by AMEs, such as aminoglycoside acetyltransferases (AACs), which chemically modify amikacin, thereby preventing its interaction with the bacterial ribosome.[5] Moreover, the acquisition of resistance genes facilitates their rapid dissemination across diverse bacterial species and environments. Notably, the aac(6')-Ib gene, encoding an aminoglycoside acetyltransferase, and other AMEs genes were frequently identified in clinical isolates of *Enterobacteriaceae*.[6,7]

The persistence and transmission of pathogenic bacteria in healthcare settings pose significant challenges to infection control and patient safety. Current research has demonstrated how inanimate hospital surfaces (IHS) influence the spread of *Enterobacteriaceae*, emphasizing the significance that environmental contamination plays in the epidemiology of hospital-acquired infections (HAIs).[8] In healthcare environments, the IHS such as bed rails, door knobs, and other frequently touched surfaces can be potential reservoirs of various pathogens including *enterobacteriaceae*. These surfaces can harbor pathogenic bacteria for extended periods, facilitating their transfer to patients, healthcare workers, and visitors.[9,10] The direct contact with contaminated surfaces by patients or healthcare workers can lead to transfer of bacteria to hands and subsequently to other surfaces or individuals. This paper aims to investigate the frequency of *Enterobacteriaceae* contamination on IHS and explore their antibiotic susceptibility patterns and aminoglycoside-resistance genes.

METHODOLOYG

Isolation and identification of bacteria

Samples were collected from exposed IHS at the surgical intensive care unit (Cairo University teaching hospital), from January 2021 to June 2022. Practically, 200 samples were collected from doorknobs, drawer handles, nurse call buttons, bedside tables, bed rails, sinks, and faucets using sterile cotton swabs. Subsequently, swabs were streaked on MacConkey agar plates (Condalab, Spain) and the plates were incubated at 35-37 °C. After 24-48 h, the developed colonies were picked and identified by matrix-assisted laser desorption-ionization time-of-flight (MALDI-TOF) mass spectrometry using a Microflex LT device and Biotyper software (Bruker Daltonics, Germany). [11]

Antimicrobial susceptibility testing

All *Enterobacteriaceae* isolates were subjected to antimicrobial susceptibility testing using the VITEK 2® automated equipment (bioMérieux, France) with Vitek2® Gram Negative Susceptibility cards (AST-GN67). The tested antibiotics were amikacin, ampicillin, ampicillin/sulbactam, cefazolin, cefepime, ceftazidime, ceftriaxone, ciprofloxacin, ertapenem, gentamicin, imipenem, levofloxacin, nitrofurantoin, piperacillin/tazobactam, tobramycin, and trimethoprim/sulfamethoxazole.

Detection of aminoglycoside-modifying genes

The presence of six aminoglycoside-resistance genes (*aac(3)-II*, *aac(6')-Ib*, *aac(6')-II*, *ant(3")-I*, *aph(3')-Ia* and *aph(3')-VI*) was detected through polymerase chain reaction (PCR) with specific primers listed in Table 1, according to previously described method.[12,13] Total DNA was extracted by the boiling lysis method.[14] In brief, fresh bacterial colony was picked by a sterile toothpick, suspended in 100 µl of nuclease-free water and boiled in a thermal block for 10 min. Following centrifugation at 16,000 rpm for 5 min, the supernatant was used as DNA template. Amplicons were analyzed by electrophoresis in 1.5% agarose gel and DNA bands of expected sizes were gel-purified and sequenced.[15]

Table 1: Primer sequences for detection of aminoglycoside resistance genes

Target gene	Primer sequence (3' → 5')	Amplicon size (bp)
aac(3)-II	F: ATATCGCGATGCATACGCGG	877
	R: GACGGCCTCTAACCGGAAGG	
aac(6')-Ib	F: TTGCGATGCTCTATGAGTGGCTA	472
	R: CTCGAATGCCTGGCGTGTTT	
aac(6')-II	F: CGACCATTTCATGTCC	542
	R: GAAGGCTTGTCGTGTTT	
ant(2")-I	F: CACAACGCAGGTCATT	220
	R: CGCTAAGAATCCATAGTCCAA	
aph(3')-Ia	F: CGAGCATCAAATGAAACTGC	623
	R: GCGTTGCCAATGATGTTACAG	
aph(3')-VI	F: ATGGAATTGCCCAATATTATT	780
	R: TCAATTCAATTCATCAAGTTT	

RESULTS

Prevalence of Bacteria

During this study, 200 swab samples were collected from various surfaces including doorknobs, drawer handles, nurse call buttons, bedside tables, bed rails, sinks, and faucets of the hospital. Of these swab samples, 192 (96.6%) were positive for growth on MacConkey agar, recovering presumptive Gram-negative bacteria. Overall, 266 bacterial colonies were recovered and subsequently identified. Of the 266 bacterial isolates, 175 (65.79%) belonged to *Enterobacteriaceae*, and the rest (n=91; 34.21%) were non-*Enterobacteriaceae* Gram-negative bacteria. MALDI-TOF/MS identification revealed 14 nosocomial bacterial species belonging to 11 genera (Table 2). Of which, seven species belonged *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Citrobacter freundii*, *Citrobacter koseri*, *Proteus mirabilis*, and *Raoultella ornithinolytica*). Oppositely, seven non-*Enterobacteriaceae* species (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Acinetobacter haemolyticus*, *Burkholderia cenocepacia*, *Aeromonas hydrophila*, *Morganella morganii*, *and Providencia stuartii*) were identified. According to the findings, the most common isolates were *K. pneumoniae* (27.06%), *E. coli* (24.43%), and *A. baumannii* (20.30%).

Table 2: Prevalence of Enterobacteriaceae isolates

Isolates		n	%
Enterobacteriaceae	*Escherichia coli*	65	24.43
	Klebsiella pneumoniae	72	27.06
	Klebsiella oxytoca	23	8.64
	Citrobacter freundii	7	2.63
	Citrobacter koseri	4	1.50
	Proteus mirabilis	3	1.12
	Raoultella ornithinolytica	1	0.37
Non-Enterobacteriaceae	*Acinetobacter baumannii*	54	20.30
	Pseudomonas aeruginosa	21	7.89
	Acinetobacter haemolyticus	6	2.25
	Burkholderia cenocepacia	5	1.87
	Aeromonas hydrophila	3	1.12
	Morganella morganii	1	0.37
	Providencia stuartii	1	0.37
Total		266	100

Antibiogram Profile

The antibiogram profiles of all *Enterobacteriaceae* isolates against16 antibiotics were investigated using Vitek 2 system and the antibiograms were tabulated (table 3). The *Enterobacteriaceae* isolates exhibited high resistance against most of the investigated antibiotics, especially, aminoglycosides, penicillins, and carbapenem. Regarding aminoglycosides, 171 (97.7%), 160 (91.4%), and 152 (86.8%) of the investigated isolates were resistant to gentamicin, tobramycin, and amikacin, respectively. In addition, all the investigated isolates were ampicillin-resistant (100%), and 83.4% of the isolates exhibited resistance to ampicillin/sulbactam. In addition, the isolates showed remarkable resistance to trimethoprim/sulfamethoxazole (92.5%), nitrofurantoin (80%), cefazolin (67.4%), and imipenem (48%), respectively. The low resistance rates were observed against piperacillin/tazobactam (15/175; 8.5%), ertapenem (16/175; 9.1%), and cefepime (17/175; 9.7%).

Table 3: Antibiotic-susceptibility patterns of *Enterobacteriaceae* isolates

Antimicrobial Categories	Antimicrobial Agents	Number of Isolates		
		S	I	R
Aminoglycosides	Amikacin (AN)	23/175	0/175	152/175
	Gentamicin (GM)	4/175	0/175	171/175
	Tobramycin (TM)	15/175	0/175	160/175
Penicillin	Ampicillin (AM)	0/175	0/175	175/175
Penicillin with β-lactamase inhibitor	Piperacillin/tazobactam (TZP)	160/175	0/175	15/175
	Ampicillin/sulbactam (SAM)	29/175	0/175	146/175
First-generation cephalosporin	Cefazolin (CZ)	57/175	0/175	118/175
Third-generation cephalosporin	Ceftazidime (CAZ)	88/175	0/175	87/175
	Ceftriaxone (CRO)	136/175	4/175	35/175
Fourth-generation cephalosporin	Cefepime (FEP)	158/175	0/175	17/175
Fluoroquinolones	Ciprofloxacin (CIP)	111/175	6/175	58/175
	Levofloxacin (LEV)	133/175	0/175	42/175
Carbapenem agents	Ertapenem (ETP)	159/175	0/175	16/175
	Imipenem (IPM)	91/175	0/175	84/175
Nitrofuran derivative	Nitrofurantoin (FT)	30/175	5/175	140/175
Diaminopyrimidine with sulfonamide	Trimethoprim/Sulfamethoxazole (SXT)	7/175	6/175	162/175

Prevalence of aminoglycosides-resistance genes

The most frequent resistance genes was *aac*(3′)-Ib (156/175; 89.1%) followed by *aph*(3′)-Ia (92/175; 52.5%) and *aac(3)-II* (88/175; 50.2%). Our results revealed that frequencies of *aph(3')-VI, ant(2")-I* and *aac(6')-II* in the investigated isolates were 29.7% (n=52/175), 21.1% (n=37/175), and 13.7% (n=24/175), respectively (table 4).

Tale 4: Distribution of aminoglycoside resistance genes among *Enterobacteriaceae* isolates

Gene	n	%
aac(3)-II	88/175	50.2
aac(6')-Ib	156/175	89.1
aac(6')-II	24/175	13.7
ant(2")-I	37/175	21.1
aph(3')-Ia	92/175	52.5
aph(3')-VI	52/175	29.7

DISCUSSION

The contaminated IHS are known sources of infections, and the germs can spread epidemically throughout hospital divisions. In this regard, a number of research have demonstrated the significant role of the IHS in spreading various nosocomial pathogens.[16,17] It has been suggested that patients may come into direct contact with polluted patient-care equipment, increasing their risk of contracting diseases, especially, with resistant types of bacteria that made it more difficult to provide medicines to treat bacterial infections.[18–20] This article addresses the implementation of MALDI-TOF/MS to identify the recovered bacteria from the IHS at Cairo University Hospital and highlights the resistance profiles of nosocomial *Enterobacteriaceae* isolates, with emphasis on their aminoglycoside-resistance genes. In this work, we found significant bacterial contamination on the IHS and equipment. Out of 200 environmental samples from swabs, 192 (96.6%) were positive for bacterial contamination. In a similar study, 223 bacterial isolated were retrieved from 137 IHS samples including bedrails, bedside table, washbasin, and hydro-alcoholic solution/soap dispensers at Edouard Herriot Hospital in France.[21] These findings agree with several studies reporting that IHS can serve as reservoirs of nosocomial pathogens.[22,23] We observed that 65.79% of the isolates belonged to *Enterobacteriaceae* and *Klebsiella* spp. were the most frequent bacteria (54.2%) followed by *E. coli* (24.43%). Noteworthy, *Acinetobacter* spp. were the most prevailing non-*Enterobacteriaceae* bacteria (34.2%) followed by *P. aeruginosa* (7.8%). These results are in harmony with previous studies reporting the high prevalence of *Klebsiella* spp., *E. coli*, *Acinetobacter* spp., and *P. aeruginosa* on the IHS as the most dominant nosocomial pathogens.[24–27] Inadequate application of common precautions including hand hygiene and contact precautions and the transfer of the organisms through airflow, could be the main causes of higher levels of bacterial contamination.

This study shed light on the higher non-susceptibility percentages to various antibiotics including the three investigated aminoglycosides; gentamicin, tobramycin, and amikacin. Our results about resistance to gentamicin, tobramycin, and amikacin were consistent with previous studies.[28,29] However amikacin, gentamycin, and tobramycin are among the first choices for treating Gram-negative infections, it has been reported that the rate of aminoglycoside-resistant *Enterobacteriaceae* has been rising globally due to the overuse of aminoglycosides.[30,31] In the present study, the most prevalent aminoglycoside-resistance gene was *aac(6')-Ib*, followed by *aph(3')-Ia* and *aac(3)-II*. The most established aminoglycoside-resistance mechanisms are mediated by enzymes that are responsible for modifying aminoglycosides such as O-adenyltransferases (ANT), N-acetyltransferases (AAC), and O-phosphotransferases (APH) and other AME-encoding genes including *aac(3)-II*, *aac(6')-I*, *ant(3")-I*, *aph(3')-II*, and *ant(2")-I*.[32–39]

CONCLUSION

This investigation demonstrated the contamination of various surfaces and equipment with antibiotic resistance bacteria that can persist on the IHS and may be spread to patients and workers. Our results highlight the importance of appropriate infection control strategies, with a focus on methods for surface disinfection and/or decontamination to prevent potential outbreaks resulting from spread of MDR bacteria.

Declarations:
Consent for publication: Not applicable
Acknowledgment: Not applicable
Conflicts of Interest: The authors declare no conflict of interest.
Funding: Authors did not receive any grants from funding agencies.
Availability of data and material: Data is provided within the manuscript and other data are available upon request.

REFERENCES

1. Oliva A, Yusuf E, Mularoni A, Thy M, Timsit JF, De Montmollin E. Aminoglycosides for the Treatment of Severe Infection Due to Resistant Gram-Negative Pathogens. Antibiotics, 2023; 12(5), 860. doi:10.3390/ANTIBIOTICS12050860
2. Rodrigues D, Baldissera GS, Mathos D, Sartori A, Zavascki AP, Rigatto MH. Amikacin for the treatment of carbapenem-resistant Klebsiella pneumoniae infections: clinical efficacy and toxicity. Brazilian Journal of Microbiology, 2021; 52(4), 1913-1919. doi:10.1007/S42770-021-00551-X/FIGURES/1
3. Zhang Y, Zhang N, Wang M, et al. The prevalence and distribution of aminoglycoside resistance genes. Biosafety and Health, 2023; 5(1), 14-20. doi:10.1016/J.BSHEAL.2023.01.001
4. Pham HN, Than TDN, Nguyen HA, Vu DH, Phung TH, Nguyen TK. Antibiotic Resistance, Biofilm Formation, and Persistent Phenotype of Klebsiella pneumoniae in a Vietnamese Tertiary Hospital: A Focus on Amikacin. Microbial Drug Resistance, 2024; 30(5), 203-209. doi:10.1089/MDR.2023.0267
5. Zárate SG, De La Cruz Claure ML, Benito-Arenas R, Revuelta J, Santana AG, Bastida A. Overcoming Aminoglycoside Enzymatic Resistance: Design of

Novel Antibiotics and Inhibitors. Molecules, 2018; 23(2), 284. doi:10.3390/MOLECULES23020284

6. Butler DA, Rana AP, Krapp F, et al. Optimizing aminoglycoside selection for KPC-producing Klebsiella pneumoniae with the aminoglycoside-modifying enzyme (AME) gene aac(6')-Ib. Journal of Antimicrobial Chemotherapy, 2021; 76(3), 671-679. doi:10.1093/JAC/DKAA480
7. Ghotaslou R, Yeganeh Sefidan F, Akhi MT, Asgharzadeh M, Mohammadzadeh Asl Y. Dissemination of Genes Encoding Aminoglycoside-Modifying Enzymes and armA Among Enterobacteriaceae Isolates in Northwest Iran. Microbial Drug Resistance, 2017; 23(7), 826-832. doi:10.1089/MDR.2016.0224
8. Patelarou AE, Mechili EA, Tchounwou PB, et al. Gram-Negative Rods on Inanimate Surfaces of Selected Hospital Facilities and Their Nosocomial Significance. International Journal of Environmental Research and Public Health, 2022; 19(10), 6039. doi:10.3390/IJERPH19106039
9. Moniruzzaman M, Hussain MT, Ali S, et al. Multidrug-resistant Escherichia coli isolated from patients and surrounding hospital environments in Bangladesh: A molecular approach for the determination of pathogenicity and resistance. Heliyon, 2023; 9(11), e22109. doi:10.1016/J.HELIYON.2023.E22109
10. Abriouel H, Manetsberger J, Lavilla Lerma L, et al. Metagenomic insights into microbial contamination in critical healthcare environments and the efficacy of a novel "HLE" disinfectant. Infection, Disease & Health, 2023; 28(4), 282-289. doi:10.1016/J.IDH.2023.07.002
11. Farahat MG. Enhancement of β-Cyclodextrin Production and Fabrication of Edible Antimicrobial Films Incorporated with Clove Essential Oil/β-cyclodextrin Inclusion Complex. Microbiology and Biotechnology Letters, 2020; 48(1), 12-23. doi:10.4014/MBL.1909.09016
12. Hu X, Xu B, Yang Y, et al. A high throughput multiplex PCR assay for simultaneous detection of seven aminoglycoside-resistance genes in Enterobacteriaceae. BMC Microbiology, 2013; 13(1), 1-9. doi:10.1186/1471-2180-13-58/TABLES/5
13. Mokhtari H, Eslami G, Zandi H, Dehghan-Banadkouki A, Vakili M. Evaluating the Frequency of aac(6′)-IIa, ant(2″)-I, intl1, and intl2 Genes in Aminoglycosides Resistant Klebsiella pneumoniae Isolates Obtained from Hospitalized Patients in Yazd, Iran. Avicenna Journal of Medical Biotechnology, 2018; 10(2), 115. Accessed June 18, 2024. /pmc/articles/PMC5960057/
14. Ghaith DM, Mohamed ZK, Farahat MG, Aboulkasem Shahin W, Mohamed HO. Colonization of intestinal microbiota with carbapenemase-producing Enterobacteriaceae in paediatric intensive care units in Cairo, Egypt. Arab Journal of Gastroenterology, 2019; 20(1), 19-22. doi:10.1016/j.ajg.2019.01.002
15. Kamel Z, Mohamed NM, Farahat MG. Optimization of culture conditions for production of B-galactosidase by Bacillus megaterium NM56 isolated from raw milk. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2016; 7(1), 366-376.
16. Patelarou AE, Mechili EA, Tchounwou PB, et al. Gram-Negative Rods on Inanimate Surfaces of Selected Hospital Facilities and Their Nosocomial Significance. International Journal of Environmental Research and Public Health, 2022; 19(10), 6039. doi:10.3390/IJERPH19106039
17. Birru M, Mengistu M, Siraj M, et al. Magnitude, Diversity, and Antibiograms of Bacteria Isolated from Patient-Care Equipment and Inanimate Objects of Selected Wards in Arba Minch General Hospital, Southern Ethiopia. Research and Reports in Tropical Medicine, 2021; 12, 39-49. doi:10.2147/RRTM.S301215
18. Tenover FC, Nicolau DP, Gill CM. Carbapenemase-producing Pseudomonas aeruginosa –an emerging challenge. Emerging Microbes & Infections, 2022; 11(1), 811-814. doi:10.1080/22221751.2022.2048972
19. Fadl MG, Farahat MG, Mohamed ZK. Optimum Biosorption and Resistance of Uranium by Metal-Resistant Bacteria Isolated from Rock Ore. Geomicrobiology Journal, 2022; 39(8), 689-696. doi:10.1080/01490451.2022.2069892
20. Freitas AR, Werner G. Nosocomial Pathogens and Antimicrobial Resistance: Modern Challenges and Future Opportunities. Microorganisms, 2023; 11(7), 1685. doi:10.3390/MICROORGANISMS11071685
21. Kuczewski E, Henaff L, Regard A, et al. Bacterial Cross-Transmission between Inanimate Surfaces and Patients in Intensive Care Units under Real-World Conditions: A Repeated Cross-Sectional Study. International Journal of Environmental Research and Public Health, 2022; 19(15), 9401. doi:10.3390/IJERPH19159401
22. Osman AH, Darkwah S, Kotey FCN, et al. Reservoirs of Nosocomial Pathogens in Intensive Care Units: A Systematic Review. Environmental Health Insights, 2024; 18. doi:10.1177/11786302241243239/ASSET/IMAGES/LARGE/10.1177_11786302241243239-FIG1.JPEG
23. Thompson E, Badu AT, Abban E, et al. Bacterial contamination on clinical surfaces and oxygen

device accessories in the emergency unit of a tertiary health facility in Ghana. BMC Infectious Diseases, 2024; 24(1), 1-9. doi:10.1186/S12879-023-08894-6/TABLES/4

24. Aliramezani A, Douraghi M, Hajihasani A, Mohammadzadeh M, Rahbar M. Clonal relatedness and biofilm formation of OXA-23-producing carbapenem resistant Acinetobacter baumannii isolates from hospital environment. Microbial Pathogenesis, 2016; 99, 204-208. doi:10.1016/J.MICPATH.2016.08.034
25. Shamsizadeh Z, Nikaeen M, Esfahani BN, Mirhoseini SH, Hatamzadeh M, Hassanzadeh A. Detection of antibiotic resistant Acinetobacter baumannii in various hospital environments: Potential sources for transmission of acinetobacter infections. Environmental Health and Preventive Medicine, 2017; 22(1), 1-7. doi:10.1186/S12199-017-0653-4/FIGURES/2
26. Decraene V, Ghebrehewet S, Dardamissis E, et al. An outbreak of multidrug-resistant Pseudomonas aeruginosa in a burns service in the North of England: challenges of infection prevention and control in a complex setting. Journal of Hospital Infection, 2018; 100(4), e239-e245. doi:10.1016/j.jhin.2018.07.012
27. Katzenberger RH, Rösel A, Vonberg RP. Bacterial survival on inanimate surfaces: a field study. BMC Research Notes, 2021; 14(1), 1-10. doi:10.1186/S13104-021-05492-0/TABLES/1
28. Ahmed OB, Asghar AH, Bamaga M, Bahwerth FS, Ibrahim ME. Characterization of aminoglycoside resistance genes in multidrug-resistant Klebsiella pneumoniae collected from tertiary hospitals during the COVID-19 pandemic. PLOS ONE, 2023; 18(7), e0289359. doi:10.1371/JOURNAL.PONE.0289359
29. Swedan S, Alabdallah EA, Ababneh Q. Resistance to aminoglycoside and quinolone drugs among Klebsiella pneumoniae clinical isolates from northern Jordan. Heliyon, 2024; 10(1). doi:10.1016/j.heliyon.2023.e23368
30. Lund D, Coertze RD, Parras-Moltó M, et al. Extensive screening reveals previously undiscovered aminoglycoside resistance genes in human pathogens. Communications Biology 2023 6:1, 2023; 6(1), 1-10. doi:10.1038/s42003-023-05174-6
31. Halawa EM, Fadel M, Al-Rabia MW, et al. Antibiotic action and resistance: updated review of mechanisms, spread, influencing factors, and alternative approaches for combating resistance. Frontiers in Pharmacology, 2023; 14, 1305294. doi:10.3389/FPHAR.2023.1305294/BIBTEX
32. Zhou K, Liang J, Dong X, et al. Identification and Characterization of a Novel Chromosomal Aminoglycoside 2′-N-Acetyltransferase, AAC(2′)-If, From an Isolate of a Novel Providencia Species, Providencia wenzhouensis R33. Frontiers in Microbiology, 2021; 12, 711037. doi:10.3389/FMICB.2021.711037/BIBTEX
33. Zárate SG, De La Cruz Claure ML, Benito-Arenas R, Revuelta J, Santana AG, Bastida A. Overcoming Aminoglycoside Enzymatic Resistance: Design of Novel Antibiotics and Inhibitors. Molecules, 2018; 23(2), 284. doi:10.3390/MOLECULES23020284
34. Rashvand P, Peymani A, Mohammadi M, et al. Molecular survey of aminoglycoside-resistant Acinetobacter baumannii isolated from tertiary hospitals in Qazvin, Iran. New Microbes and New Infections, 2021; 42, 100883. doi:10.1016/J.NMNI.2021.100883
35. Moussa AA, Nordin AFM, Hamat RA, Jasni AS. High Level Aminoglycoside Resistance And Distribution Of The Resistance Genes In Enterococcus faecalis And Enterococcus faecium From Teaching Hospital In Malaysia. Infection and Drug Resistance, 2019; 12, 3269-3274. doi:10.2147/IDR.S219544
36. Azimi L, Armin S, Samadi Kafil H, et al. Evaluation of phenotypic and genotypic patterns of aminoglycoside resistance in the Gram-negative bacteria isolates collected from pediatric and general hospitals. Molecular and Cellular Pediatrics, 2022; 9(1), 1-8. doi:10.1186/S40348-022-00134-2/TABLES/4
37. Mancini S, Marchesi M, Imkamp F, et al. Population-based inference of aminoglycoside resistance mechanisms in Escherichia coli. eBioMedicine, 2019; 46, 184-192. doi:10.1016/J.EBIOM.2019.07.020
38. Ahmadian L, Norouzi Bazgir Z, Ahanjan M, Valadan R, Goli HR. Role of Aminoglycoside-Modifying Enzymes (AMEs) in Resistance to Aminoglycosides among Clinical Isolates of Pseudomonas aeruginosa in the North of Iran. BioMed Research International, 2021; 2021(1), 7077344. doi:10.1155/2021/7077344
39. Landman D, Babu E, Shah N, et al. Activity of a novel aminoglycoside, ACHN-490, against clinical isolates of Escherichia coli and Klebsiella pneumoniae from New York City. Journal of Antimicrobial Chemotherapy, 2010; 65(10), 2123-2127. doi:10.1093/JAC/DKQ278