REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 24, No. 4 (2023)
http://www.veterinaria.org
Article Received: 15 October 2023; Revised: 28 November 2023; Accepted: 22 December 2023

Antimicrobial Usage in Contemporary Cattle Farming: Exploring the Threat of Resistance and Strategies for Sustainable Management

Dr. Pravesh Belwal[1]*, Dr. Anuradha Rohinkar[2], K Suneetha[3]

*[1]Assistant Professor, School of Engineering and Computer, Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand, India, Email Id- ece.pravesh@dbuu.ac.in, Orcid Id- 0000-0003-2119-1494

[2]Assistant Professor, Department of Biochemistry, Parul University, PO Limda, Vadodara, Gujarat, India, Email Id: anuradha.rohinkar82125@paruluniversity.ac.in

[3]Professor, Department of Computer Sceince and Information Technology, Jain (Deemed to be University), Bangalore, India, Email Id- k.suneetha@jainuniversity.ac.in, Orcid Id- 0000-0001-6738-3921

Abstract

Antimicrobial resistance (AR) presents an existential threat to worldwide public health, compromising the effectiveness of clinical antimicrobial (Antimic) treatments. The spread of resistance from cattle to people by the food chain and environmental variables exacerbates this problem. The practice of cattle farming heavily depends on the use of Antimic additives in animal feed to ensure well-being and improve efficiency. In this research, we investigate the actual state of antibiotic (ABX) utilization in contemporary cattle farming. This study examines the harmful effects of AR. It explores the complex ways in which people might develop resistance through consuming animal products or exposed to contaminated surroundings, such as water, air, soil, or manure. The review emphasizes the necessity of using sustainable management measures to counteract the spread of ABX resistance in cow production. The report seeks to integrate current knowledge on the topic to achieve a complete comprehension of the situation and suggest comprehensive strategies for combat. It is crucial to prioritize the investigation of long-term alternatives and the appropriate use of Antimics in cattle to protect public health, guarantee food safety and maintain the effectiveness of Antimic treatments.

Keywords: Antimic resistance, Cattle Farming, Food animals

INTRODUCTION

Agricultural production, animal welfare and public health are intersected in the ever-changing world of modern cow farming when it comes to the use of ABX. Antimic medicines have a long history of use in animals, helping to cure and prevent infections that can affect individual animals and herds as a whole (1). The responsible use of ABX in cattle ranching has become a hotly debated topic due to the growing global concerns about ABX resistance and sustainable agriculture. A large portion of the worldwide demand for meat and dairy products is supplied by cattle farms (2). ABX has been crucial in managing and preventing infectious diseases in cattle populations, given the current context of heightened efficiency and escalating customer expectations. One popular tactic for protecting animal health and reducing financial losses caused by disease outbreaks is the preventative use of ABX (3).

The development of bacterial strains that are resistant (R) to Antimics is a significant concern due to the careless and extensive use of these drugs, which endangers the health of humans and animals (4, 6). Together, farmers, animals and politicians can reduce the possibility of ABX resistance while protecting animals' well-being. Developing alternative disease preventive strategies, improving management practices and responsibly using Antimics when necessary are part of the multi-faceted approach that is necessary to address this (5, 7, 8). Furthermore, a worldwide movement has been raised in response to the public health concerns raised by the rise of ABX resistance. There has been an increase in the awareness among cattle farmers of the interdependence of animal, human and ecological well-being (6).

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 24, No. 4 (2023)
http://www.veterinaria.org
Article Received: 15 October 2023; Revised: 28 November 2023; Accepted: 22 December 2023

Animal-to-human transfer of AR

Excessive utilization of Antimics results in the development of drug resistance, posing a significant risk to the well-being of animals and people. There has been a growing prevalence of ABX resistance against "sulphonamides (SULFA), β-lactams and penicillin."An investigation conducted on E.coli samples obtained from 175 cattle revealed a significant prevalence of R to both "ampicillin and tetracycline," as well as a substantial presence of "E. coli strains expressing extended-spectrum β-lactamases (ESBLs)" (7, 8).

There has been a worldwide growth of multiple drug-R pathogens. Antimics have led to over a million infections and 21,500 fatalities in the USA, as well as 24,000 deaths in Europe, on an average year (9). Additionally, pneumococcal disease leads to a 31.2% failure rate in the initial treatment. Studies have shown that AR presents a substantial risk to public health worldwide (15).

Extended utilization of ABX in animals develops optimal circumstances for the emergence and dissemination of R variants. ABX in animals can be transmitted to humans through various means, such as food, water and mud, which can be used as fertilizers (7). Indeed, there is indisputable evidence that various animal-derived foods and the phases of food processing enclose a significant quantity of ABX bacteria (Bactria). Homologous connections have been established between drug-R Bactria found in humans and animals, specifically in prevalent food borne like "methicillin-R Staphylococcus aureus (MRSA)" (10).

Hence, HGT performs a substantial role in facilitating the swift dissemination of resistance. Individuals in occupations such as farm and butcher workers, veterinarians and others who have frequent interaction with farmers are very susceptible to contracting ABX-R Bactria due to their regular exposure to infected animals (11). A study conducted in 1952 initially discovered that when the chickens were provided with a meal containing tetracycline as a supplement, the gut Bactria of nearly all the birds exhibited resistance to tetracycline within one week of consuming the food. The study revealed that, during a period of four to seven months, 33.9% of the faecal samples collected from individuals living on farms possessed a concentration of tetracycline-R Bactria above 75%. Between 2003 and 2008, a total of 41 strains of E. coli that were R to apramycin were discovered randomly. These strains were collected from six farms. It was observed that the apramycin R DNA of the aac (3)-IV type had a 97.6% similarity between humans and animals.

Nevertheless, in 1997, apramycin was authorized for use in livestock in Asian countries, although its use in humans was not permitted. Moreover, out of the MRSA, six of them possessed mec-A, which is the mutation that causes "methicillin resistance in S. aureus," and this gene was the same as the infections found in humans. An extensive genomic analysis demonstrated the presence of identical ColV/ColBM plasmids in both "mcr-1-positive E. coli (MCRPEC) isolates" from poultry (9, 12 and 13). However, the positive tendency was reversed once the use of ABX was resumed. These investigations have verified the transfer of ABX-R microorganisms from animals to farmers. The findings exposed the frequency of resistance between workers prior to subsequent to the implementation of ABX in their professional environment (8, 10, 14 and 19). While the restricted transmission seems not to endanger the overall population's health, the transfer of drug-R genetic factors into "the community and hospital" settings could be dangerous.

In addition, consumers run the risk of contracting R Bactria from arriving in touch with or eating animal foods. There is strong evidence indicating that meals obtained from different meat sources throughout the whole preparation process contain substantial quantities of robust bacteria and genes linked to resistance (12, 14 and 15). A strain of Salmonella typhimurium carrying the blaNDM-5 gene was initially identified. MRSA has been discovered in cattle, meat and various other animal products acquired from the retail market. AR genes identified in food borne illnesses were detected in people, therefore verifying the risk associated with consuming meat products contaminated with AR Bactria that are resistant to ABX. Table (1) provides additional evidence of the transmission of AR from animals to humans (10, 16).

Table (1). Proof of ABX resistance in humans transmitted by animal foods (Source: Author)

Proof	Resistance	Animal	Reference
Animals were found to have Mcr-1/2	MDR	Cambodia pigs, chicken	(9)
Farmers were found with R strains	MDR	Pig	(11)
Phenotypic and genotypic investigations revealed the connection between microorganisms recovered from patients and food.	Ciprofloxacin (CIPRO)	Chicken Sandwich	(13)
RAPD and PFGE research revealed that several R humans were identical to chicken isolates	CIPRO	Spanish-Style Chicken	(15)
Human mcr-1-positive strains were combined with pig	MDR	Sweet and Sour Chinese Pork	(19)
ABX-R E. coli strains with transferred plasmids have been identified	Tetracycline	American Chicken	(5)
R strains were found in farmers, pigs and agricultural surroundings	MDR	Aussie Pork Delicacy	(8)

There is compelling evidence that when humans consume food containing Bactria that is R to ABX, they can get diseases that are R to ABX, either directly or indirectly. At the beginning of 1979, a woman who was 69 years old passed away due to an infection called Salmonella enteritis and sepsis. Unfortunately, her condition did not improve despite receiving therapy with chloramphenicol (5, 17). The Campylobacter jejuni variant obtained from chicken products at retail establishments exhibited significant genetic similarity to the strain isolated from human patients in the USA (18). A study examined the frequency of the "mc-1 gene in Salmonella strains" attained since the investigation of individuals with diarrhoea in Asian countries between 2005 and 2013. The majority of the strains that tested positive for mcr-1 were closely related to themes found in pork, indicating that consuming pork was the leading cause of this disease. A compelling study is Hummel's 1983 report, which monitored the dissemination of nourseothricin resistance (1, 10, 19). Pigs had a low incidence of resistance to nourseothricin.

Nevertheless, following several years of administering "nourseothricin," a strain of E. coli that existed immune to the drug was discovered not only in pigs that had been treated (38%) but also in fertilizer seas, food and the intestinal micro-biota of farmers (19%), the relatives of formers (15%) and patients seeking medical care (19%). This strain was responsible for 3% of the cases of urinary tract infections. Table (2) contains a list of ABX residues established in the faeces of pigs, fowl and cattle (18, 20).

Table (2). Animal fertilizer containing ABX residues (Source: Author)

Animal	Residues (mg/kg)	ABX
Pigs	3.85	Macrolides
Pigs, Cattle	0.25 / 22.54	SULFA
Pigs, Cattle	29.64/ 66.45	Tetracyclines
Pigs	48.15	Oxytetracycline
Pigs, Cattle	15.26 / 12.48	CIPRO
Chicken	523.32	Norfloxacin
Chicken	56.89	Fleroxacin

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 24, No. 4 (2023)
http://www.veterinaria.org
Article Received: 15 October 2023; Revised: 28 November 2023; Accepted: 22 December 2023

AR prevention strategies

The European Union (EU) implemented one of the initial prohibitions on the utilization of Antimic growth agents (AGA) by imposing a ban on tetracycline in mid-1965 (4, 9, 12 and 22). Table (3) shows that the use of ABX as growth promoters in animals raised for human consumption is restricted or outright forbidden in several nations. Following the prohibition of using tetracycline in animal diets for nutritional purposes, there has been an increase in the prevalence of tetracycline-R strains in pigs and human individuals. The EU implemented a prohibition on the agricultural utilization of avoparcin in 1996, citing the high occurrence of "vancomycin-R Enterococcus (VRE) among patients." In 1998, the developed countries implemented a prohibition on the utilization of "bacitracin, spiramycin, tylosin and virginiamycin" as AGAs due to their concurrent usage in human medicine. As of 2004, the developed countries have implemented a complete prohibition on the use of AGA (3, 6 and 7).

Table (3). Timeline to implement the legalization of AGAs in animal food production (Source: Author)

Year	Ban	Countries
1973	Virginiamycin	Denmark
1987	Avoparcin	EU
1996	All AGAs	China
1997	Every AGAs	Mexico
1998	Arsanilic acid	EU
1999	Avoparcin	Sweden
2000	Colistin	Denmark
2001	Significant Antimics	USA
2007	AGAs	China
2008	Virginiamycin	EU
2018	Avoparcin	Germany
2018	Every AGAs	Denmark
2020	Penicillin	European
2021	All AGAs	China

During the mid-1990s, there was a direct correlation between the increased usage of virginiamycin in Danish broilers and a significant increase in the prevalence of R E. faecium, which increased from 29% to 65%. After the prohibition of avoparcin in 1995, many studies revealed a significant decrease in the occurrence of VRE in Denmark, dropping from a range of 69%–75% to 7%–4% (15, 19, 20 and 21).

Following the prohibition of AGAs, a significant concern arose regarding the potential rise in illness occurrence among animals, which could, therefore, cause an increase in therapeutic usage. The occurrence of "necrotizing enteritis (NE) in chickens and pigs rose" quickly after the prohibition of AGAs in a particular country (20, 22). There was a notable increase in the overall quantity of ABX utilized in the pig business. The intensity of therapy, as measured by the prescribed daily dose, remained consistent. Despite an initial rise in the overall usage of therapeutic ABX following the restriction, no enduring adverse impacts were observed in relation to death rates, daily average growth in weight, or animal output. Nevertheless, in the majority of other nations, animal production remains reliant on the extensive utilization of Antimics (11).

Implementing a sudden and comprehensive prohibition on the use of Antimics in food animals might result in significant repercussions for animal well-being, productivity, welfare and food costs (5). Nevertheless, advancements in sanitation and the regulation of animal nutrition have been documented to mitigate the detrimental consequences of these prohibitions on the well-being and efficiency of animals. Furthermore, it is

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 24, No. 4 (2023)
http://www.veterinaria.org
Article Received: 15 October 2023; Revised: 28 November 2023; Accepted: 22 December 2023

noteworthy that the early advantageous impacts of AGAs, such as increased weightiness and improved food productivity, have declined (19).

"The Food and Agriculture Organization (FAO), the World Organization for Animal Health (OIE) and the World Health Organization (WHO)" are collaborating to regulate the utilization of Antimics in animals. Attempts have been initiated by "global monitoring systems, such as the National AR Monitoring System (NARMS) for Enteric Bactria and the European AR Surveillance Network, to gather data on the use of Antimics and the development of AR" (5). The government prioritizes the matter of AR and has implemented various initiatives to enhance Antimic stewardship. Several documents concerning the case have been published. The following documents will contribute to the improvement of Antimic management in multiple areas: "Antimic Management will be Enhanced in Multi-areas (2013), Five Year Action Plan for the Comprehensive Management of Veterinary Drugs in Asian countries (2014–2018), National Action Plan to Contain AR (2017–2019) and Work Program for the Reduction of the Use of Antimics in Animals (2017–2022)" (1, 8, 15, 19, 21, 22, 23, 24). These documents provide comprehensive evidence that the government will enhance oversight of the manufacturing, supplies and utilization of Antimics (3, 25). Table (4) indicates that an Asian country has achieved notable advancements in diminishing the use of Antimics in animal production.

Table (4). ABX use from 2013 to 2022 (Source: Author)

Year	2013	2015	2017	2019	2022
Compared with 2013 (%)	-	-29.60	-23.89	-54.52	-45.54
Compared with before (%)	-	-29.60	-48.51	-6.56	-59.45
Total (tons)	65,256.52	65,562.58	89,452.56	56,451.00	54,456.45

CONCLUSION

AR poses a significant worldwide public health issue. Antimics provide a selective solid impact on the development of resistance. Growing data indicates that the improper and excessive use of ABX in animals contributes to the development of AR. To address the problem, it is necessary to prohibit the use of AGAs and develop specific protocols for administering Antimics to animals for therapeutic purposes. To mitigate financial losses, it is imperative to enhance animal health conditions and identify effective methods for alleviating animal discomfort. It is necessary to provide consistent instruction on the appropriate use of Antimics, improve Antimic stewardship and enforce stringent "infection control measures." Specifically, minimizing the utilization of extra antimic medications could help to prevent the appearance and dissemination of drug-R microorganisms. Furthermore, significant investigation has been conducted on the utilization of substitutes for Antimics, revealing their efficacy and potential to enhance the animal breeding field.

REFERENCES

1. Borka Balas, R., Meliț, L.E. and Mărginean, C.O., (2023). Current Worldwide Trends in Pediatric Helicobacter pylori Antimicrobial Resistance. *Children*, *10*(2), p.403.https://doi.org/10.3390/children10020403
2. Salam, M.A., Al-Amin, M.Y., Salam, M.T., Pawar, J.S., Akhter, N., Rabaan, A.A. and Alqumber, M.A., (2023), July. AR: A severe growing threat to global public health. In *Healthcare* (Vol. 11, No. 13, p. 1946). MDPI.https://doi.org/10.3390/healthcare11131946
3. Lianou, D.T. and Fthenakis, G.C., (2022). Use of ABX against Bactrial infections on dairy sheep and goat farms: Patterns of usage and associations with health management and human resources. *ABX*, *11*(6), p.753.https://doi.org/10.3390/antibiotics11060753
4. Vidovic, N. and Vidovic, S., (2020). AR and food animals: Influence of livestock environment on the emergence and dissemination of AR. *ABX*, *9*(2), p.52.https://doi.org/10.3390/antibiotics9020052
5. Carson, C., Li, X.Z., Agunos, A., Loest, D., Chapman, B., Finley, R., Mehrotra, M., Sherk, L.M., Gaumond, R. and Irwin, R., (2019). Ceftiofur-R Salmonella enterica serovar Heidelberg of poultry origin–

a risk profile using the Codex framework. *Epidemiology & Infection*, *147*, p.e296.https://doi.org/10.1017/S0950268819001778

6. European Food Safety Authority and European Centre for Disease Prevention and Control, (2020). The European Union Summary Report on Antimicrobial Resistance in zoonotic and indicator bacteria from humans, animals and food in 2017/2018. *EFSA Journal*, *18*(3), p.e06007.https://doi.org/10.3390/vaccines10091372
7. Elbediwi, M., Wu, B., Pan, H., Jiang, Z., Biswas, S., Li, Y. and Yue, M., (2020). Genomic characterization of mcr-1-carrying Salmonella enterica Serovar 4,[5], 12: i:-ST 34 clone isolated from pigs in China. *Frontiers in bioengineering and biotechnology*, *8*, p.663.https://doi.org/10.3389/fbioe.2020.00663
8. Lee, T., Jordan, D., Sahibzada, S., Abraham, R., Pang, S., Coombs, G.W., O'Dea, M. and Abraham, S., (2021). AR in porcine enterococci in Australia and the ramifications for human health. *Applied and Environmental Microbiology*, *87*(10), pp.e03037-20.https://doi.org/10.1128/AEM.03037-20
9. Sodagari, H.R., Agrawal, I., Yudhanto, S. and Varga, C., (2023). Longitudinal analysis of differences and similarities in antimicrobial resistance among commensal Escherichia coli isolated from market swine and sows at slaughter in the United States of America, 2013–2019. *International Journal of Food Microbiology*, *407*, p.110388.https://doi.org/10.1016/j.ijfoodmicro.2023.110388
10. Ahmad, I., Malak, H.A. and Abulreesh, H.H., (2021). Environmental AR and its drivers: a potential threat to public health. *Journal of Global AR*, *27*, pp.101-111.https://doi.org/10.1016/j.jgar.2021.08.001
11. Möller, V., Östholm-Balkhed, Å., Berild, D., Fredriksson, M., Gottfredsson, M., Holmbom, M., Järvinen, A., Kristjansson, M., Rydell, U., Sönksen, U.W. and Kolmos, H.J., (2021). ABX resistance among major pathogens compared to hospital treatment guidelines and ABX use in Nordic hospitals 2010–2018. *Infectious Diseases*, *53*(8), pp.607-618.https://doi.org/10.1080/23744235.2021.1910338
12. EFSA Panel on Biological Hazards (BIOHAZ), Koutsoumanis, K., Allende, A., Álvarez-Ordóñez, A., Bolton, D., Bover-Cid, S., Chemaly, M., Davies, R., De Cesare, A., Herman, L. and Hilbert, F., (2021). Role played by the environment in the emergence and spread of AR (AMR) through the food chain. *EFSA Journal*, *19*(6), p.e06651.https://doi.org/10.2903/j.efsa.2021.6852
13. Abbasi, K., Tajbakhsh, E. and Momtaz, H., (2021). AR and biofilm encoding genes amongst the Staphylococcus aureus Bactria isolated from meat and meat products. *Egyptian Journal of Veterinary Sciences*, *52*(1), pp.55-62.https://doi.org/10.21608/ejvs.2020.39385.1186
14. Ibrahim, M., Ahmad, F., Yaqub, B., Ramzan, A., Imran, A., Afzaal, M., Mirza, S.A., Mazhar, I., Younus, M., Akram, Q. and Taseer, M.S.A., (2020). Current trends of Antimics used in food animals and aquaculture. In *ABX and AR genes in the environment* (pp. 39-69). Elsevier.https://doi.org/10.1016/B978-0-12-818882-8.00004-8
15. López-Alonso, V., Ortiz, S., Corujo, A. and Martínez-Suárez, J.V., (2020). Analysis of benzalkonium chloride resistance and potential virulence of Listeria monocytogenes isolates obtained from different stages of a poultry production chain in Spain. *Journal of food protection*, *83*(3), pp.443-451.https://doi.org/10.4315/0362-028X.JFP-19-289
16. Serwecińska, L., (2020). Antimics and ABX-RBactria: a risk to the environment and to public health. *Water*, *12*(12), p.3313.https://doi.org/10.3390/w12123313
17. Ma, Z., Lee, S. and Jeong, K.C., (2019). Mitigating ABX resistance at the livestock-environment interface: a review.https://doi.org/10.1109/ISEMANTIC.2019.8884272
18. Zalewska, M., Błażejewska, A., Czapko, A. and Popowska, M., (2021). ABX and ABX resistance genes in animal manure–consequences of its application in agriculture. *Frontiers in Microbiology*, *12*, p.640.https://doi.org/10.3389/fmicb.2021.610656
19. Wierup, M., Wahlström, H. and Bengtsson, B., (2021). Successful prevention of antimicrobial resistance in animals—a retrospective country case study of Sweden. *Antibiotics*, *10*(2), p.129.https://doi.org/10.3390/antibiotics10020129
20. Lima, T., Domingues, S. and Da Silva, G.J., (2020). Manure as a potential hotspot for ABX resistance dissemination by horizontal gene transfer events. *Veterinary sciences*, *7*(3), p.110.https://doi.org/10.3390/vetsci7030110

21. Thapa, S.P., Shrestha, S. and Anal, A.K., (2020). Addressing the ABX resistance and improving the food safety in food supply chain (farm-to-fork) in Southeast Asia. *Food Control*, *108*, p.106809.https://doi.org/10.1016/j.foodcont.2019.106809
22. Haulisah, N.A., Hassan, L., Bejo, S.K., Jajere, S.M. and Ahmad, N.I., (2021). High levels of ABX resistance in isolates from diseased livestock. *Frontiers in veterinary science*, *8*, p.652351.https://doi.org/10.3389/fvets.2021.652351
23. Palma, E., Tilocca, B. and Roncada, P., (2020). AR in veterinary medicine: An overview. *International Journal of Molecular Sciences*, *21*(6), p.1914.https://doi.org/10.3390/ijms21061914
24. Wang, X., Biswas, S., Paudyal, N., Pan, H., Li, X., Fang, W. and Yue, M., (2019). ABX resistance in Salmonella Typhimurium isolates recovered from the food chain through national AR monitoring system between 1996 and 2016. *Frontiers in microbiology*, *10*, p.985.https://doi.org/10.3389/fmicb.2019.00985
25. Hoque, R., Ahmed, S.M., Naher, N., Islam, M.A., Rousham, E.K., Islam, B.Z. and Hassan, S., (2020). Tackling AR in Bangladesh: A scoping review of policy and practice in human, animal and environment sectors. *PloS one*, *15*(1), p.e0227947.https://doi.org/10.1371/journal.pone.0227947