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Mini Review

Wild Boars Carry Antimicrobial Resistant Enterobacteriaceae of Zoonotic Importance

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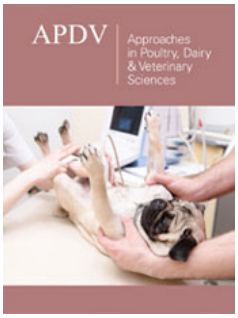

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Antibiotics belonging to the β-lactam class are the most commonly used antimicrobials in human and veterinary medicine [1]. Bacteria initially susceptible to β-lactams can develop resistance by modifying the β-lactams' targets (mutation or alteration of penicillin binding proteins), reducing cell permeability (downregulation of porins required for β-lactam entry), overexpressing efflux systems or producing β-lactamases [2]. β-lactamases are enzymes capable of hydrolyzing the amide bond of the β-lactam ring, therefore rendering the antimicrobial ineffective [3]. The emergence of Extended Spectrum Beta Lactamase (ESBL) and Carbapenemase-Producing Enterobacteriaceae (CPE) is causing an unprecedented public health crisis, leaving few treatment options and affecting not only hospitalized patients, but also long-term care facilities and the community [4].

Genes encoding ESBLs and carbapenemases are typically located on transferable plasmids, which can be mobilized between the same or different bacterial species [5]. Additionally, clonal and horizontal gene transfer have contributed to the dissemination of β-lactamase-mediated Antimicrobial Resistance (AMR) from humans to animals or the environment and vice versa [6]. Thus, the capacity of such AMR determinants to transmit among various hosts raises concerns on a One Heath perspective.

Wild boar (Sus scrofa) has been identified as an important reservoir of zoonoses and food-borne pathogens [7-9]. Interest has been drawn to the species due to its "invasive" behavior, the great increase of its population densities, its omnivorous diet and close proximity to anthropized environments (farms and pastures) that could favor health risks resulting from the transmission of infections across the wildlife-domestic animal-human interface [10]. In recent years, research has been conducted to identify carriage of genes conferring resistance to human last-resort antibiotics, including ESBL and carbapenem-resistance genes, from wild boars. Results indicate the dissemination of public health significant antimicrobial resistance determinants, such as those responsible for fluoroquinolone and colistin resistance [11,12]. For instance, quinolone resistant *Escherichia coli* (*E. coli*) isolates harboring plasmid-mediated genes of the qnr group (qnrS1/qnrS3) have been identified in Poland [12].

Regarding ESBLs, their dispersion among wild boars has been documented in several European and African countries, while data from other regions are not available. The overall rate of ESBL-Enterobacteriaceae fecal carriage among the sampled animals in the existing studies has been described to vary widely from 0.9% in Poland to 15.9% in Italy and from 28.1% in Tunisia up to 44.4% in Algeria [11-14]. Variants of the CTX-M family predominate in most of the studies, with CTX-M-1 being the heretofore most prevalent ESBL enzyme in *E. coli* isolates reported from European countries and in particular from Germany, Portugal, Spain and Czech Republic [15-19]. On the other hand, variant CTX-M-15 has been identified as the most prevalent in both *E. coli* and *Klebsiella pneumoniae* strains in Algeria [13]. Other ESBLs

have also been reported, though to a lesser extent, and include CTX-M-14, SHV-12, SHV-28 and TEM-52b [14,19,20]. Concerning the transposable elements responsible for the respective ESBL genes' diffusion, few information is available and describes the presence of class 2 integrons among two *E. coli* strains [19]. Finally, different sequence types and incompatibility groups of plasmids have been associated with ESBLs in wild boars in the aforementioned studies.

The overuse and misuse of β-lactam molecules in both human and veterinary medicine as well as the ability of antibiotic residues and of resistant bacteria originating from human or animal excrements to accumulate in numerous environmental niches have been highlighted as the main causes of ESBL carriage by wild boars [11]. ESBLs were more frequently isolated from the urban and peri-urban wild boars in Spain than from the forest ones and increased human population density led to an increase of blaTEM prevalence in wild boars in Italy [14,20]. These facts indicate the great influence of humans in AMR diffusion. CPE colonization in wild boars has only been described by a sole report in Algeria, to date [21]. Plasmid located blaOXA-48 was identified in ST635 *E. coli* strains, whereas the same OXA variant was chromosomally encoded in ST13 Klebsiella pneumoniae. Transmission to wild boars was associated with their feeding habits in the Algerian warm and humid habitat that favors the preservation of contaminating bacteria of human and animal origin.

Overall, it is evident that β-lactamase resistance is not confined to human and livestock settings but has also arisen in wild fauna. Natural habitats become increasingly invaded by humans, forcing wildlife into greater direct and indirect contact with them and ultimately elevating the risk of AMR transmission among populations [22], especially as regards commensal, ubiquitous bacteria such as Enterobacteriaceae. Further research is required to fully unveil the role of wild boars as reservoirs and amplifiers of β-lactamase genes and their capacity to diffuse AMR back to humans. Special attention should be given during wild boar hunting and manipulation of wild boar meat, since the rising, complex challenge of AMR now requires a holistic and multidisciplinary approach.

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Conflicts of Interest

The authors declare no conflict of interest.

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