



Avian Colibacillosis, Multidrug Resistance, Antibiotic Alternatives: an Updated Review

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Abstract

COLIBACILLOSIS is the most prevalent infectious microbe affecting avian species resulting in financial losses. Also, Colibacillosis is frequently one of the most common illnesses mentioned in surveys regarding the health of poultry or complaints made during processing. Colibacillosis denotes any systemic or localized infection induced partly or entirely by avian pathogenic *Escherichia coli* (APEC), which includes coli-septicemia, coligranuloma (Hjarre's disease), air sac disease [chronic respiratory disease (CRD)], venereal colibacillosis (acute vaginitis in turkey), swollen-head syndrome, and coliform cellulitis, peritonitis, salpingitis, osteomyelitis/ synovitis, pan-ophthalmitis, omphalitis, enteritis and lymphocytic depletion of the bursa and thymus. Often colibacillosis is among the most frequently reported diseases in surveys of poultry health or condemnations at processing. The majority of APEC isolated from chickens are certain types that are only harmful to birds and pose little risk of infection to other animals or humans. Recently, avian colibacillosis has a wide range of multidrug resistance, and the world directed to the usage of antibiotic alternatives to overcome this problem. Thus, the current review on the current status of colibacillosis among poultry farms, drug resistance, and the possible solutions via using safe natural antibiotic alternatives.

Keywords: Antibiotic alternatives, Chicken, *E. coli*, Genes, Probiotics, Serotypes.

Introduction

Avian pathogenic *Escherichia coli* is the cause of different illness conditions in birds as fatal septicemia and local infections [1,2], Airsacculitis, perihepatitis, pericarditis, peritonitis [3,4], and salpingitis [5]. APEC bacteria have been recovered as a complicated factor in cases of complicated chronic respiratory disease (CCRD) [6]. Likewise, modern analysis of APEC genome sequences has similarities to *E. coli* strains that can cause people extraintestinal illness like renal illness, sepsis, and neonatal meningitis [7,8].

Control of APEC infections in poultry is crucial. Strict hygienic measures are important, and if infection occurs, treatment with antibiotics selected based on sensitivity testing is recommended.

However, antibiotic resistance has become a major problem on many poultry farms, with multi-drug resistant *E. coli* strains, involving those producing cephalosporin-resistance, extended-spectrum beta-lactamases (ESBLs), and plasmid-mediated quinolone resistance (PMQR) [9,10].

Vaccination has emerged as a valuable tool for controlling colibacillosis. Both inactivated and live attenuated *E. coli* vaccines have shown promise. Inactivated *E. coli* vaccines administered subcutaneously can elicit high antibody titers and provide protection in layer chickens and turkeys [11]. Live attenuated vaccines, such as the AaroA mutant strain, have also been found to be safe and effective when used in broiler chickens [12].

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Avian colibacillosis

E. coli, is a normally detected bacteria in the intestines of animals, involving chickens [13, 14]. While many strains of *E. coli* are harmless, some can cause illness and infections [15]. *E. coli* has a lot of pathotypes that cause a variety of diseases and syndromes associated with colibacillosis can vary and include acute fatal septicemia, airsacculitis, pericarditis, perihepatitis, peritonitis, and lymphocytic depletion of the bursa and thymus. [16].

Economic importance

APEC is a critical illness in avian species inducing financial losses due to increased mortalities, cost of medication, and indirectly due to reduced final weight, elevated FCR as well as, high condemnation rates of avian carcass [17]. Furthermore, MDR developed quickly to *E. coli* [18] which led to severe losses by increasing treatment costs during the disease course and mortalities [19]. In chickens, APEC induces colibacillosis, and the disease induces financial losses to the poultry industry all over the world [20]. Additionally, APEC causes a burden on broiler breeders, with decreased fertility, hatchability, and egg production as well as increased mortality [20,21].

E. coli virulence factors

The virulence factors of pathogenic *E. coli* can influence a vast range of cellular processes in eukaryotic cells, involving ion secretion, cell signaling, mitosis, protein synthesis, mitochondrial action, and cytoskeletal function [16,22,23]. The virulence factors encoded on mobile genetic elements like plasmids, bacteriophages, transposons, as well as pathogenicity islands, which transfer between different *E. coli* strains, creating a new merge of virulence factors [23 and 24]. The genomic makeup of sequenced pathogenic *E. coli* strains shows a mosaic pattern, with up to 2,000 genes found in 247 islands in one pathotype that are absent from the non-pathogenic K-12 strain. Conversely, up to 0.53 MB of DNA present in K-12 can be missing from pathogenic *E. coli* [16, 24]. The virulence factor genes in pathogenic *E. coli* are regulated by both pathotype-specific regulators that are away from the commensal type of *E. coli*, as well as more general 'housekeeping' regulators that are present in both pathogenic and non-pathogenic strains [16,23, 25].

According to Dho-Moulin and Fairbrother [26]; Johnson and Nolan [27], and Mellata [8], *E. coli* strains isolated from chickens can possess various virulence factors that contribute to their pathogenicity including:

Adhesins: Adhesins are surface proteins that enable *E. coli* to adhere to specific receptors on host cells, facilitating colonization and infection. Different adhesins have been known in pathogenic *E. coli* strains, including those obtained from chickens.

Examples of adhesins associated with *E. coli* pathogenicity include type 1 fimbriae, P fimbriae, and curli fibers.

Colonization factors: certain strains of *E. coli* possess colonization factors that enhance their ability to colonize specific sites within the host, such as the intestines. For example, strains of APEC can possess colonization factors such as F1C fimbriae, S fimbriae, and APEC O78-specific fimbriae, which contribute to their ability to colonize the avian respiratory and urinary tracts.

Toxins: while verotoxins are not commonly associated with *E. coli* strains isolated from chickens, other toxin types can be present. For instance, some *E. coli* strains produce heat-labile toxins (LT) & heat-stable toxins (STa & STb), which can contribute to diarrheal disease in chickens. These toxins can disrupt normal intestinal function and contribute to the development of diarrhea.

Verotoxins/Shiga Toxins, verotoxigenic *E. coli* (VTEC), also identified as Shiga toxin-producing *E. coli* (STEC), are strains of *E. coli* that possess certain virulence factors known as verotoxins or Shiga toxins. These toxins are a family of cytotoxins produced by certain strains of *E. coli*, particularly VTEC/STEC. There are different types of verotoxins identified, including Shiga toxin 1 (Stx1), Shiga toxin 2 (Stx2), and their variants. These toxins are classified as AB₅ toxins, where the A subunit mediates the cytotoxic effect, and the B subunit facilitates binding to specific receptors on host cells [28]. These toxins-producing microbes can induce severe illness in humans, like hemolytic uremic syndrome and hemorrhagic colitis [29-31]. Verotoxins encoded by genes located on temperate bacteriophages (bacterial viruses) that have integrated into the *E. coli* genome. The genes responsible for Shiga toxin production are typically located within the pathogenicity islands of the bacterial chromosome or plasmids. The presence of these genes is one of the key virulence determinants that differentiate VTEC/STEC strains from other harmless *E. coli* strains [32].

Iron Uptake Systems: Iron is an elements nutrient for bacterial multiplication, and *E. coli* strains have developed various iron uptake systems to compete for iron in the host environment [33]. Pathogenic *E. coli* strains isolated from chickens often possess specific iron uptake systems, such as sit (iron ABC transporter) and iro (salmochelin siderophore system), which aid in their survival and colonization within the host [34].

Factors assist *E. coli*'s ability to establish and persist in the chicken host

The survival and colonization of *E. coli* strains in chickens can be influenced by various factors were

sate following Semenov et al. [35], Braz et al. [36], and Pokharel et al. [37] as follows:

Adherence and Colonization Factors

The ability of *E. coli* strains to adhere to and colonize specific sites within the chicken host is crucial for their establishment. Adherence factors, such as fimbriae and other adhesins, enable *E. coli* to bind to host cells and tissues, facilitating colonization. Different *E. coli* strains may possess specific adherence factors that contribute to their colonization in specific sites, such as the intestinal tract or respiratory system.

Iron Acquisition

As previously mentioned, iron is an important nutrient for bacterial multiplication, and its availability in the host environment is restricted. *E. coli* strains employ various iron uptake systems, including the production of siderophores and the expression of specific receptors and transporters, to acquire iron from the host. Efficient iron acquisition mechanisms can enhance the existence & competitiveness of *E. coli* strains in the chicken host.

Immune Evasion

The immune system of chickens plays a critical role in defense against bacterial infections. *E. coli* strains that possess mechanisms to evade or subvert the host immune response can have an advantage in survival and colonization. For example, some strains may produce immune-modulating proteins or possess mechanisms to resist phagocytosis by immune cells, allowing them to avoid clearance and establish persistent infections.

Toxin Production

Certain *E. coli* strains produce toxins that can contribute to their survival and colonization in chickens. For instance, some strains produce cytotoxic proteins that can damage host cells, disrupt tissue barriers, and facilitate bacterial dissemination. Toxins can also modulate the host immune response, enabling the bacteria to evade immune clearance and establish infection.

Antimicrobial Resistance

The emergence of antimicrobial-resistant *E. coli* strains poses a significant challenge in the control of bacterial infections in chickens [38]. Strains that are resistant to commonly used antimicrobial agents can persist and colonize the chicken gut, potentially leading to the spread of resistant strains within poultry populations.

Host Factors

Host-related factors, such as age, immune status, and gut microbiota composition, can likewise affect the existence and colonization of *E. coli* strains in chickens. Younger chickens with immature immune

systems may be more susceptible to colonization and infection. Additionally, the presence of commensal bacteria in the gut can compete with *E. coli* for nutrients and colonization sites, affecting their establishment.

The virulence genes associated with chicken pathogenic E. coli

Pathogenic *E. coli* strains isolated from chickens can possess a variety of virulent genes that contribute to their ability to cause disease. These genes encode factors like adhesins, toxins, iron acquisition systems, & other virulence-related proteins. The presence and combination of specific virulence genes can determine the pathogenic potential of *E. coli* strains [26,39-41].

Antibiotic resistance gene in avian pathogenic E. coli strains

Most APEC isolates (75–100%) carried virulence genes including *ial*, *fimH*, *crl*, *papC*, and *cjrC*. The presence of *papC*, and *cjrC* genes, as well as the phylotypes D2 and B2, showed a significant association with colibacillosis. Phylogenetic analysis revealed two distinct clades (clade A & B) of APEC, with clade A sharing 98–100% similarity with APEC O78 & *E. coli* EHEC strains, & clade B having the closest correlation with *E. coli* O169:H41 strain. Intriguingly, phylogroups B2 & D2 were present in APEC strains from both clades, while strains from phylogroups A1 and 7 B1 were only found in clade A [70]. Investigated that the pathotypes and antibiotic resistance gene of pathogenic *E. coli* strains from chicken included adhesins (e.g., *iha*, *fimH*), toxins (e.g., *hlyA*, *astA*), & iron acquisition systems (e.g., *iutA*, *fepA*) among the isolates.

Pathogenic *E. coli* isolates from chickens can harbor antibiotic-resistant genes, which contribute to their ability to survive and proliferate in the presence of antibiotics [42,43]. These genes are acquired through horizontal gene transfer, allowing bacteria to rapidly develop resistance to various antibiotics [44]. The prevalence and characterization of plasmid-mediated quinolone resistance genes (e.g., *qnrA*, *qnrB*, *qnrS*) in *Salmonella* strains recovered from poultry in China. It highlights the presence of these resistance genes, which can also be found in pathogenic *E. coli* strains [45]. In investigating the identification of extended-spectrum β -lactamase (ESBL) genes in *E. coli* isolates from ducks & ecological samples on a duck farm. ESBL genes, such as *bla*_{CTX-M}, are associated with resistance to cephalosporins and other beta-lactam antibiotics [46]. *E. coli* isolated from laying hens in Shandong Province, China. It identifies multiple antibiotic resistance genes, including those associated with resistance to fluoroquinolones (e.g., *qnrS*, *qnrB*), sulfonamides (e.g., *sul1*, *sul2*), and tetracyclines (e.g., *tetA*, *tetB*) [47].

The diversity of virulence genes

The diversity of virulence genes in APEC strains obtained from chicken strains can vary depending on factors such as strain prevalence, geographical location, host population, and environmental conditions and can have different potential implications [37, 48].

Variability in Pathogenicity

The presence and combination of different virulent genes can influence the pathogenic potential of *E. coli* strains. Some virulence genes encode factors such as adhesins, toxins, and iron acquisition systems, which contribute to colonization, tissue invasion, and immune evasion [23]. The diversity of virulence genes among strains can result in variations in the severity and type of diseases they cause in chickens, ranging from mild intestinal infections to more severe systemic infections [49].

Host Tropism and Adaptation

The diversity of virulent genes can contribute to host tropism and adaptation. Certain virulence genes may be more prevalent or associated with specific *E. coli* strains isolated from chickens, indicating their adaptation to the avian host [39]. These genes can enable the bacteria to colonize and cause disease in chickens, while potentially having reduced virulence or no impact on other host species [41].

Antibiotic Resistance

Virulence genes and antibiotic resistance genes can sometimes be co-located on similar mobile genetic elements, like plasmids or transposons [50]. The diversity of virulence genes in *E. coli* strains isolated from chickens can be associated with the presence of antibiotic-resistance genes [51]. This co-occurrence of antibiotic resistance genes & virulence genes poses challenges in the treatment and control of bacterial infections, as it limits the effectiveness of antibiotics commonly used in poultry production [52- 54].

Vaccine Development: The diversity of virulence genes can impact the development of effective vaccines against pathogenic *E. coli* strains in chickens. Vaccines targeting specific virulence factors or combinations of virulence genes may need to be tailored to match the prevalent virulence profiles in the circulating *E. coli* strains [51,55,56].

Zoonotic importance

E. coli infections in chickens can potentially be transmitted to humans' certain strains of *E. coli*, such as certain serotypes of STEC, can cause illness in humans through the ingestion of polluted poultry products or direct contact with diseased birds or their feces [57]. These strains can cause a range of symptoms in humans, including diarrhea (often

bloody), abdominal cramps, & in some cases, more severe complications such as hemolytic uremic syndrome, which results in renal failure [58, 59].

Transmission

The primary routes of APEC infection include fecal-oral where the bacteria shed in the feces of infected birds contaminate the environment, feed, and water sources. Chickens can become infected with APEC through a few main routes. They can ingest contaminated feed or water or come into direct contact with feces from infected birds, either through the respiratory tract or the ascending vaginal/cloacal route [26]. The fecal-oral and respiratory transmission routes have been studied the most in cases of colibacillosis [41]. There is also evidence of vertical transmission of APEC from infected parent birds to their offspring through the eggs. This can lead to increased mortality in the first week of life for the chicks, as well as subsequent horizontal transmission within the hatchery [20,41].

Epidemiology and occurrence of the E. coli

Normally *E. coli* inhabits bird's gut, unfortunately that disease could be triggered by numerous events including stress together with immunosuppressive viruses as Gumboro, Marek's disease (MD), & Chicken Anemia virus (CIA) [60], moreover *E. coli* is considered the main complicating agents for different lesion in poultry industries as it was found that 88.2% of Airsacculitis cases in 100 poultry farms in Jordan, were identified as *E. coli* [1]. In day old chicks, it was found that APEC resulted in higher mortality (28.4–31.4%) in birds because of yolk sac infection [61].

Loop-mediated isothermal amplification (LAMP) assays were developed to rapidly detect three virulence genes associated with APEC: *stx*A, *tra*T, & *omp*T. These LAMP assays were shown to be highly specific, repeatable, & sensitive, able to detect as few as 1,000 bacterial cells/mL in various sample matrices. The LAMP method was demonstrated to be applicable for on-site testing, as it was used to successfully detect the three virulence genes in animal swabs, tissues, & ecological samples collected from commercial poultry farms. The virulence genes were found at high rates (over 85%) in samples from chickens with clinical symptoms of colibacillosis. Remarkably, the genes were also found at high prevalence (over 75%) in samples from clinically healthy broiler flocks, but lower prevalence (less than 75%) in other healthy chicken flocks. Overall, the study shows these three LAMP assays provide a rapid (results in < 35 min), sensitive, and robust method for on-site detection of APEC virulence factors in various sample types. This can enable prompt implementation of necessary measures to mitigate APEC outbreaks [62].

Congo red binding

The Congo red binding (CRB) ability has been applied as a phenotypic marker to differentiate between pathogenic, invasive coli-septicemic *E. coli* strains and non-pathogenic, commensal *E. coli* strains in poultry. This serves as an epidemiological tool to discriminate virulent APEC from harmless *E. coli*. Yadav et al. [63] examined the CRB ability & plasmid profiles of 70 *E. coli* isolates from birds. The majority, 92.86% of isolates, were able to CRB dye, while only 7.14% did not bind the dye even after 72 hours. The ability to CRB has been directly linked to bacterial cell surface hydrophobicity and virulence. *E. coli* strains that CRB are considered more pathogenic and capable of causing septicemic infections, particularly in APEC [64]. Multiple studies have reported a positive correlation between CR binding and the pathogenicity of *E. coli*. This phenotypic marker has been applied routinely *in vitro* to evaluate the virulence of *E. coli* isolates [65- 68]. CR-positive *E. coli* colonies were recovered from pericardium, air sacs, hepatic tissue, lung, synovial fluid, and heart blood of chickens with coli-septicemia [69].

Further research using molecular typing methods like RAPD, BOX-PCR, and ERIC-PCR classified the APEC isolates that bound CR into distinct genotypes. Phylotyping also revealed these CR-binding APEC strains belonged to major pathogenic phylogroups like B2 and D. By utilizing 3 phylogenetic markers (chuA, yjaA, & DNA fragment TspE4.C2), the APEC isolates were classified into phylotypes A1 (33.91%), B23 (37.36%), B22 (9.20%), D2 (11.49%), & B1 (8.05%) [70].

Serotyping of E coli from poultry

Sero-grouped *E. coli* was obtained successfully from samples collected from infected hearts, lungs, air sacs, liver, spleen, ovaries, kidney, oviduct, intestine, and bursa of Fabricius of turkey together with septicemic cases Osman et al. [71], moreover several serogroups of *E. coli* from fecal swabs of apparently healthy chickens, which were found to be enteropathogenic strains. Serogroups O142, O78, O111, O114, O44, O126, O124, O127 and O128 were isolated from skin samples of slaughtered chicks. Also, serogroups O111, O44, O128, O142, O124, and O127 were obtained from muscle samples [72]. It is recommended for the successful isolation of *E. coli* the sample must be from freshly dead and diseased birds [38]. Isolation of *E. coli* to about year season from apparently healthy flocks or diseased cases was found that in the fall season, *E. coli* was isolated from broilers at 57.3%, 64%, and 76% in apparently healthy, diseased, and freshly dead, respectively. While in summer it recovered from 26.6%, 40%, and 55% from apparently healthy, diseased, and freshly dead. The serogroups of *E. coli* were O1, O2, O26, O78, O127, O91 and O153. [73].

Conventional methods for Isolation and characterization of E. coli

The results of multiplex PCR found that the eaeA (intimin *E. coli* attaching and effacing) gene detected in O1, O26, O2, and O153, ompA gene found in all *E. coli* serogroups O1, O2, O26, O78, O91, and O127. Stx1 gene was detected in O2, O78, O26, & O91. While, Stx2 gene was found in O127, O78, & O91 [73].

Polymerase chain reaction (PCR) for multidrug-resistant genes

According to a study by Momtaz et al. [74] APEC exhibited multidrug resistance due to the distribution of various antibiotic resistance genes. Specifically, the tet(A) and tet(B) genes were found in 52.63% of the isolates, the dfrA1, qnrA, catA1, & cmlA genes were found in 36.84% of the isolates, and the sul1& ere(A) genes were present in 47.36% of the isolates. Additionally, 15.78% of the strains were resistant to a single antimicrobial agent, while 19.29% showed resistance to 2 antimicrobial products. Furthermore, multi-resistance, defined as resistance to three or more tested agents, was detected in 64.91% of the *E. coli* strains. The data show that isolates harbored one or more antibiotic-resistance genes, & the PCR assay was an effective method for determining the presence of these genes.

More recently, Hornsey et al. [75] described the genotypic & phenotypic features of an MDR APEC ST69 isolate (APECA2) obtained from infected broilers. The isolate was resistant to different antibiotics, including colistin. The MCR-1 gene, which confers colistin resistance, was found on a mobile genetic element detected on an IncHI2/ST4 plasmid. Furthermore, Mohammed et al. [73] demonstrated that *E. coli* remains the main pathogen responsible for illness in broilers. The *E. coli* were found to be pathogenic and multidrug-resistant, with various resistance genes, such as CITM, ere, tet(A), aac(3) -(IV), dfr(A1), tet(B), & aad(A1), found in a proportion of the tested isolates.

Pathogenicity of E. coli in poultry

Karmy et al. [76] investigated the pathogenicity of *E. coli* O78:K80 in 4 weeks old broilers. They inoculated about 10⁶ CFU through the intratracheal route. Some groups were subjected to chemotherapy and others were kept without any medication. The groups without any medication showed rhinitis and airsacculitis in 80% of cases, pericarditis in 50%, and perihepatitis in 30% of the slaughtered cases with only 10% mortality. Prevalence, pathogenicity, and sensitivity of *E. coli* infection were studied from October 1988 to November 1989. In the study, 315 diseased flocks, 198 broilers, and 117 layers comprised 9,000 435 birds. Of these, a total of 945 dead and 1565 sick birds were examined by ante- and PM examination, and observations were recorded. Of

315 diseased flocks, colibacillosis was recorded in 37 flocks (11.74%). The prevalence was higher in broilers (13.13%) compared with layers (9.40%). Among layers, it was higher in hens of up to 18 weeks of age (11.94%) followed by 18-30 weeks of age (9.68%) and above 30 weeks of age (5.2%). It was higher in broilers of up to 3 weeks of age (17.20%) as compared to 3-6 weeks of age (10.53%) and more than 6 weeks of age (6.9%). The selected strains of *E. coli* (45) showed pathogenicity both by chemical and chick inoculation methods and the isolates were sensitive to gentamicin, ampicillin, and neomycin [77]. *E. coli* serotypes O2, O8, O9, O17, O18, O20, O23, O61, O63, O73, O77, O85, O102, O114, O118, O121, O132, O161, O167 rough, was evaluated for pathogenicity by chick I/P test. Serotypes O8, O63, O73, O167 were highly pathogenic; while serotypes O2, O9, O17, O18, O61, O118, O132 were moderately pathogenic; while serotypes O121, O23, O21 and O77 were the least pathogenic [78]. According to Mellata et al. [8], APEC can cause colibacillosis in chickens through respiratory tract infection. APEC strains have been associated with various virulence factors, involving type 1 (F1A), P (F11) fimbriae, curli, aerobactin, K1 capsule, & temperature-sensitive haemagglutinin (Tsh), as well as plasmid DNA regions. The study investigated the role of these virulence factors in serum resistance and pathogenicity in chickens using mutants of APEC strains TK3, MT78, and chi 7122, which belong to serogroups O1, O2, & O78, respectively. Furthermore, Ask et al. [79] conducted a study in which they challenged 192 chicks intratracheally with *E. coli* on the 7th day old, while 160 chicks were used as controls. The researchers examined the surviving chicks at 14 or 15 days and calculated parameters such as daily mortality, body weight lesion scores, at various time points, and feeding behavior. The results showed that increasing susceptibility to colibacillosis, defined by the presence of lesions, airsacculitis, systemic lesions, and mortality, was associated with increasing growth retardation.

A total of 150 fresh and frozen chicken meat and meat products, for the presence of *E. coli* serotypes. The pathogenicity of selected strains against mice was also determined. It was shown that 54 of 61 isolates belonged to serogroups O1, O9, O37, O42, O53, O60, O62, O73, O100, O101, and O170, while the rest were rough or un-typeable. Serogroups O1 and O9 resulted in 100% mortality in mice, while serogroups O60 and O101 resulted in 83.33 and 66.67% mortality, respectively. The lowest, highest, and zero mortalities were recorded after 96, 24-48, and 12 h infection, respectively. Postmortem examination showed gross lesions in the internal organs. It was suggested that the variation in pathogenicity between serogroups may be due to differences in the production of virulence factors [80].

According to the study conducted by Hussein et al. [81], 219 *E. coli* strains obtained from 84 avian *E. coli* flocks in Egypt were subjected to phylogenetic grouping and virulence genotyping. This included 153 APEC, 30 avian fecal *E. coli* (AFEC), & 36 ecological. Additionally, a subgroup of 50 isolates (30 APEC from coli septicemia & 20 AFEC) underwent more extensive description. This involved sero-grouping, antimicrobial susceptibility analysis, screening for 7 intestinal *E. coli* virulence genes, multilocus sequence typing (MLST), pulsed-field gel electrophoresis (PFGE), & *in vivo* virulence examination. Moreover, experimental infection with *E. coli* O78 by Abd El-Tawab et al. [82]. The clinical signs showed listlessness, the tendency to huddle together, loss of appetite, depression, ruffled feathers, dropping of wings, foul-smelling diarrhea, respiratory signs including gasping (mouth breathing), sneezing, rales, and birds showed loss of weight. Cafosfomycin-treated groups showed gradual improvement and subsiding of clinical signs and chickens were normal after the course of treatment. Infected groups showed moderate to severe lesions of enteritis, air sacculitis, pericarditis, congestion and hemorrhage in the liver, and congestion in the spleen. While the Cafosfomycin treated group showed nearly complete recovery.

Antibiogram

Results from *in vitro* antibiogram profiling indicated that all *E. coli* isolates were resistant to at least three antibiotics, with varying resistance percentages was noticed among different phylotypes [83]. The phylotype B22 exhibits the maximum resistance to ampicillin, nalidixic acid tetracycline & nitrofurantoin at rates of 90.91%, 90.11%, 83.72%, & 65.12%; respectively. Correspondence analysis established significant correlations between phylotypes and CRB, biofilm formation, drug resistance, and virulence genes. The study emphasizes that phylotypes B2 & A1 are the predominant circulating APEC phylotypes, while phylotypes B2 and D2 are associated with pathogenicity. The high incidence of APEC antibiotic-resistant strains across the various phylotypes suggests the need for the implementation of organic antimicrobial compounds, metals, & rotational use of antibiotics in poultry [70].

Histopathological findings of *E. coli* infection

Bajwa et al. [84] mentioned that histopathological studies in birds challenged with *E. coli* post-Mycoplasma showed cellular infiltration & sloughing of the mucosa of the trachea. In the lungs, congestion, and focal necrosis with emphysema were observed, in every case. Congestion, hemorrhages & leukocytic infiltration were found in sections of hepatic tissue from many birds. Eman Hassan et al. [85] reported significant histopathological changes in the trachea, lungs, hepatic tissue, & intestine of 12-

day-old chickens inoculated with *E. coli* (O78). The portal veins & liver central were moderately to markedly dilated & congested. Hepatic parenchyma showed diffuse marked vascular degeneration. Intestine showing diffused mucosal degeneration & desquamation of the epithelial cells. Moreover, Dutta et al. [86] found microscopically, severe congestion and hemorrhages in different organs (of pigeons infected with *E. coli*) like lungs, liver, kidney, and intestine. In some cases, a thick fibrinous exudate with a substantial number of heterophils over both liver and heart surfaces with degenerative changes and focal necrosis. Chaudhari and Kariyawasam [87] described histopathological changes in ovarian and oviducts including severe inflammation like infiltration of mononuclear cells & edema. While Kapakin et al. [88] studied a total of 48 Lohmann White strains (53 weeks old) infected with *E. coli* for histopathologic examinations in the liver, marked degenerative changes of the hepatic cell were seen, while some were noticed as necrotic. Furthermore, Riaz et al [89] used Multiplex PCR for confirmation of three serogroups O1, O2 & O78 were found in percentages of 33%, 8% & 0%. While the photomicrography of liver and lung from experimentally inoculated birds with *E. coli* serogroup (O2) at 14 & 21 days of age showed congestion, hepatomegaly, coagulative necrosis, & infiltration of inflammatory cells in infected hepatic, and lung tissues were congested & there were macrophages, lymphocytes, & heterophils.

Antibiotic Resistance

Studies have reported high resistance rates to clinically important antimicrobials among *E. coli* isolates recovered from broilers, chicken, and turkey meat a high resistance rates to third-generation cephalosporins, fluoroquinolones, or colistin among *E. coli* isolates from these source [90- 92]. Koju et al. [93], found that 89% of the 190 collected chicken cecum samples were subjected to culture and drug sensitivity testing, & *E. coli* was isolated from 94% of the samples. Of the 159 *E. coli* isolates, 71% had resistance to three or more antimicrobial classes. The most prevalent resistance was noticed against tetracycline (86%) and ciprofloxacin (66%). Brätfelan et al. [94], 30% of collected chicken samples were positive for *E. coli*. Most of the isolates showed high resistance to ampicillin (80%), tetracycline (80%), chloramphenicol (70%), sulfamethoxazole (73.33%), & nalidixic acid (60%). Strong resistance was also detected against ciprofloxacin (56.66%), trimethoprim (50%), cefotaxime (46.66%), ceftazidime (43.33%), & gentamicin (40%). Only one *E. coli* strain was resistant to colistin. The antimicrobial resistance determinants detected among the *E. coli* isolates, like tetA (53.33%), blaTEM (36.66%), tetB (46.66%), & sul1 (26.66%), were consistent with their resistance phenotypes.

Prevalence of antibiotic-resistant *E. coli* in Chicken

Numerous studies have revealed a high incidence of MDR *E. coli* in chicken populations. An investigation conducted by Guerra et al. [95] studied the antibiotic resistance patterns of *E. coli* strains isolated from chicken meat across Europe. The results demonstrated a widespread presence of resistance to multiple antibiotics, including tetracycline, ampicillin, and sulfonamides. Similarly, Manges et al. [96] the incidence of antibiotic-resistant *E. coli* in retail meat chicken in Canada and found high rates of resistance to various antibiotics, such as fluoroquinolones and extended-spectrum cephalosporins.

Recently, Ahmed et al. [96] isolated *E. coli* serotypes O2, O44, O91, O78, O128, and O124, from broiler chickens in Egypt, these strains were related to EHEC, EPEC, ETEC, and EIEC also, these *E. coli* showed MDR to extensively drug-resistant, the virus have genes tsh, papC, iss, iutA, and hlyF were detected in 50% of isolates having 5 genes and 50% having 4 genes. All the tested isolates showed MDR genes 60% of isolates were positive for 5 resistance genes, 20% were positive for 4 resistance genes and 20% were positive for resistance 3 genes. These genes confer resistance to various classes of antibiotics, involving β -lactams, aminoglycosides, fluoroquinolones, tetracyclines, & sulfonamides.

The prevalence and diversity of antibiotic-resistant genes in chicken *E. coli*:

It can be attributed to different factors, like the use of antibiotics in poultry production and horizontal gene transfer [94, 97]. The antibiotic-resistant genes in chicken *E. coli* can be collectively summarized as follows [37,98,99]:

- β -lactam Resistance:** Genes encoding β -lactamases, such as blaTEM, blaSHV, and blaCTX-M, are commonly found in chicken *E. coli* isolates. These genes enable resistance to penicillins and cephalosporins.
- Fluoroquinolone Resistance:** The presence of genes such as qnr, aac(6')-Ib-cr, & mutations in the quinolone resistance-determining regions (QRDR) of gyrA & parC contribute to fluoroquinolone resistance in chicken *E. coli*. These genes confer resistance to fluoroquinolones, a critically important antibiotic class.
- Aminoglycoside Resistance:** Genes such as aac(3)-IIa, aac(6')-Ib, & aph(3')-Ia have been identified in chicken *E. coli*. These genes mediate resistance to aminoglycosides, including gentamicin and kanamycin.
- Tetracycline Resistance:** The tet(A), tet(B), & tet(C) genes are frequently detected in chicken *E. coli* and confer resistance to tetracyclines.

- e. Sulfonamide Resistance: Genes such as *sul1* and *sul2* are commonly found in chicken *E. coli* isolates. These genes are associated with resistance to sulfonamide.

Mechanisms of Antibiotic Resistance

The presence of antibiotic-resistant genes in chicken *E. coli* could be attributed to various mechanisms, including chromosomal mutations and horizontal gene transfer.

- a. Chromosomal Mutations: Mutations in target genes, such as *gyrA* and *parC*, can lead to resistance to fluoroquinolones. Similarly, mutations in other chromosomal genes can confer resistance to different antibiotic classes.
- b. Horizontal Gene Transfer: The transfer of antibiotic resistance genes between bacteria plays a crucial role in the dissemination of resistance. Plasmids, integrons, and transposons facilitate the horizontal transfer of antibiotic-resistant genes among chicken *E. coli* and other.

Factors Affect Use of antibiotic in Poultry Production

The widespread use of antibiotics in poultry farming is a major driver of antibiotic resistance in chicken *E. coli*. Antibiotics are commonly used in poultry for disease treatment, prevention, and growth promotion [100]. This extensive use exerts selective pressure on microbes, favoring the survival and proliferation of resistant strains [101]. Agga *et al.* [102] demonstrated a significant relationship between antibiotic use in poultry farms & the prevalence of antibiotic-resistant *E. coli* in chickens.

Horizontal Gene Transfer

E. coli can acquire resistance genes through horizontal gene transfer, where resistance genes are shared between bacterial cells, even across species [103]. This facilitates the spread of resistance determinants in the poultry environment, including *E. coli* and other bacteria [104]. Horizontal gene transfer plays a crucial role in the dissemination of antibiotic resistance genes between bacteria. Mobile genetic elements, such as plasmids and transposons, carry resistance genes and facilitate their transfer between bacterial strains [105]. *E. coli* harbouring antibiotic resistance genes can transfer these genes to other bacteria, involving pathogenic strains, through horizontal gene transfer mechanisms [106]. This process contributes to the rapid spread of antibiotic resistance in chicken *E. coli*. A study by Johnson *et al.* [107] identified plasmids carrying broad-spectrum beta-lactamase genes in *E. coli* obtained from chickens, highlighting the potential for horizontal gene transfer in promoting antibiotic resistance.

Biofilm Formation

E. coli's ability to form biofilms, which are communities of bacteria embedded in a self-

produced extracellular matrix, can enhance their resistance to antibiotics and survival in the poultry environment [108]. Biofilms protect bacteria from antimicrobial agents and host immune responses [109].

Environmental Contamination

Antibiotic-resistant *E. coli* can be discharged into the environment through poultry waste, contaminating soil, water, and other animals [110]. This environmental reservoir further propagates the spread of resistance genes [111].

Poor Biosecurity Measures

Inadequate biosecurity practices on poultry farms, such as poor hygiene, improper waste management, and limited control of animal movements, can facilitate the transmission of resistant *E. coli* within and between farms [112].

Implications for Public Health:

The presence of antibiotic-resistant *E. coli* in chickens has significant implications for public health. Consumption of contaminated chicken meat or eggs can be a source of antibiotic-resistant *E. coli* infections in humans. Likewise, the transfer of resistance genes from chicken *E. coli* to human pathogenic microbes raises concerns about the limited effectiveness of antibiotics in treating infections [96].

Prevention and control

E. coli infections in chickens require a multi-faceted approach, including good management practices and biosecurity measures [26]. Implementing biosecurity measures on poultry farms is crucial to reduce the risk of *E. coli* contamination and other infectious diseases [113]. It is important to note that biosecurity measures should be adopted according to the specific needs and poultry farm conditions. It is important to note that biosecurity measures should be tailored to the specific needs and conditions of each poultry farm [114, 115]. The usage of antibacterial. Prebiotics and vaccination are effective in the prevention and control of *E. coli* in poultry farms [116, 117, 118].

Probiotics, prebiotics and Synbiotic

Probiotics and prebiotics play a vital role in protecting against gut pathogens. Pivnick *et al.* [119] recorded that the competitive exclusion included the introducing of gut microbes from adult birds into newly hatched chicks. Several years later, Petrariu *et al.* [120] identified probiotics as live microorganism cultures taken orally to act positively on host health by improving gut immunity, inhibiting pathogens, & protecting the gut microflora. The probiotics stimulated chicken immunity in two ways: The probiotic flora migrated via the gut wall & multiplied to a limited extent, or antigens released by dead

probiotic microbes were absorbed & stimulated the immunity [121,122]. Garriga et al. [123] demonstrated that 77 strains of lactic acid bacteria from the gut of 50 chicks inhibited enteric indicator strains (*S. enteritidis* & *E. coli*). Eight different strains recognized as *L. salivarius* had the can stop all the indicator strains, had high adhesion efficacy to chicken epithelial cells, and were resistant to multiple antibiotics. Mack et al. [124] proposed that the capability of probiotics to prevent the adherence of attaching & effacing microbes to the gut epithelium was mediated via their capability to enhance the expression of MUC2 & MUC3 gut mucins. La Ragione et al [125] showed that *B. subtilis* py79 spores given to chicks at first day of age for 24 hours prior to challenge with an APEC O78 resulted in a significant decrease in the gut colonization and reduced fecal shedding of the challenge *E. coli*. Ahn et al [126] reported that *L. acidophilus* pfo1 & Cfo7 stopped the growth of *E. coli* K88 & K99, *S. enteritidis* & *S. typhimurium*. Further studies revealed that administration of Lactobacillus-based probiotics resulted in the activation & enhancement of local cell-mediated immune response against specific enteric pathogens via the secretion of cytokines & alterations in lymphoid cells in the chicken gut [127].

Murry et al [128] found that *L. plantarum* & *L. salivarius* contained in probiotics could ferment carbohydrates in avian ration to produce pH degree & levels of lactic acid that stop the multiplication of *C. perfringens*, *E. coli*, & *S. typhimurium*. Ogunbanwo et al. [129] reported the therapeutic efficacy of bacteriocin in control of *E. coli* infection in broiler chickens was due to reduction in the severity of clinical signs, improved growth rate, and lower *E. coli* re-isolation. Related results were found by Ramarao et al. [130], who concluded that probiotics or gut acidifiers could safely replace antibiotics in broiler chicken ration with beneficial effects on the immunity, gut microbial colonization, & resistance to *E. coli* experimental infection. A study on Lactobacillus species was reported by Lonkar et al. [131] who stated that *L. acidophilus* and *L. sporogens* exhibited antibacterial activity against four pathogens, *E. coli*, *Proteus* species, *P. aeruginosa* and *Salmonella* species. Hanaa [132] evaluated the effect of probiotics (*L. sporogens* and *B. subtilis*) in concurrent infection with *E. tenella* & *E. coli* on 3-week-old chicks. They demonstrated that probiotics had a protective role against invasion and colonization with *E. coli* on the other hand probiotics had effect on *Eimeria* infection where they might decrease the severity of *Eimeria tenella* by decreasing caecal lesion scores and oocyst count. Amer et al. [133] concluded that the using of probiotics help for the prevention of pathogenic intestinal Enterobacteriaceae and improve the body performance even the chicken infected and increase the immunity of the chicks. Moreover, Gao et al.

[134] stated that adding *B. subtilis* at 200 mg/kg to the broiler diet increased feed efficiency, improved growth performance, reduced harmful bacteria in the intestinal tract, and regulated serum index.

Multi-strain and single strain probiotic uses were investigated, multi-strains containing *L. acidophilus* (2.5×10^7 cfu/g), *L. casei* (2.5×10^7 cfu/g), *B. thermophilum* (2.5×10^7 cfu/g) and *E. faecium* (2.5×10^7 cfu/g) while single-strain probiotic contains *P. acidilactici* (1×10^{10} cfu/g) both used in order to study broiler breeder performance and gastrointestinal health, results revealed that feed treatments had no impact on total hatching egg production, shell weight, yolk color index, egg weight, mortalities, body weight gain, hatchability, fertility, stroma & oviduct weight, none of the jejunum morphological features, ileal protein digestibility & ileal Lactobacillus count were impacted by supply with probiotics, while ileum *E. coli* number was lowered by addition of feed probiotics [135].

Antibiotics and Antibacterials

Khalid [136] recorded that *E. coli* strains from chicken origin were markedly resistant to ampicillin, streptomycin, tetracycline, trimethoprim, & sulfamethoxazole but completely sensitive to flumequine, gentamycin and nitrofurantoin. While Char and Rao [137] studied the drug sensitivity tests of 880 strains of *E. coli* isolated from wild and domestic animals & poultry, all isolates were sensitive to Nitrofurantoin but none to Penicillin.

Later, Ngeleka et al [138] examined the antibiotic sensitivity of 104 isolates from internal organs & the cloacae of broilers, results revealed that more than 10% of *E. coli* isolates were resistant to most of the used antibiotics. Moreover, Huff et al. [139] evaluated the treatment efficacy of bacteriophage and/or enrofloxacin separately & in combination to treat colibacillosis. Both provided effective treatments. Enrofloxacin was better than bacteriophage in decreasing airsacculitis lesion scores, mortality, and lesion in surviving birds. Synergism between bacteriophage and enrofloxacin treatments was recorded suggesting that treatment with combined bacteriophage with antibiotic had significant value.

In an antimicrobial resistance and susceptibility study by Zhao et al [140], most of the 95 APEC-tested isolates showed resistance to sulfamethoxazole, tetracycline, streptomycin, gentamicin, and nalidixic acid at rates of 93%, 87%, 86%, 69%, and 59%; respectively. Further. trials were performed later to check emerged resistant strains including Zhang et al. [141] who investigated resistance of 205 *E. coli* isolates in North China to commonly used clinical aminoglycoside antibiotics. The isolates had varying degrees of resistance to kanamycin, streptomycin, gentamicin, neomycin,

amikacin, & spectinomycin, the resistance rates of the former 3 antibiotics exceeded 40%. Moreover, Amare et al. [61] made an in-vitro drug sensitivity test for YSI-infected chicks, and evaluated microbial isolates were showed high susceptibility to chloramphenicol, gentamycin, and streptomycin. Abd El Tawab et al. [142] stated that *E. coli* isolates showed resistance to gentamicin, erythromycin, tetracycline, ciprofloxacin, ampicillin, and florfenicol rate of 46.6%, 63.3%, 80%, 40%, 73.3%, and 53% respectively. Prevalence of Broad-spectrum Cephalosporin resistance in *E. coli* isolated from healthy broilers at farms markedly declined within a year post the controlled removal from Ceftiofur usage at hatcheries. This denotes that BSC resistance in *E. coli* isolates from broilers could be controlled by limiting the use of CTF at the hatcheries [143]. Investigations by Jahantigh et al. [144] observed that susceptibility of *E. coli* against lincospectin (41%), oxytetracycline and doxycycline (3%), gentamycin (81%), cefuroxime (16%), norfloxacin (9%), trimethoprim/sulfamethoxazole (10%), ciprofloxacin (7%), colistin and nalidixic acid (0%). Zehor et al [145] isolated 156 *E. coli* strains & antimicrobial susceptibility test showed an increased level of antibiotic resistance to flumequine (91.5%), tetracyclines (94.12%), sulfamethoxazole-trimethoprim (88.89%), nalidixic acid (85.62%), enrofloxacin (86.27%), ampicillin (83.01%) & doxycycline (75.81%), with medium resistance to amoxicillin-clavulanic acid (43.13%) & chloramphenicol (39.22%). All the strains were susceptible to cefotaxime, also the data of MDR cleared that all strains were resistant to 2 antibiotics & 66.66% of strains were resistant to seven antibiotics at least. Callens et al. [146] recommended that national antimicrobial use-lowering campaigns have a positive impact on the overall resistance degree. Analyses were adopted on small datasets, though, and care must be taken while making inferences. For more detailed analysis, antibiotic use data at an animal species level is recommended. Moreover, Mohamed et al. [147] found that 56 samples (35 %) were positive for *E. coli*, data of the CR procedure showed that 20 isolates of 56 (35.7%) were positive & 36 isolates (64.3%) were negative, the characterization of *E. coli* serotypes of CR-positive isolates were O78, O24, O44, O55, O124, O86, O127, & O158.

Strategies for Mitigation

To address the issue of antibiotic resistance in chicken *E. coli*, several strategies can be implemented:

a. Reduction in Antibiotic Use: Implementing strict regulations and guidelines to minimize the usage of antibiotics in avian production can help reduce the selective pressure for antibiotic-resistant microbes.

b. Improved Farm Management Practices: Enhanced biosecurity measures, hygiene protocols, and vaccination programs can minimize the risk of bacterial infections, thereby reducing the need for antibiotics.

c. Alternative Approaches: Exploring alternative approaches such as probiotics, prebiotics, and bacteriophages as alternatives to antibiotics can help maintain gut health and prevent bacterial colonization by antibiotic-resistant strains [148].

Probiotics and Bacteriophages for preventing antibiotic-resistant E. coli colonization in chickens:

Alternative approaches such as probiotics and bacteriophages have gained attention as potential strategies for preventing *E. coli* colonization by antibiotic-resistant strains in chickens [149, 150].

Probiotics

Probiotics are live microbes that, when given in adequate counts, provide health advantages to the host, in the context of poultry production, probiotics have shown promise in reducing *E. coli* colonization by antibiotic-resistant strains [151- 153]. Various mechanisms contribute to the effectiveness of probiotics in preventing colonization [154].

Mycoplasma gallisepticum (MG) and/or *E. coli* challenge along with vaccination hindered the NDV antibodies formation & lowered the vaccines regulated cytokine genes. The vaccinated mixed infected group showed lower antibody levels & cytokines expressions contrasted to those in the single infected groups. These data show a new insight into the immunosuppression action of MG & *E. coli* challenge in birds vaccinated against NDV [155].

A study was conducted to detect the effect of *S. enteritidis* and/or *E. coli* O78 and /or synbiotic on the immunity of broiler chickens challenged with salmonella & *E. coli*. A significant decrease in phagocytic index, phagocytic activity, & weight of spleen, bursa, and thymus in infected groups, but a significant elevation in ND HI titer & bursal weight, thymus, & spleen in synbiotic groups [82]. Among the different alternatives to the use of antibiotics is the incorporation of either prebiotics, probiotics, or Synbiotics into ration and/or drinking water. Probiotics had an antagonistic impact via the secretion of substances that inhibited the development of pathogens [156]. Prebiotics show their impact via attachment to pathogens in the gut lumen & therefore block the adhesion of those microbes to the epithelium [157]. Synbiotic stimulate positive bacteria & enhance gut health [158]. Chickens infected with *E. coli* had reduced antibody titers and delayed seroconversion after ND vaccination compared to non-infected chickens. This indicates that *E. coli* infection can interfere with the

chicken's ability to generate a robust immune response to the vaccine [159].

Antibiotic supply in ration has been continued for the aforementioned 60 years as treatment use, they can enhance the growth & feed efficiency in the chickens, supply with antibiotics resulted in microbial resistance, & moreover, the genes can relocate to microbes involving *Campylobacter* & *Salmonella*, resulting in hazard of food poisoning [160]. Antibiotics are either from natural sources or synthetic that have a critical action in the gut protection against pathogens, antibiotics were widely found in avian production for a long period, and they cause a lowering in gut microbes and their toxic metabolites [161].

Bacterial resistance poses a threat to antibiotic-resistant genes and may also interchange plasmids between species, making treatments for humans and animals vulnerable [162,163].

In poultry production, a variety of antibiotic substitutes have been developed, such as enzymes, organic acids, prebiotics, probiotics, & herbs, to control pathogens by promoting intestinal microflora. The goal of these substitutes is to preserve feed and have antimicrobial activity [164, 165].

An alternative strategy modulates the expression of antimicrobial proteins (AMPs) as β -defensin gallinacin-6 on the mucosal surface of the chicken gut [166]. Currently, several chicken antimicrobial peptides, belonging to the cathelicidin, hepatic-expressed antimicrobial peptide (LEAP), & β -defensin families, have been noticed [166,167].

a. Competitive Exclusion: Probiotic strains compete with *E. coli* antibiotic-resistant for adhesion sites in the chicken gut, thereby limiting their colonization. Mountzouris et al. [168] demonstrated that broiler chickens supplemented with a probiotic mixture exhibited reduced colonization of antibiotic-resistant *E. coli* strains.

b. Modulation of Gut Microbiota: Probiotics can modulate the structure & action of the gut microbiome, promoting a healthier microbial balance. This creates an unfavorable environment for *E. coli* strains, limiting their growth and survival. The administration of a probiotic mixture to chickens reduced the abundance of antibiotic-resistant *E. coli* in the ceca [169].

c. Production of Antimicrobial Substances: Probiotics produce antimicrobial substances including bacteriocins and organic acids, which inhibit the growth of antibiotic-resistant *E. coli*. These substances create a hostile environment for the colonization and proliferation of resistant strains. Awad et al. [170] demonstrated that the administration of a probiotic strain in chickens reduced the counts of antibiotic-resistant *E. coli* isolates in the ceca.

Bacteriophages

Bacteriophages are viruses that specifically infect & kill bacteria, including antibiotic-resistant *E. coli* strains [171]. The phage therapy holds the potential to prevent *E. coli* colonization in chickens [149].

a. Specificity: Bacteriophages exhibit host specificity, targeting specific bacterial strains or species while sparing beneficial bacteria. This selective action allows for the targeted elimination of antibiotic-resistant *E. coli* strains without disrupting the overall gut microbiota. Loc-Carrillo and Abedon [172] highlighted the specificity of phages in combating *E. coli* infections.

b. Self-Replication: Bacteriophages can replicate within bacterial hosts that can infect and kill other bacterial cells. This self-replication property enhances the efficacy of phage therapy in reducing *E. coli* colonization. The successful use of phages in reducing antibiotic-resistant *E. coli* in broiler chickens was demonstrated [173].

c. Potential for Co-evolution: Bacteriophages could co-evolve with bacteria, including antibiotic-resistant strains to overcome these defenses. The co-evolutionary dynamics between phages and *E. coli* were discussed in a study by Torres-Barceló et al. [174].

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داء العصيات القولونية في الطيور، مقاومة الأدوية المتعددة، بدائل المضادات الحيوية: مراجعة محدثة

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⁴مدير عام شركة القاهرة A3 للدواجن، مصر.

الملخص

يشير داء العصيات القولونية إلى أي عدوى موضعية أو جهازية تسببها كليًا أو جزئيًا بكتيريا الإشريكية القولونية المسببة للأمراض في الطيور (APEC)، والتي تشمل تسمم الدم القولوني، والورم الحبيبي القولوني (مرض هجار)، ومرض كيس الهواء [مرض الجهاز التنفسي المزمن (CRD)]، وتورم الرأس. متلازمة، داء العصيات القولونية التناسلية (التهاب المهبل الحاد في تركيا)، والتهاب النسيج الخلوي القولوني (عملية التهابية)، التهاب الصفاق، التهاب البوق، التهاب الخصية، التهاب العظم والنقي / التهاب الغشاء المفصلي (معدن التهاب العظم والنقي في تركيا)، التهاب عموم العين، التهاب السرة (عدوى الكيس المحي)، والتهاب الأمعاء. يعد داء العصيات القولونية أكثر الأمراض البكتيرية المعدية شيوعًا بين الدواجن، كما أن عدوى الإشريكية القولونية بأشكالها المختلفة مسؤولة عن خسائر اقتصادية كبيرة. غالبًا ما يكون داء العصيات القولونية من بين الأمراض الأكثر شيوعًا في الدراسات الاستقصائية لصحة الدواجن أو الإذانات أثناء المعالجة. معظم APEC المعزولة من الدواجن هي أنواع نسيلية محددة مسببة للأمراض للطيور فقط وتمثل خطرًا منخفضًا للإصابة بالمرض بالنسبة للأشخاص أو الحيوانات الأخرى. في الآونة الأخيرة، أظهر داء العصيات القولونية لدى الطيور مجموعة واسعة من المقاومة للأدوية المتعددة وتوجه العالم إلى استخدام بدائل المضادات الحيوية للتغلب على هذه المشكلة. وبالتالي، تركز المراجعة الحالية على الوضع الحالي لداء العصيات القولونية بين مزارع الدواجن، ومقاومة الأدوية والحلول الممكنة باستخدام بدائل المضادات الحيوية الطبيعية الآمنة.

الكلمات المفتاحية: بدائل المضادات الحيوية، فرخة، بكتيريا قولونية، الجينات، البروبيوتيك، الأنماط المصلية.