Antimicrobial Drug Resistance in Poultry Pathogens: Challenges and Opportunities

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ABSTRACT

Antimicrobial resistance (AMR) is widely acknowledged to be a global public health issue, and poultry raising is a key contributor. Antimicrobial medications are used in the treatment and prevention of disease in chickens as well as in the prevention of it. As a result of their work, human ailments may be avoided or addressed. Antimicrobials are overused and misused in human and animal health due to excessive dependence on them. Antimicrobial resistance was previously measured using disc diffusion tests for bacteria and fungi and phenotypic fluorescence-based techniques (for viruses). Once they had been cultivated under growth conditions, the viruses were able to thrive in embryonic chicken eggs or certain cell lines. Many previously undiscovered antimicrobial resistance genes have been discovered using metagenomics and next-generation sequencing (NGS). Systematic evaluations of studies on AMR in different poultry illnesses were carried out using MEDLINE, EMBASE, and CINAHL library sources. According to this list of sources, 103 studies were eligible for inclusion in the protocol. For our research into antimicrobial resistance, we're also looking at new methods for preventing disease and promoting development in food animals like chickens as well. As a result, it is imperative that efforts to harmonize testing methods, give open access to information and data on AMR, and monitor the spread of AMR in poultry illnesses be bolstered.

Keywords: AMR, antibiotics, antifungals, antivirals, enteric, multidrug resistance

Introduction

Public health officials must address antimicrobial resistance (AMR) as soon as feasible. In recent years, a slew of studies have demonstrated that animal antibiotic usage is a major contributor to the rise of antibiotic resistance (Marshall and Levy, 2011). Antimicrobial overuse in animal food production is the leading cause of foodborne illness in humans. Consumption is likely to grow sharply since agricultural methods in most emerging countries have advanced dramatically (Van Boeckel, et al., 2015). Predictions and data on AMR's emergence and prevalence among animals in the food supply chain are based on organisms that often cohabit with poultry and foodborne zoonotic diseases (Luna-Galaz, et al., 2016; Bortolaia, Espinosa-Gongora, and Guardabassi, 2016). Except in a few rare cases, nothing is known about the mechanisms and prevalence of AMR in pathogenic bacteria isolated from chickens and other foodstuffs.

In the world's biggest food industry, the production of chickens is the most common kind of poultry. Chicken meat is produced at a rate of more than 90 billion tonnes per year (Food and Agriculture Organization of the United Nations, 2017). Few, if any, religious or cultural limitations on their use are in place, and their production costs are quite low. Increasing output and development, as well as preventing and curing illnesses, are all goals in the chicken farming industry around the world. Antimicrobials are often administered orally. This was the conclusion of a study published in 2015 by Landoni and Albarellos. Antimicrobials are critical to human health, according to the World Health Organization (2017).

Indiscriminate antimicrobial use in animal husbandry has been linked to both commensal and pathogenic microbial resistance (AMR). eggs and meat that include antimicrobial ingredients present health issues in addition to concerns about the development of AMR in poultry illnesses (Reig and Toldra, 2008). Poultry illnesses and economic losses due to the high cost of ineffective antimicrobials are other concerns.

A systematic review technique was used to examine data on antibiotic resistance in poultry bacteria, fungi, and viruses. Health care for food animals like chicken is also evaluated, with the purpose of identifying trends and uncovering weaknesses and information gaps in the system.

Antimicrobial Drug use and Resistance in Poultry

To boost feed efficiency and growth rates, poultry has depended largely on antimicrobial treatments since the 1950s (Niewold, 2007; Torok et al., 2011). Using these items may also help to lessen the incidence of chicken diseases (Torok et al., 2011). More than three-quarters of the antimicrobial agents available in the majority of retail outlets are used on animals raised for food (Van Boeckel et al., 2019). Antimicrobial chemicals in feed and drinking water are used in a variety of ways across the world and in different regions (Gyles, 2008). Antimicrobial medication usage in food animals is ubiquitous, except in the European Union (EU) and the United States, where it was banned in 2006 and 2017 respectively (Roth et al., 2019). There are several methods in which antimicrobial medications are used to keep chickens healthy.

In human therapeutics, animal husbandry, and aquaculture, the overuse and/or misuse of antimicrobial medicines is the result of an excessive dependence on these drugs (Livermore, 2002; Sommer et al., 2009; Yuan et al., 2019). Consequently, the selection of resistant species is more likely to occur (Yang et al., 2004).

In the battle against antibiotic-resistant microorganisms, fluoroquinolone resistance is a critical concern. These antimicrobials are very effective in treating human infections due to their low toxicity and wide range coverage (Angulo et al., 2000; Livermore et al., 2002; Yang et al., 2004).

Globally, increasing numbers of researchers and policymakers believe that antimicrobial resistance (AMR) is a serious threat to public health that has resulted in more than 2 million cases of antibiotic-resistant disease and the deaths of dozens of individuals. "Superbugs," or germs that can tolerate multiple different kinds of antibiotics, are anticipated to worsen the situation (McKenna, 2013; Yuan et al., 2019). A major danger to both human and animal health is the development of antibiotic-resistant diseases that prolong illness and impair productivity owing to increasing morbidity and mortality (Yang et al., 2004).

Transmission and Spread of Antimicrobial Resistance

There is little doubt that antimicrobial resistance is a natural and ancient phenomena. Antimicrobial compounds are commonly used by bacteria to prevent competition (Newman et al., 2003; Yuan et al., 2019) and microorganisms' production of antimicrobial agents has developed over millions of years (Baltz, 2008; Yuan et al., 2019). Genes for antibiotic resistance (AMR) have a high amount of variation, which suggests that there may be several sources of resistant bacteria, or gene flow across strains as a consequence of mobile genetic components. As a result, antibiotic manufacturers must have systems in place to safeguard themselves against the dangers posed by the antibiotics of their rivals (Cordero et al., 2012; Wright, 2007; Yuan et al, 2019). Point mutations, re-assortment, and horizontal gene transfer (HGT) are all ways in which this resistance might develop (Hoelzer et al., 2017). An important role for AMR generation and transmission is played by enteric pathogens and normal gut microbiota under external stress through HGT (Zhou et al., 2012), which is mediated by mobile genetic elements (MGE). Antimicrobial resistance and transmission of zoonotic pathogen resistance have also been linked to the gut microbiome, as shown by research (Fricke et al., 2009; Nandi et al., 2004; Oakley et al., 2014). Numerous ARGs that have been widely studied may be found in methicillin-resistant enterococci (MGEs) (Allen et al., 2010; Yuan et al., 2019). Different ARG subtypes linked with the same antibiotic class may have varied effects on the bacteria that they affect (Kraupner et al., 2013; Yuan et al., 2019).

According to Wee, Muloi, and van Bunnik (2020), the primary source of AMR has been cattle, and the risk factors for transmission have been deemed to include environmental edges and close contact with regard to animals. It is possible that antimicrobials used to treat different infectious illnesses in livestock may be comparable to those used to treat people, which might contribute to the development and transmission of AMR in humans who are near to these animals/livestock (Novais& Freitas, 2020). The increasing use of disinfectants and metals in the environment may also be a role in the selection of AMRs in the future (Novais& Freitas, 2020). There are many ways for AMR-causing microorganisms and genes to spread from one place to another. These include direct contact with food, manure and wastewater, as well as indirect contact with the environment and animals. This allows for the continuous exchange of genetic material, as well as for the recombination of AMR features.

Methods Used to Study Antimicrobial Resistance

Chicken microbiome studies were stymied by high costs and outdated methodologies until recently (Penders et al., 2013). The degree of antibiotic susceptibility of indicator microorganisms was previously established through culturing bacteria of interest and performing antimicrobial sensitivity tests to assess their resistance to various antimicrobial agents. The selection of indicator microorganisms was based mostly on their clinical significance and cultivability (Penders et al., 2013). Only approximately 20% of the enteric microbiota has been cultured using these methods because of the finicky nature of gut microbes, which typically need unknown growing conditions (Clavijo and Florez, 2017; Gaskins et al., 2002).

Polymerase chain reaction (PCR) techniques may also be used to identify antimicrobial resistance genes. With these methods, it is possible to identify antimicrobial resistance more rapidly and with better sensitivity. There is a downside of PCR, which is that it tends to over- or under-represent the genes and processes linked with known resistance (Penders et al., 2013). An evaluation of the whole resistome in poultry's gastrointestinal system cannot be done using this approach (Zoetendal et al., 2004; Clavijo and Florez, 2017).

For AMR samples, functional metagenomics is an extra helpful technique. What's going on here?gene expression in non-homologous hosts after cloning of DNA fragments from one vector into another (often Escherichia coli). Transformed organisms are cultivated on antibiotic-containing media at safe doses for the wild-type host strain to see whether they are resistant to antibiotics. It has now been decoded the genomes of antibiotic-resistant clones (Penders et al., 2013; Schmieder and Edwards, 2012). This strategy's major shortcoming is that each gene may be expressed in surrogate hosts. What we don't know is whether the surrogate host has resistance genes that are not expressed (false negatives). When a foreign gene interacts with the host's cell machinery in unanticipated ways, it might create false positives (Penders et al., 2013; Schmieder and Edwards, 2012).

Analyzing AMR using sequence-based metagenomics is one of the most reliable methods since it does not need the cultivation of any organisms in order to extract, fragment, and separate DNA (Penders et al., 2013). By comparing the obtained sequences to the global sequence databases, it is possible to identify resistance genes (Penders et al., 2013; Schmieder and Edwards, 2012). While Sanger sequencing (SGS) has been largely replaced by NGS platforms including Illumina's Genome Analyzer (IGA), Roche's 454 sequencer, and Applied Biosystem'sSOLiD system, there has been a considerable rise in the number of metagenomic sequencing studies (Penders et al., 2013). However, despite the fact that most NGS technologies have shorter contiguous read lengths and need more genome coverage, their high-throughput reduces the cost and number of sequencing runs (Niedringhaus et al., 2011; Penders et al., 2013). DNA from the sample is amplified and then sequenced using either the 16S rRNA gene or the internal transcribed spacer (ITS) region, depending on the kind of bacteria or fungi. Direct shotgun sequencing of DNA samples is also becoming more popular due to its high sensitivity, reproducibility,

and ability to sequence the whole microbial community.

Antibacterial Resistance in Poultry

As a hazard to livestock productivity, food safety and the general public's health, bacteria may cause sickness in both animals and people (Taylor et al., 2001; Wolfe et al., 2007; Woolhouse and Gowtage-Sequeria, 2005; Zhou et al, 2012). Salmonella, Campylobacter, avian pathogenic Escherichia coli, and enterococci are only a few of the enteric zoonotic bacteria found in poultry (Gyles, 2008). Bacterial AMR in poultry and other animals has been the subject of several investigations.For example, the authors of a recent research on AMR in Salmonella from the poultry sector in Ethiopia (Abdi et al., 2017) found that prevalence was greater in bedding and staff hand swabs (33.3%) than in the cloaca (14.8 percent). This exposed the shoddy biosecurity and hygiene standards at chicken processing facilities. However, more importantly for this review, the authors found that all isolates were resistant to the antibiotics kanamycin and sulfamethoxazole-trimethoprim, as well as varying degrees of resistance to nalidixic acid, ampicillin and cefoxitin, as well as to the antibiotics streptomycin and tetracycline. Concern was raised when they discovered that the majority of isolates had developed resistance to several drugs (MDR). Antimicrobial resistance in Salmonella isolated from chicken has been studied in similar ways in Belgium, Ghana, and the United States (Vinueza-Burgos et al., 2019), as well as the United Kingdom (Andoh et al., 2016). (Velasquez et al., 2018). The prevalence of Salmonella and AMR was studied by Bailey et al. (2020) by collecting ambient samples, carcass rinses, and faecal samples in a longitudinal research. In the early phases of processing, organic chickens were shown to be associated with statistically significant levels of Salmonella. According to Bailey et al. (2020), Salmonella infection may be more likely to occur when using organic techniques, however proper processing may reduce this risk. This is consistent with the results of Kamaruzzaman and Saeed (2020) that multidrug resistant (MDR) Salmonella spp. and E. coli are prevalent in poultry in eastern Malaysia. Farms raising these broilers may have overused antimicrobial treatments, contributing to the problem. There have been several research done in Canada and the United States on the frequency of AMR of Salmonella in chicken (Varga et al., 2019). (Fricke et al., 2009).

In Kenya, a study of backyard and small-scale hens found that 77.4%, 71.0%, and 71.0% of Campylobacter jejuni isolates were resistant to nalidixic acid, tetracycline, and ciprofloxacin, respectively (Nguyen et al., 2016). Gentamicin and chloramphenicol had lower resistance of 25.8%, whereas multidrug resistance was found in 61.3 percent of the isolates. Despite the fact that Campylobacter species were shown to be prevalent in both conventional and organic poultry management systems, the antimicrobial resistance rates were significantly different between the two systems (Luangtongkum et al., 2006). According to the researchers, organically reared chicken had less Campylobacter strains that were resistant to antimicrobial agents compared to those from conventionally maintained poultry. Campylobacter strains isolated from conventionally raised turkeys were also found to have multidrug resistance. Unregulated use of antimicrobial drugs on chicken farms was clearly shown to have a harmful

effect. Marotta et al., 2019 and Wimalarathna et al., 2013 conducted similar investigations in Italy and the United Kingdom, with varying results. Antimicrobial resistance has risen as a consequence of overuse and misuse of antimicrobials in human and veterinary medicine, according to these research.

APEC isolates from broilers during the slaughter period in a processing factory, Kenya, were also studied by Adelaide, Bii, and Okemo (2008) to explore MDR and virulence-related genes. According to the findings, MDR and virulent APEC are prevalent in Kenyan broilers. E. coli clinical isolates from poultry and cattle were studied in China between 2004 and 2012 as part of another research of AMR in E. coli isolates (Yassin et al., 2017). Researchers found that 94% of the isolates were drug-resistant, and 83% were resistant to three or more antimicrobial classes. Antibiotic resistance is frequent among E. coli isolates from poultry and animals, which is why the authors stressed the need of rationalising and restricting the overuse of antibiotics in China's food supply. APEC was also isolated, identified, serogrouped and genotyped from broilers, as well as their antibiotic resistance profile and indicated genetic features, and the relevant risk factors were evaluated by Ibrahim and colleagues (2019). A total of 54 percent of broilers were considered to be infected, and APEC was isolated from their visceral organs. According to the data, 68 percent of the APEC isolates had at least five to eight antimicrobial resistance genes. MDR APEC in broiler chickens is connected to the presence of two risk factors: proximity to neighbouring farms and the use of ground water as a source of drinking water. APEC isolates with high levels of antimicrobial resistance and identification of resistance genes, according to Ibrahim et al. (2019), demonstrate the significance of closely monitoring ARG development in the environment, particularly in Jordanian poultry farms. Homjan et al. (2018) performed a research to determine the antibiotic resistance of E. coli isolates from colibacillosis lesions, and the results focused on the appearance of MDR and AMR among APEC or E. coli isolates. The goal of this study was to better understand the need of frequent AMR monitoring and the practical use of antimicrobial drugs in chicken production. E. coli resistance to antibiotics in broiler production was also examined in depth by Roth et al. (2019) in their study. APEC isolates from poultry have also been studied in Belgium (Smet et al., 2008), Canada (Varga et al., 2019), Iran (Momtaz et al., 2012), Jordan (Ibrahim et al., 2019), and the United States (Smet et al., 2008, Varga et al., 2019). (Musgrove et al., 2006; Zhao et al., 2005).

In a study of Enterococcus spp. from Nigerian poultry and cattle farms, vancomycin was shown to be effective against all of the isolates examined. However, 61 percent, 61 percent, 45,1 percent, and 32,7 percent of the isolates were resistant to tetracycline, erythromycin, ampicillin, and gentamicin (Ngbede et al., 2016). In addition, 53.1 percent of the isolates were shown to be resistant to several drugs. Some of the isolates had genes for antibiotic resistance and pathogenicity (asa1, gelE and cylA). Authors reasoned that the Enterococcus species in the research regions were capable of virulence and resistance traits that may be spread to other organisms by way of the poultry, livestock, and dung. The United States has also carried out research on AMR, virulence factors, and the genetic profiles of Enterococcus from poultry (Jackson et al., 2014; Kilonzo-Nthenge et al., 2016; Tyson et al., 2017).

Numerous poultry bacterial infections have also been studied in depth by researchers. While Apostolakos

and Picirillo (2018) give a wealth of information on the present state of knowledge and issues associated with colistin resistance in chicken production, Threlfall (2002) sought to investigate AMR in Salmonella. In contrast, Gautier-Bouchardon (2018) focused on the AMR of Mycoplasma spp. in their study. Human health hazards linked with antimicrobial medication usage in food-producing animals were also addressed by Hoelzer et al. (2017), while Saliu et al. (2017) investigated the kinds and prevalence of Enterobacteriaceae that produce extended-spectrum beta-lactamase (ESBL) in chicken. Antibiotics become ineffective because ESBL enzymes, which are generated by certain bacteria, break down the active components. Other researchers, on the other hand, focus on a broader range of bacterial infections in poultry when studying AMR (Nhung et al., 2017; van Boeckel et al., 2015; van Boeckel et al., 2019).

Antifungal Resistance in Poultry

It is becoming more common for domestic and wild birds to carry human fungus that have the potential to cause disease (Subramanya et al., 2017). People's health may be jeopardised if they are exposed to pathogenic fungus found in birds, such as Cryptococcus, Geotrichum, Rhodotorula, and Trichosporon (Wojcik et al., 2013; Subramanya et al., 2017). Synanthropic birds may be a source of drug-resistant fungus, raising concerns about the transmission of zoonotic infections from birds to people (Subramanya et al., 2017).

It was shown that both domestic and commercial hens' gut bacteria had virulence factors and antifungal sensitivity patterns in a research conducted in Nepal (Subramanya et al., 2017). The MIC values of fluconazole (8-512 vs 0.031-16) and amphotericin B (0.5-64 vs 0.031-6) were found to be higher in biofilm cells than in planktonic cells in this investigation.

It is 0.062-16 for voriconazole and caspofungin, vs 0.062-8 and 0.031-1, respectively. The widespread use of antimicrobials and growth promoters in commercial chicken feed has been blamed for the rise in antibiotic resistance. A similar study in Saudi Arabia found the presence of Cryptococcus, Saccharomyces, Rhodotorula, Candida, Meyerozyma, Cyberlindnera, Rhodosporidium, Millerozyma, and Lodderomyces in rock pigeon faecal droppings, but none of the identified yeast isolates exhibited any resistance to the antifungal drugs tested, despite the presence of these pathogenic and opportunistic yeast species (Abulreesh et al., 2019). No Cryptococcus species tested positive for virulence markers including urease activity, growth at 37°C, melanin formation, or the PLB and CAP genes, according to Abulreesh and colleagues.

In a previous study in Poland, all 85 Aspergillus fumigatus strains isolated from domestic geese and their environment were found to be resistant to miconazole, regardless of source, in vitro susceptibility to amphotericin B, clotrimazole, voriconazole, itraconazole, enilconazole, and ketoconazole and tioconazole (Ziolkowska et al., 2014). The remaining azoles and amphotericin B were resistant to 90.6 to 70.6 percent of the test samples. Voriconazole and enilconazole were shown to be completely resistant. The researchers also found that the most resistant viruses were found in lung samples (100 percent for amphotericin B and clotrimazole and 35.7 percent for itraconazole). There have been similar studies done on the resistance of Aspergillus fumigatus to itraconazole and the susceptibility of Aspergillus niger strains to several antifungal

medications in Poland (Nawrot et al, 2019). (Tokarzewski et al., 2012).
Macrorhabdusornithogaster (an anamorphic ascomycete) was shown to be resistant to Amphotericin B therapy in Australian cage birds, according to a separate investigation (Baron et al., 2018).

Antiviral Resistance in Poultry

Additionally, there is no evidence that chickens are resistant to antiviral medication. Only recombinant feline interferon, an immune-modulator, has been licenced for use on farm animals globally, which may explain the dearth of information on antiviral resistance among a number of poultry viral diseases (Hussein and Abdelwhab, 2016). In contrast, antivirals have a considerably smaller scope of action and can only target a single virus (Hussein and Abdelwhab, 2016). Virus genomes, on the other hand, are subject to a lot of random mutations. Changing the antiviral drug's target might result in a mutation that renders it ineffective, resulting in the emergence of resistant strains (Hussein and Abdelwhab, 2016). A surge in amantadine-resistant HPAI H5NI viruses in Chinese poultry has been attributed to unlawful and irresponsible containment of H5NI and H9N2 influenza infections in chickens (Abdelwhab and Hafez, 2012; Cyranoski, 2005; He et al., 2008; Huang et al., 2009; Parry, 2005). Egypt's reemergence of resistant H5N1 viruses was also tied to an unlimited use of amantadine in Egyptian poultry farms, which made this therapy worthless for human avian influenza treatment and prevention (El-Shesheny et al., 2016). (El-Shesheny et al., 2016).

Oseltamivir, an important antiviral drug in the fight against the pandemic flu, is excreted and released into the environment by Swedish sewage treatment plants (Fick et al., 2007). According to the data, UV light radiation has no influence on the breakdown of oseltamivir carboxylate. Consequently, it permeates the environment and promotes the development of drug resistance since it is discharged into the waste water that exited the facility. Oseltamivir (Gilman, 2015a; Jarhult, 2011) resistance mutations H274Y, I222T, and R292K in influenza A/H1N1, H7N9, and H6N2 were further investigated in mallard birds (Gilman et al., 2015b; G. An influenza virus resistant to drugs was found in ducks living near sewage treatment facilities, according to these studies. The scientists voiced fear that oseltamivir resistance may transmit to human-adapted populations with pandemic potential if influenza viruses can bypass species barriers. As a consequence, the essential pandemic-prevention drug oseltamivir would be rendered ineffective. As a result, they claimed that tracking resistance over time necessitated observing wild birds. In order to lower the amounts of oseltamivir carboxylate in the environment, greater sewage treatment and judicious usage of antivirals are needed. Results from a Swedish investigation on flu viruses acquired from wild mallards indicated alterations related to oltamivir and azidothymidine resistance as well (Orozovic et al., 2014).

The remaining 67 H5N1 viruses discovered in India between 2006 and 2012 were found to have an unique NA I117T amino acid substitution (N2 numbering) and eight previously known neuraminidase inhibitors (NAI) resistance marker mutations (I117V; E119D; N294S) in their genomes (Kode et al., 2019). A total of 13.4% of those who took part in the study refused therapy. Flu viruses in birds should

continue to be monitored for influenza viruses, since NA inhibition tests demonstrated cross-resistance in the I117T amino acid substitution isolate to both of the two medicines studied. (Kode et al., 2019) In a similar experiment, oseltamivir-resistant H5N1 avian influenza viruses were tested in India using embryonated chicken eggs (Tare et al., 2019). The antiviral medication susceptibility of avian influenza viruses has also been studied in China, Egypt, India, and the United Kingdom, among other countries (Bialy and Shelton, 2020).

Alternatives to Antimicrobial Agents in Poultry Production
Probiotics
A probiotic is a combination of living microbes that, when taken in sufficient quantities, have a beneficial effect on the person taking them (Clavijo and Florez, 2017; Smith, 2014). Beneficial microbiota, which limit and prevent the colonisation of pathogens in the gut, promote epithelial health, boost digestive capacity and aid in tissue maturation in animal hosts, are stimulated by them. Clavijo and Florez have examined the health advantages of these supplements in depth in their research (2017).

Since 1973, probiotics have been used in poultry to reduce Salmonella in broiler chickens (Clavijo and Florez, 2017; Nurmi and Rantala, 1973). A drawback to this early use of probiotics was the possibility that infections were also conveyed, which might have harmed the helpful microbes. According to Clavijo and Florez (2017), a wide variety of probiotics have been created, with different efficacy. Most commercially marketed probiotics are a mix of Lactobacillus and Bacillus species.

In Kenya, a study was carried out to determine the effect of dietary probiotics on poultry's natural Immunoglobulin levels (Khobondo et al., 2015). Researchers dissolved 5ml of probiotic Molaplus into containers of various sizes, ranging from 250 to 2,000 ml of drinking water, for 150 2-month-old chicks in this investigation. Indirect enzyme-linked immunosorbent assay (ELISA) was used to measure Immunoglobulin concentrations. Immunoglobulin binding to keyhole limpet hemocyanin was shown to be unaffected by dietary probiotic supplementation, according to the results (KLH). According to Atela et al. (2015), treating indigenous chickens in Kenya with probiotics in their drinking water may dramatically enhance their weights.

Prebiotics
Prebiotics are substances that encourage the growth of helpful microorganisms in the intestines of the host (Clavijo and Florez, 2017). They're less expensive to make than probiotics, have less negative effects on the host, and are simpler to prepare and administer than those latter products (Clavijo and Florez). Generally speaking, prebiotics work by adhering to pathogens and acting as a source of carbon for fermentation. Additionally, this causes macrophage activity to be stimulated, and short-chain fatty acids (SCFAs) to be produced, which in turn affects the immune system (Clavijo and Florez, 2017; Patel and Goyal, 2012).

In most cases, they are synthetic oligosaccharides comprising one or more sugar molecules, as well as combinations of simple sugars such as glucose, fructose and xylose that are not digested by humans. However,

when employed in large-scale production systems, responses to prebiotic supplements have been uneven (Clavijo and Florez, 2017). A variety of factors have been suggested, including differences in the quality and amount of the chemicals and the unique environment of each farm.

Adding organic acids to broiler chickens' drinking water enhanced their feed conversion ratio and gastrointestinal health in a Kenyan poultry farm study, according to Odede (2016), who conducted the research on broiler chickens near Nairobi. By increasing beneficial bacteria and decreasing coliform levels, these acids made this feasible. Because of this, the author concluded that organic acids are an excellent alternative to antibiotics for improving broiler chicken health and production.

Bacteriophages

Bacteriophages are infectious viruses that specifically target bacteria and are known as such. Phage therapy refers to the use of phages in the treatment of bacterial infections (Clavijo and Florez, 2017). In 1915, bacteriophages were discovered, and the first known human usage of them was recorded (Abedon et al., 2011; Clavijo and Florez, 2017). Multidrug-resistant diseases have recently made the natural, harmless alternative treatment of bacteriophages a realistic option (Clavijo and Florez, 2017). A advantage of targeted treatment is that it doesn't disrupt the general microbiota in any way. Since the risk of secondary infections as a consequence of the use of antibiotics is decreased (Clavijo and Florez, 2017). antibiotic-resistant and antibiotic-resistant bacteria may both benefit from the use of bacteriophages (Clavijo and Florez, 2017; Loc-Carrillo and Abedon, 2011; Nilsson, 2014). phages with connection to humans, animals, plants, and food have been thoroughly explored by Clavijo and Florez (2017). In 2006, the US Food and Drug Administration approved the use of an anti-Listeria phage combination in foods designed for human consumption (Clavijo and Florez, 2017; Sulakvelidze, 2013). The use of bacteriophages in live animals, on the other hand, is still prohibited. Bacteriophage therapy have been studied in many animal models, including the prevention of Salmonella and Campylobacter.

With phage therapy, there is a wide range of results that may be obtained. A phage may become resistant to its target microorganism because of its low infection multiplicity, or it may be inaccessible to the target microorganism because the host has activated the phage (Clavijo and Florez, 2017). They can't be used on farms since they haven't been cleared for use with animals. Because of its new development, the treatment's acceptance by the producer community is uncertain (Clavijo and Florez, 2017). A study of the effectiveness of phages in commercial industrial farming settings, such as those seen in meatpacking plants, was suggested by Grant et al.

Challenges and Future Prospects

Many researchers believe that poultry AMR induced by common indicator diseases should be a matter for concern. For antimicrobials used in animal production, such as penicillin and tetracyclines, resistance rates are the highest. ' According to Van Boeckel et al, the rapid loss in our capacity to identify novel and effective antimicrobial medications used in livestock husbandry would have a negative impact on both

animal and human health (2019). The post-antibiotic era is even more frightening due to a dearth of new antimicrobials and even fewer that have been approved for usage. Developing countries like Kenya and Africa, where resistance is frequent, need international engagement and cooperation since research budgets and prospects are limited.

It is important not to abuse antimicrobial medications as a treatment for poultry infections. Antimicrobials should be used at every stage of the poultry production process. An example of an alternative treatment is phage therapy. Chickens should be fed probiotics and prebiotics in order to promote their general health and well-being. The use of antibiotics to treat illness or promote growth has reduced. Natural and synthetic antimicrobial peptide development may also be a topic of discussion. Biosecurity measures and a healthier diet may help raise healthy birds and reduce their need on antimicrobials.

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