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Invited Review Article

A holistic approach to combating antimicrobial resistance (AMR) in poultry production

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Abstract

Antimicrobials (antibiotics) are used in sub-therapeutic levels in the poultry sector to promote growth performance and prevent infectious bacterial diseases. The sub-therapeutic use of antibiotic growth promoters could promote the development of antimicrobial resistance bacteria, which is presently a global public health threat. Research has been focused on the development of antimicrobial alternatives that can maintain optimum poultry health and performance. The different categories of antimicrobial alternatives described include postbiotics, probiotics, prebiotics, essential oils, bacteriophages and organic acid. Holistic nutritional practices (antibiotic alternatives) coupled with good poultry farm management, biosecurity measures, proper vaccination programs, and provisions of high-quality feed and water will be the key to maximizing poultry production and improving health.

Keywords: Alternative, Antimicrobial, Poultry, Resistance

Highlights

- Antimicrobial resistance is a global public health threat.
- The sub-therapeutic use of antibiotic growth promoters has led to the development of antimicrobial resistance.
- Feed interventions coupled with good poultry farm management practices will be the key to optimising poultry health and production.
- A holistic intervention strategy can contribute to lowering the risk of poultry diseases and, hence, the use of antimicrobials.

INTRODUCTION

Antimicrobial resistance (AMR) is one of the greatest global health threats to human and animal health, and food security in this century (WHO, 2017). AMR occurs naturally as bacteria encounter antimicrobials. Overuse of antimicrobials in human medicine and use of antimicrobials in livestock production to maintain health and productivity are linked to antimicrobial resistance in humans and livestock. The antimicrobial drugs used in livestock production globally were estimated to amount to 99,502 tonnes in 2020 and are expected to increase to 107,472 tonnes (by 8%) by 2030 (Mulchandani *et al.*, 2023) because of the rising demand for livestock products by the human population in middle-income countries.

Poultry, meat and eggs are important sources of animal protein and are a source of safe and high-quality protein in human nutrition. Poultry meat and egg production are considered precious throughout the world (Shang *et al.*, 2018). By 2050, the world population is expected to be about 9.6 billion (Borda-Molina *et al.*, 2018). To match the demands of a growing global population, the production of chicken meat and eggs is expected to grow exponentially, especially in Asia, Africa, and South America due to recent changes in diet for a more animal protein option (Van Boeckel *et al.*, 2019). AMR is a growing concern in the poultry industry, as the use of antibiotics and other antimicrobial agents in poultry production can contribute to the development of resistant bacteria. For the last few decades, antibiotic growth promoters (AGPs) have been used in poultry feed to improve production performance. The use of antibiotic growth promoters at subtherapeutic level in poultry feed could promote the development of antibiotic resistant bacteria (Rahman *et al.*, 2022). In spite of the positive outcomes of poultry development, there are many limitations associated with poultry production that need to be addressed to tackle antimicrobial resistance. These limitations include adequate infrastructure, lack of capital, ineffective implementation of the existing policies, a lack of training and awareness programs, poor feed and water quality, low biosecurity in the semi-commercial or backyard poultry farms and a lack of economic AGPs alternatives (Wong *et al.*, 2017; Mondal *et al.*, 2020). These circumstances have ensured a search for holistic

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interventions to combat antimicrobial resistance.

Antimicrobial resistance transmission pathways

Humans, animals (domestic animals as well as wildlife), and birds continuously interact with each other and share a specific environment, combined with limited biosecurity measures, which can increase AMR transmission (Hedman *et al.*, 2020). Resistant bacteria exposure between chicken breeds and intensive poultry farming has been linked to AMR transmission between various domestic and wild animal species (Pornsukarom *et al.*, 2018). Resistant bacteria cross host species barriers and cross species AMR transmission can be mediated by rodent and insect vectors in intensive poultry farming system (Leibler *et al.*, 2009). Zoonotic AMR transmission is also facilitated by foodborne transmission and occupational exposure (Nguyen *et al.*, 2016a). A systems framework has been applied to evaluating the AMR transmission pathways in the poultry sector by Hedman *et al.* (2020) (Table. 1).

Table 1. AMR transmission pathways originating from poultry sector in Asian, African and South American countries (Heddman *et al.*, 2020)

Country	Area	Operation size	AMR transmission pathway	Findings	Reference
India	Urban	Large	Intensive chicken farming	High prevalence of ESBL -producing *Escherichia coli* (87%) and multidrug resistance (94%)	Brower *et al.*, 2017
	Rural	Small	Indirect transmission to backyard poultry	High prevalence of multidrug resistance and avian pathogenic *E. coli* associated virulence genes 75.5% from backyard layer chickens and their environment.	Samanta *et al.*, 2014
Vietnam	Rural	Small Medium	Intensive chicken farming; Occupational exposurem	Reported antimicrobial resistant *Salmonella* spp. in farmers and intensively farmed poultry.	Nguyen *et al.*, 2016a
Indonesia	Rural	Small Medium	Intensive chicken farming	Documented high prevalence of multidrug resistance (53.57%) *Klebsiella pneumoniae* isolates.	Prematasari *et al.*, 2020
Bangladesh	Urban	LargeMedium	Intensive chicken farming; Zoonotic	Isolated multidrug resistant *E. coli* from intensive poultry, poultry husbandry environments, and hands of poultry workers.	Sarker *et al.*, 2019
Kenya	Rural	Small Large	Intensive chicken farming	Documented drug-resistant thermophilic *Campylobacter* spp. originating in small-scale family operated poultry systems.	Nguyen *et al.*, 2016b
		Small	Indirect transmission to backyard poultry	Detected presence of class 1 integrons beta-lactamase genes from *E. coli* and *Salmonella* spp. from backyard chicken feces.	Langata *et al.*, 2019
Zimbabwe	Rural Urban Peri-urban	Small Large	Intensive chicken farming	Detected multidrug resistant (12.1%) *Salmonella enteritidis* isolates, presents public health risk of salmonellosis.	Makaya *et al.*, 2012

Cont. Table 1.

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Country	Area	Operation size	AMR transmission pathway	Findings	Reference
Nigeria	Urban	Large	Cross-species AMR transmission	High prevalence of antimicrobial resistant and virulent *Enterococcus* spp. sampled from poultry and cattle excreta suggesting cross-species transmission.	Ngbede *et al*., 2017
Ecuador	Rural	Small	Cross-breed AMR transmission; Zoonotic AMR transmission	High prevalence (66.1%) of beta-lactamase CTX-M-producing *E. coli* of backyard chickens not fed antibiotics after the village-scale introduction of broiler chickens. Sequenced blaCTX-M demonstrated close relatedness of backyard chicken, broiler chicken, and human samples from the villages which could suggest antimicrobial resistant zoonotic transmission.	Ochoa *et al*., 2016

Holistic interventions to combat antimicrobial resistance in poultry production

Farm management biosecurity practices: Farm management and biosecurity measures are crucial in reducing the need for the use of antibiotics in poultry. Poor disease prevention and control strategies and low or inadequate biosecurity practices result in high mortality and poor performance due to disease outbreaks (Abdelqader *et al*., 2007). Strict on-farm biosecurity practices and standard poultry house management are essential to prevent the transmission of infectious diseases between and within farms, maintain optimum production performance (Bailey, 2019) and decrease the need for antimicrobial treatment. This includes measures such as poultry shed cleaning and a disinfection plan, separating sick and healthy birds, restricting people's movement and proper disposal of dead birds. Poultry health, disease resistance and optimum production performance are dependent on initial development of immune system (Mondal *et al*., 2020). For proper development of the immune system, early access to feed, water and optimal brooding conditions are required. Delayed responses in terms of all immunity parameters are observed in the caeca and colon and on the colonization of lymphocytes in the bursa when the birds are exposed to feed and water after 48 hours of hatching (Bar-Shira *et al*., 2005). This will lead to improper immune activity during the first two weeks of life. Good farm management, strict biosecurity, proper cross ventilation, litter management, proper stock density and lighting programs play a vital role in maintaining good health and performance (Dawkins *et al*., 2004; Olanrewaju *et al*., 2006; Dunlop *et al*., 2016; Wang *et al*., 2016; Bailey, 2019; Caekebeke *et al*., 2020).

Feed quality: Feed is an essential component in poultry production. Poor quality or contaminated feed can increase the risk of infections in birds, resulting in the use of antimicrobials to manage or prevent disease outbreaks. This can lead to the selection of AMR bacteria in the birds' gut microbiome, which may be transferred to other birds, the environment or even to humans. AMR concerns have led to antibiotic-free production (ABF). In that scenario, feed quality, dietary components and feed formulation play key roles to maintain bird's health and production performances. Bird's health and productivity are directly related to gastrointestinal tract (GIT) health and immunity. The intestinal microbiota balance is influenced by raw ingredients, nutrient density and the form of the feed. High levels of indigestible, water-soluble non-starch polysaccharides (NSPs) in the diet can increase viscosity in the intestinal lumen and decrease digesta passage rate. The source and level of dietary protein may also affect intestinal microbiota balance. Feeding with high levels of anti-nutritional factors could lead to more undigested protein in the intestinal lumen which in turn favors the growth of *Clostridium perfringens*. This may cause necrotic enteritis in birds (Timbermont *et al*., 2011). The risk of bacterial enteritis can be reduced by supplementation of enzymes in the diet. Alterations in normal intestinal function such as intestinal barrier function, nutrient absorption and reduction in immunity were reported in birds fed feed with mycotoxins (Grenier and Applegate, 2013).

Water quality: Water quality and water line management can also have an impact on poultry health and performance. Contaminated water can be a potential source of pathogenic bacteria that can colonize the bird's gut and cause disease. The water quality is essential for the maintenance of gut health and performance, which minimizes the need for antimicrobials. Water quality depends upon the source, hardness, pH, and mineral content of the water (Bailey, 2019). The pH is a key factor that can influence microbial populations in water and in the gut, thus maintaining a natural balance of gut microbiota. The water pH should be between 5 and 7 because alkaline pH reduces the activity of digestive enzymes (Ovideo-Rondon, 2019). A proper water hygiene, sanitation program and water quality testing should be followed to optimize poultry health and performance, which reduces antimicrobial use.

Breeder health, hatchery hygiene and chick quality: Breeder's health is critical to produce healthy chicks, and good breeder management programs ensure the birds are kept in optimal condition. Breeding stock that is free from any potential pathogens can lead to healthy chicks, which require fewer antibiotics. For proper development of their progeny, optimum nutrition of the breeder birds is necessary (Calini and Sirri, 2007). Egg nutrients obtained from the hen are considered to be important for embryonic development. Breeder hens transfer intestinal microbes and immunity to their progeny (Inoue *et al*., 2008; Leandro *et al*., 2011a,b). Intestinal microbiota can be acquired in the pre-hatching phase directly from the oviduct of the hen (Gantois *et al*., 2009) or from the environment through the pores in the eggshell. The gut microbiota composition may also be influenced by maternal antibodies. Maternal immunity can provide protection against enteric pathogens in chicks until 14 days of age (Grindstaff *et al*., 2003; Hamal *et al*., 2006). The high hygiene levels of hatcheries influence the development of the GIT and immune system (Wineland *et al*., 2006a,b; Leksrisompong *et al*., 2007). Proper hatchery sanitation, including cleaning and disinfection of the hatchery, is essential to reduce the infections in the hatchery and limit the need for antibiotics. Additionally, effective management of hatching eggs in the hatchery including proper storage, cleaning and sanitation of hatching egg can ensure healthy chick development.

Vaccination program: A potential tool that offers unique advantages in fighting against the development and spread of antimicrobial resistance is the development and use of vaccines against infectious diseases (Abbott, 2017). Vaccination can also help to control and prevent disease outbreaks, reducing the need for antibiotics. Reductions in antimicrobial use and bacterial resistance were observed after the introduction of a vaccination program (Fireman *et al*., 2003). An effective vaccination program can be tailored to meet the specific needs of poultry farms and can help to reduce the number of birds exposed to antibiotics.

Alternatives to antibiotic growth promoter: Many different classes of alternatives to antibiotic growth promoter have been tested and used in poultry production, and these include postbiotics, probiotics, prebiotics, essential oil, bacteriophages and organic acid.

Postbiotics- Postbiotics are used as alternatives to antibiotics in poultry and are a new promising solution in antibiotic free production (Humam *et al*., 2019). Postbiotics are the bioactive compounds resulting from the fermentation processes by food-grade microorganisms (Wegh *et al*., 2019). Inclusion of a postbiotic in the diet reduced intestinal lesions, enhanced immunity, improved health and growth performance of poultry (Roto *et al*., 2017; Nelson *et al*., 2018). Use of a postbiotic as an alternative intervention reduced the colonization of potential pathogenic microbes such as *Salmonella* sp., *Eimeria* sp. and *Escherichia coli* in poultry (Abd EI-Hack *et al*., 2022; Chaney *et al*., 2022; Kalani *et al*., 2022). In poultry, a postbiotic showed antioxidative activity under heat stress condition (Humam *et al*., 2019). Recent literature demonstrated that the postbiotic modulates host immunity and gut microbiome, resulting in improved poultry health and production performance (Chaney *et al*., 2022).

Probiotics- Probiotics are alternative feed additives used to modulate intestinal microbiota and control pathogens, and improve bird performance (Yegani and Krover, 2008; Mondal, 2018). Probiotics are live microorganisms that can improve bird's health by colonizing the gut and providing a more balanced microbiota (Murate *et al*., 2015). Probiotics can modulate both cell-mediated and humoral immune responses (Shang *et al*., 2008). Inclusion of a probiotic in a poultry diet improved nutrient digestibility and illeal and caecal microbiota composition in the intestinal lumen (Mountzouris *et al*., 2010). Probiotics act by multiple mechanisms of action, viz. competitive exclusion of pathogenic bacteria, improved immune response, improved gut barrier function, production of bacteriocins, and improved microbiota homeostasis (Gaggia *et al*., 2010; Mondal, 2018).

Prebiotics- Prebiotics are oligosaccharides and popularly known as 'non-digestible feed ingredients' but are utilized by specific population of gut microorganisms. They are used to modulate the composition and metabolism of intestinal microbiota selectively (Piniero *et al*., 2008). Prebiotics enhance the growth of *Bifidobacteria* and other species, thereby improving gut health (Scott *et al*., 2020). Prebiotics can improve birds' health by enhancing the production of metabolites like lactic acid, modifying microbial metabolism, and increasing cell integrity of the epithelium (Neupane *et al*., 2019; Yaqoob *et a*l., 2021). These can be potential feed additives to modulate gut microbiota for better growth and improved poultry health.

Essential oils- The phytogenic feed additives (PFAs) may act as antibacterial or immune-stimulating agents. One category of PFA is a mixture of essential oil compounds (EOC) (Hashemi and Davoodi, 2010). Essential oils are important due to their antiviral, antimicrobial, antiparasitic and antioxidant capabilities. Inclusion of essential oils in the poultry diet improved poultry performances and carcass characteristics (Khattak *et al*., 2014). Essential oil can mitigate pathogens such as *Salmonella* and *E. coli* in the intestine. These EOCs, viz. carvacrol, thymol and cinnamaldehyde, possess selective antimicrobial properties (Guo *et al*., 2004; Lee *et al*., 2004). Essential oil compounds can reduce the growth of *Clostridium perfringens* and control Coccidia infections (Guo *et al*., 2004; Mitsch *et al*., 2004; Oviedo-Rondón *et al*., 2005, 2010). EOC maintain the intestinal barrier function. Essential oils can improve poultry health and production by enhancing the activity of digestive enzymes, nutrient digestibility, pathogen reduction and enhancing antioxidant capacity and immune function (Algawany *et al*., 2021; Abd El Ghany *et al*., 2022).

Bacteriophages- Bacteriophages, known as bacteria eaters, are viruses that selectively infect and kill bacteria. Bacteriophages require a host cell to replicate. They are highly specific and can infect and kill closely related bacteria (de Jonge *et al*., 2019). With the increasing concern of antimicrobial resistance, bacteriophages have been an alternative tool to modulate innate and acquired immunity and prevention of pathogenic bacteria in poultry (Sarrami *et al*., 2022). Supplementation of bacteriophage in poultry diet improved egg production in layer and growth performance in broiler (Sarrami *et al*., 2022). Bacteriophages have positive impacts on the growth performance, immunity, and gut microbiota in broilers.

Organic acids- Organic acids are used to fight against bacterial and fungal contamination in feed. Organic acids are useful in maintaining gastrointestinal health and improving the production performance of birds. They efficiently mitigate pathogenic bacteria, such as *E. coli*, *Salmonella*, *Campylobacter*, *C. perfringens* and others (Banupriya *et al*., 2016). These acids enhance the growth of beneficial bacteria such as *Lactobacillus* in ileum and caecum of poultry (Saki *et al*., 2012). The inclusion of organic acids in feed and in water positively affects the prevention of enteric diseases and enhances the immunity, nutrient digestibility and overall production performances of poultry. Therefore, organic acids can alternate AGPs in poultry production (Abdelrajek *et al*., 2016).

Conclusion

A holistic disease prevention strategy can contribute to lower the risk of poultry diseases and hence, the use of antimicrobials. Farm management, biosecurity measures, water and feed quality, breeder's health, hatchery hygiene and chicks' quality, proper vaccination program and use of antimicrobial alternative feed additives such as postbiotics, probiotics, prebiotics, organic acids, essential oils and bacteriophages, can play a vital role to reduce the need of antimicrobial use. The issue of antimicrobial resistance in poultry is a complex and multifaceted problem that requires a comprehensive strategy to ensure that antimicrobial agents are used responsibly and sustainably. Failure to address this issue could have a negative impact on public health and global food security.

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Author's contributions: AM: Manuscript writing; VWN: Manuscript review and editing; JS: Manuscript review.

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