



Editorial

The battle against colistin-resistant *E. coli* and the need for a one health approach

The emergence and spread of antibiotic-resistant bacterial strains pose a significant threat to the global healthcare system. The recent emergence of colistin-resistant *E. coli* strains is cause of concern [1,2]. Colistin, an antibiotic of last resort, has been a vital weapon in our fight against multidrug-resistant bacteria [3]. However, the discovery of bacteria that can evade this last line of defense raises alarm bells.

Urinary tract and bloodstream infections are frequently caused by *E. coli*, which is the most prevalent bacterial agent responsible for both community- and hospital-acquired infections. However, no evidence describing the association between colistin resistance in clinical isolates of *E. coli* and its administration has been provided by any observational studies [4]. Conversely, a correlation was found between colistin use and resistance in livestock agriculture. According to reports by the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC), fattening pigs, calves, broilers, and turkeys is associated with a prevalence of colistin resistance of 0.3%, 0.8%, 1.7%, and 5.7%, respectively [5,6]. China, which is one of the key consumers and producers of colistin worldwide, is trying to drastically decrease its use [7]. In India, which is another consumer of colistin, the colistin resistance in *E. coli* causing hospital-acquired infections was 1.1% [8]. Alarming, 70% of *E. coli* isolated from hospital wastewater was resistant to colistin [9].

In Australia and the USA, colistin has never been marketed for livestock animals. The percentage of resistant *E. coli* isolates from Australian patients was 0.39% [10]. In 2019, the clinical prevalence of colistin resistance in North, Central, and South America, Africa, and Asia was 0.3%, 0.3%, 0.3%, 0.19%, and 1.2%, respectively [11].

Colistin has been effective against strains resistant to other antibiotics [12]. However, colistin resistance emerged in China in 2015, primarily driven by a gene known as mobile colistin resistance-1 (*mcr-1*) [13]. Resistance to colistin occurs through modifications of the Lipopolysaccharide (LPS), resulting in an increased positive charge of the LPS, which reduces its attraction to colistin [14]. [15]. Moreover, the *mcr-1* gene can spread to other bacteria through horizontal gene transfer [16]. Some colistin-resistant isolates from livestock animals lacked *mcr-1* gene suggesting that there may be other mechanisms contributing to the resistance of these isolate to colistin [17].

The spread of colistin-resistant *E. coli* strains hinders therapeutic options, leading to clinical complications (e.g., sepsis or pneumonia), longer hospital stays, increased healthcare costs, and higher mortality [18].

Moreover, *E. coli* can be found in the intestines of animals and humans, and food. Colistin-resistant *E. coli* in livestock can contaminate meat and other animal products; should they are not handled or cooked properly, great risks to human health can occur [19].

In addition, the administration of more potent antibiotics in both humans and animals for treating colistin-resistant *E. coli* can increase the likelihood of other antibiotic resistance [20].

The emergence of colistin resistance in *E. coli* can be attributed to several factors: Overuse and misuse of antibiotics in both humans [21] and veterinary medicine [22] have played a significant role. The inappropriate use of colistin in agriculture as a growth promoter in livestock has contributed to the selection of resistant strains. Inadequate infection control practices, poor sanitation, and international migration of people and animals have also contributed to the global spread [23]. All of them emphasize the need for a comprehensive, One Health approach focused on antibiotic stewardship in healthcare settings, cautious use in agriculture, and hygiene [24].

Concerted efforts are required: Enhanced surveillance systems to monitor the prevalence [25] and to detect hotspots and outbreaks.

Implementing robust infection control measures in healthcare facilities, livestock production, and food processing industries is vital. Emphasizing hand hygiene, proper sanitation, and responsible waste management can help curtail the spread of resistant bacteria [27–29].

Continued investment in research and development is needed to discover new antibiotics and alternative therapies [30]. Efforts should also focus on developing innovative strategies such as phage therapy and immunotherapy which could improve our armamentarium against antibiotic-resistant bacteria [31–33].

Authors contribution

All authors participated in the drafting and revision of the manuscript and the approval of the final version.

Declaration of competing interest

None.

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References

- [1] Zafer MM, El-Mahallawy HA, Abdulhak A, Amin MA, Al-Agamy MH, Radwan HH. Emergence of colistin resistance in multidrug-resistant *Klebsiella pneumoniae* and *Escherichia coli* strains isolated from cancer patients. *Ann Clin Microbiol Antimicrob* 2019;18(1):40.
- [2] Bastidas-Caldes C, Guerrero-Freire S, Ortuno-Gutierrez N, Sunyoto T, Gomes-Dias CA, Ramirez MS, et al. Colistin resistance in *Escherichia coli* and *Klebsiella*

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- pneumoniae in humans and backyard animals in Ecuador. *Rev Panam Salud Pública* 2023;47:e48.
- [3] Nation RL, Li J. Colistin in the 21st century. *Curr Opin Infect Dis* 2009;22(6):535–43.
- [4] European Centre for Disease P, Control, European Food Safety A, European Medicines A. ECDC/EFS/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals: joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Report. 2017.
- [5] European Food Safety A, European Centre for Disease P, Control. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in. 2017. 2019.
- [6] European Food Safety A, European Centre for Disease P, Control. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in. 2016. 2018.
- [7] Wang Y, Xu C, Zhang R, Chen Y, Shen Y, Hu F, et al. Changes in colistin resistance and mcr-1 abundance in *Escherichia coli* of animal and human origins following the ban of colistin-positive additives in China: an epidemiological comparative study. *Lancet Infect Dis* 2020;20(10):1161–71.
- [8] Walia K, Madhumathi J, Veeraraghavan B, Chakrabarti A, Kapil A, Ray P, et al. Establishing antimicrobial resistance surveillance & research network in India: journey so far. *Indian J Med Res* 2019;149(2):164–79.
- [9] Bardhan T, Chakraborty M, Bhattacharjee B. Prevalence of colistin-resistant, carbapenem-hydrolyzing proteobacteria in hospital water bodies and out-falls of West Bengal, India. *Int J Environ Res Publ Health* 2020;17(3):1007.
- [10] Ellem JA, Ginn AN, Chen SC, Ferguson J, Partridge SR, Iredell JR. Locally acquired mcr-1 in *Escherichia coli*, Australia, 2011 and 2013. *Emerg Infect Dis* 2017;23(7):1160–3.
- [11] Binsker U, Käsbohrer A, Hammerl JA. Global colistin use: a review of the emergence of resistant Enterobacteriales and the impact on their genetic basis. *FEMS (Fed Eur Microbiol Soc) Microbiol Rev* 2021;46(1).
- [12] Poirel L, Jayol A, Nordmann P. Polymyxins: antibacterial activity, susceptibility testing, and resistance mechanisms encoded by plasmids or chromosomes. *Clin Microbiol Rev* 2017;30(2):557–96.
- [13] Aghapour Z, Gholizadeh P, Ganbarov K, Bialvaei AZ, Mahmood SS, Tanomand A, et al. Molecular mechanisms related to colistin resistance in Enterobacteriaceae. *Infect Drug Resist* 2019;12:965–75.
- [14] Mlynarcik P, Kolar M. Molecular mechanisms of polymyxin resistance and detection of mcr genes. *Biomed Pap Med Facul Palacky Univ Olomouc* 2019;163(1).
- [15] Forde BM, Zowawi HM, Harris PNA, Roberts L, Ibrahim E, Shaikh N, et al. Discovery of mcr-1-mediated colistin resistance in a highly virulent *Escherichia coli* lineage. *mSphere* 2018;3(5).
- [16] Yamamoto Y, Higashi A, Ikawa K, Hoang HTT, Yamaguchi T, Kawahara R, et al. Horizontal transfer of a plasmid possessing mcr-1 marked with a single nucleotide mutation between *Escherichia coli* isolates from community residents. *BMC Res Notes* 2022;15(1):196.
- [17] Nikkahi F, Robatjazi S, Niiazadeh M, Javadi A, Shahbazi GH, Aris P, et al. First detection of mobilized colistin resistance mcr-1 gene in *Escherichia coli* isolated from livestock and sewage in Iran. *New Microb New Infect* 2021;41:100862.
- [18] Wangchinda W, Pati N, Maknakhon N, Seenama C, Tiengrim S, Thamlikitkul V. Collateral damage of using colistin in hospitalized patients on emergence of colistin-resistant *Escherichia coli* and *Klebsiella pneumoniae* colonization and infection. *Antimicrob Resist Infect Control* 2018;7(1):84.
- [19] Barlaam A, Parisi A, Spinelli E, Caruso M, Taranto PD, Normanno G. Global emergence of colistin-resistant *Escherichia coli* in food chains and associated food safety implications: a review. *J Food Protect* 2019;82(8):1440–8.
- [20] Magiorakos A-P, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infection* 2012;18(3):268–81.
- [21] Syed B, Ishaque S, Imran A, Muslim O, Khalid S, Siddiqui AB. Emergence of colistin-resistant gram-negative rods in intensive care units: a cross-sectional study from a developing country. *SAGE Open Med* 2022;10:20503121221132358.
- [22] Dawadi P, Bista S, Bista S, Chediack JG. Prevalence of colistin-resistant *Escherichia coli* from poultry in South Asian developing countries. *Vet Med Int* 2021;2021:1–5.
- [23] Bastidas-Caldes C, de Waard JH, Salgado MS, Villacís MJ, Coral-Almeida M, Yamamoto Y, et al. Worldwide prevalence of mcr-mediated colistin-resistance *Escherichia coli* in isolates of clinical samples, healthy humans, and livestock-A systematic review and meta-analysis. *Pathogens* 2022;11(6).
- [24] Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: one health approach. *Vet World* 2022;15(3):743–9.
- [25] Kawamoto Y, Kaku N, Akamatsu N, Sakamoto K, Kosai K, Morinaga Y, et al. The surveillance of colistin resistance and mobilized colistin resistance genes in multidrug-resistant Enterobacteriaceae isolated in Japan. *Int J Antimicrob Agents* 2022;59(1):106480.
- [26] Tsuji BT, Pogue JM, Zavascki AP, Paul M, Daikos GL, Forrester A, et al. International consensus guidelines for the optimal use of the polymyxins: endorsed by the American college of clinical pharmacy (ACCP), European society of clinical microbiology and infectious diseases (ESCMID), infectious diseases society of America (IDSA), international society for anti-infective pharmacology (ISAP), society of critical care medicine (SCCM), and society of infectious diseases pharmacists (SIDP). *Pharmacotherapy. J Human Pharmacol Drug Ther* 2019;39(1):10–39.
- [27] Halaby T, Al Naiemi N, Vandenbroucke-Grauls CM. Reply to "selective digestive tract decontamination and spread of colistin resistance: antibiotic prophylaxis is not a substitute for hygiene". *Antimicrob Agents Chemother* 2014;58(6):3576–8.
- [28] Halim MMA, Eyada IK, Tongun RM. Prevalence of multidrug drug resistant organisms and hand hygiene compliance in surgical NICU in Cairo University Specialized Pediatric Hospital. *Egypt Pediatr Associat Gazette* 2018;66(4):103–11.
- [29] Anyanwu MU, Okpala COR, Chah KF, Shoyinka VS. Prevalence and traits of mobile colistin resistance gene harbouring isolates from different ecosystems in Africa. *BioMed Res Int* 2021;2021:6630379.
- [30] Humphrey M, Larrouy-Maumus GJ, Furniss RCD, Mavridou DAI, Sabnis A, Edwards AM. Colistin resistance in *Escherichia coli* confers protection of the cytoplasmic but not outer membrane from the polymyxin antibiotic. *Microbiology (Read)* 2021;167(11).
- [31] Wang X, Loh B, Gordillo Altamirano F, Yu Y, Hua X, Leptihn S. Colistin-phage combinations decrease antibiotic resistance in *Acinetobacter baumannii* via changes in envelope architecture. *Emerg Microb Infect* 2021;10(1):2205–19.
- [32] Kim J, Park H, Ryu S, Jeon B. Inhibition of antimicrobial-resistant *Escherichia coli* using a broad host range phage cocktail targeting various bacterial phylogenetic groups. *Front Microbiol* 2021;12.
- [33] Xiao X, Wu H, Dall'Acqua WF. Immunotherapies against antibiotics-resistant *Klebsiella pneumoniae*. *Hum Vaccines Immunother* 2016;12(12):3097–8.

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