EBioMedicine 42 (2019) 10–11

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

EBioMedicine
Published by THE LANCET

MCR-1-producing *Salmonella* Typhimurium ST34 links animal foods to human community infections

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Polymyxins are a group of cationic antimicrobial cyclic peptides (including colistin) that are extensively used in agricultural production, veterinary medicine, and clinical therapies during the past decades [1]. However, the discovery of mobile colistin resistance determinant, *mcr-1*, in Southern China led to the official banning of colistin as a feed additive in China [2]. Subsequently, global dissemination of *mcr-1* appeared as a challenge to public health and caused international consternation [1]. *Mcr-1* has been predominantly detected in animal isolates of *Escherichia coli* (*E. coli*), whereas only a few cases involve the human isolates of *E. coli* [3]. It remains a missing knowledge gap in the prevalence and dissemination of MCR-1-producing Enterobacteriaceae in the context of community-acquired infections.

In this issue of *EBioMedicine*, Lu et al. 2019 systematically investigated the *mcr-1* incidence in 12,053 *Salmonella* strains from the diarrhea of outpatients in Shanghai, China, from 2006 to 2016 [4]. This large-scale epidemiological survey revealed the low, but rapidly-increasing prevalence of *mcr-1*-harboring *Salmonella* in community-acquired diarrheal cases. It raises a possibility that *mcr-1*-positive *Salmonella* constitutes an emerging threat in enteric infection and food safety. This study also provides a baseline for the prevalence of *mcr-1*-harboring *Salmonella* from human infections prior to the formal withdrawal of colistin in China. Intriguingly, an expansion of *mcr-1*-containing *Salmonella* after 2012, is noted especially in patients aged <5 years old. This is generally consistent with the fact that a high prevalence of *mcr-1*-bearing Enterobacteriaceae isolates occur in the intestinal flora of children from Hangzhou, China [5]. A similar study led by Berglund and colleagues reported the distribution of *mcr-1*-expressing *Klebsiella pneumoniae* at a paediatric hospital in Vietnam [6]. Among them, *mcr-1* is found to coexist with other resistance genes, such as Extended-Spectrum β-Lactamase (ESBL) or carbapenemase. The fact that a substantial portion of the *mcr-1*-positive multi-drug resistant (MDR) Enterobacteriaceae strains was determined in the low-age children, suggests that the spread of *mcr-1*-harboring MDR Enterobacteriaceae poses a real threat for children <5 years old. Given the unexpected rapid spread of MCR-1-producing MDR Enterobacteriaceae isolates in children, efforts on the rational use of polymyxins among children must be fortified, to prolong its clinical longevity.

Clonal expansion of *Salmonella enterica* Serovar Typhimurium Sequence Type 34 (ST34) contributes to the spread of *mcr-1* gene among food animals in China [7]. Phylogeny of *S.* Typhimurium strains from human community-infections, swine, and poultry sources show that 34 ST34 human strains are closely-related to the swine isolates, particularly those from Thailand and China. Therefore, it is concluded that pork consumption but not poultry is likely the major contamination source. Whole-genome sequencing of all *mcr-1*-harboring plasmids from human isolates also confirmed that *mcr-1* is mainly located on IncI2 or IncHI2-like plasmids as previously described [7]. It implies that the *mcr-1*-harboring *S.* Typhimurium triggers outbreaks and subsequent expansion of colistin-resistant strains in the community. Thus, active surveillance is required to prevent further spread of colistin resistance in animals and humans.

Recently, a growing number of *mcr*-like family (*mcr-1* to *mcr-8*) have been identified, which poses a heavy risk for public health including food safety. Despite the divergent origins [8], it seems to functionally unify within the MCR family [9]. More efforts are demanded to elucidate how prevalent these *mcr*-like genes (such as *mcr-3* [10]), are in *Salmonella*. Unfortunately, Lu et al. failed to report the carriage and dissemination of *mcr*-like agents other than *mcr-1* in this epidemiological investigation [4]. In addition, *mcr*-carrying plasmids possess various abilities of transmission among different serotypes of *Salmonella*, although the microbiological factors causing plasmid transformation and survival differences are still largely unknown. Given that the spread of *mcr-1*-harboring MDR *Salmonella* poses a threat for young children, what is needed is the evaluation of risk factors of such infection patterns, as well as the transmission mode(s) and contamination source(s). Since China has banned colistin as a growth promoter in animals [2], continued surveillance on colistin resistance of *Salmonella* isolates from animals and humans are necessary for probing the effect of this action.

In conclusion, this study sheds light on the prevalence of *mcr-1*-harboring *Salmonella* in outpatients with community-acquired diarrhea, and on its genomic characteristics and plasmid profiles. To enhance

DOI of original article: https://doi.org/10.1016/j.ebiom.2018.07.027.
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https://doi.org/10.1016/j.ebiom.2019.03.073
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infection control measures and clinical awareness, the spread of MCR-producing *Salmonella* ST34 needs to be closely monitored in multiple sectors consisting of animal products, foods, communities, and hospitals.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (31830001, 31570027 and 81772142, YF), and National Key R&D Program of China (2017YFD0500202, YF). Dr. Feng is a recipient of the national "Young 1000 Talents" Award of China.

Conflict of interest

The authors declare no conflicts of interest.

References

[1] Sun J, Zhang H, Liu YH, Feng Y. Towards understanding MCR-like colistin resistance. Trends Microbiol 2018;26(9):794–808.

[2] Walsh TR, Wu Y. China bans colistin as a feed additive for animals. Lancet Infect Dis 2016;16(10):1102–3.

[3] Zheng B, Xu H, Yu X, et al. Low prevalence of MCR-1-producing Klebsiella pneumoniae in bloodstream infections in China. Clin Microbiol Infect 2018;24(2):205–6.

[4] Lu X, Zeng M, Xu J, Zhou H, Gu B, Li Z, Jin H, Wang X, Zhang W, Hu Y, Xiao W, Zhu B, Xu X, Kan B. Epidemiologic and genomic insights on *mcr-1*-harbouring *Salmonella* from diarrhoeal outpatients in Shanghai, China, 2006-2016. EBioMedicine 2019 Mar 21(19). https://doi.org/10.1016/j.ebiom.2019.03.006 (pii: S2352-3964(19)30146-X, [Epub ahead of print]).

[5] Hu YY, Wang YL, Sun QL, et al. Colistin resistance gene *mcr-1* in gut flora of children. Int J Antimicrob Agents 2017;50(4):593–7.

[6] Berglund B, Hoang NTB, Tarnberg M, et al. Colistin- and carbapenem-resistant *Klebsiella pneumoniae* carrying *mcr-1* and bla_{OXA-48} isolated at a paediatric hospital in Vietnam. J Antimicrob Chemother 2018;73(4):1100–2.

[7] Yi L, Wang J, Gao Y, et al. *mcr-1*-harboring *Salmonella enterica* Serovar Typhimurium sequence type 34 in pigs, China. Emerg Infect Dis 2017;23(2):291–5.

[8] Wei W, Srinivas S, Lin J, et al. Defining ICR-Mo, an intrinsic colistin resistance determinant from *Moraxella osloensis*. PLoS Genet 2018;14(5):e1007389.

[9] Zhang H, Zong Z, Lei S, et al. A genomic, evolutionary and mechanistic study of MCR-5 action suggests functional unification across the MCR family of colistin resistance. Adv Sci 2019 [Accepted].

[10] Xu Y, Zhong LL, Srinivas S, et al. Spread of MCR-3 colistin resistance in China: an epidemiological, genomic and mechanistic study. EBioMedicine 2018;34:139–57.