Egyptian Journal of Veterinary Sciences

https://ejvs.journals.ekb.eg/

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

Ahmed A. Ahmed[1,2], Heba M. Salem[3*], Mohamed M. Hamoud[3,4] and Mohamed M. Amer[3]

[1] *MVSc student, Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, P.O. 12211, Giza, Egypt.*
[2] *Quality Assurance - Cairo Poultry Co., Egypt.*
[3] *Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, P.O. 12211, Giza, Egypt.*
[4] *General manager of Cairo 3A Poultry Co., Egypt.*

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, coli-granuloma (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. col*i 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].

*Corresponding authors: Mohammed M. Amer, E-mail: profdramer@yahoo.com Tel.: +201011828228
(Received 02 July 2024, accepted 05 August 2024)
DOI: 10.21608/EJVS.2024.300945.2216

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 verodoxins 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 verodoxins 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 verodoxins identified, including Shiga toxin 1 (Stx1), Shiga toxin 2 (Stx2), and their variants. These toxins are classified as AB_5 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]. Verodoxins 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 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: sitA, traT, & ompT. 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 10^6 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 airsaculitis 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 01, 09, 037, 042, 053, 060, 062, 073, 0100, 0101, and 0170, while the rest were rough or un-typeable. Serogroups 01 and 09 resulted in 100% mortality in mice, while serogroups 060 and 0101 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, fuel-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 saculitis, 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%). Brătfelan 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]:

a. 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.

b. 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.

c. 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.

d. 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 florfenicolin 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].

Acknowledgments

Not applicable

Authors' contributions

A.A.A and H.M.S. collected data from the available published paper , M.M.H. and M.M.A. supervised the work. All team members wrote, revised the original draft, and approved the final manuscript.

Funding statement

Not applicable

Availability of data and materials

Not applicable

Declarations

All data included in this paper is an original obtained from the available free published papers .

Ethics approval and consent to participate

Not applicable

Competing interests

The authors declare that they have no competing interests.

Author details

Ahmed A. Ahmed: MVSc student, Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, P.O. 12211, Giza, Egypt. Quality Assurance - Cairo Poultry Co., Egypt. E-mail address: drahmedaliahmed.2016@gmail.com

Heba M. Salem: BVSc, MVSc, PhD, Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, P.O. 12211, Giza, Egypt. dr.hebasalem@cu.edu.eg mobile: +201018489282; ORCID ID https://orcid.org/0000-0002-4453-7884

Mohamed M. Hamoud: BVSc, MVSc, PhD, Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, P.O. 12211, Giza, Egypt. General manager of Cairo 3A Poultry Co., Egypt. e-mail address: mohamed.hamoud@cairo3 apoultry.com

Mohamed M. Amer: BVSc, MVSc, PhD, Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, P.O. 12211, Giza, Egypt. Email: profdramer@yahoo.com. Mobile +201011828228. ORCID: 0000-0001-8965-7698

References

1. El-Sukhon, S. N., Musa, A. and Al-Attar, M. Studies on the bacterial etiology of airsacculitis of broilers in northern and middle Jordan with special reference to *Escherichia coli*, *Ornithobacterium rhinotracheale*, and *Bordetella avium*. *Avian Disease*, **46**(3): 605- 612 (2002), https://doi:10.1637/0005-2086(2002)046[0605:SOTBEO]2.0.CO;2.

2. Popy, N., Asaduzzaman, M., Miah, M.S., Siddika, A., Sufian, M.A., and Hossain, M.M. Pathological study on the upper respiratory tract infection of chickens and isolation, identification of causal bacteria. *The Bangladesh Veterinarian*, **28**(2): 60 – 69 (2011). https://www.cabidigitallibrary.org/doi/pdf/10.5555/20123197780

3. Vandemaele, F., Assadzadeh, A., Derijcke, J., Vereecken, M., and Goddeeris, B.M. Aviaire pathogene Escherichia coli (APEC) [Avian pathogenic Escherichia coli (APEC)]. *Tijdschrift Diergeneeskunde*. **127**(19):582-588 (2002) https://pubmed.ncbi.nlm.nih.gov/12389466/

4. Ewers, C., Janssen, T., and Wieler, L.H. Avian Pathogenic Escherichia coli [APEC]. *Berliner und Münchener Tierärztliche Wochenschrift*, **116**(9-10): 381-395 (2003).

5. Barnes, H.J., Vaillancourt J.P. and Gross, W.B. Newcastle disease, 631-656. In: Ibid. [Ed.], Diseases of Poultry. 11th ed. Iowa State University Press, Ames (2003),

6. Sivaseelan S., Malmarugan S., and Balasubramaniam G.A. Synergistic Pathological Effect of *Mycoplasma gallisepticum* with other Infectious Organisms in Layer Chickens. *Brazilian Journal of Veterinary Pathology,* **6**(2): 44-47 (2013). https://bjvp.org.br/wpcontent/uploads /2015/07/DOWNLOAD-FULL-ARTICLE-12-20881_2013_8_16_0_38.pdf

7. Johnson, T.J., Wannemuehler, Y., Johnson S.J., Stell, A.L., Doetkott, C., Johnson, J.R., Kim, . K.S., Spanjaard, L., and Nolan, L.K. Comparison of extraintestinal pathogenic *Escherichia coli* strains from human and avian sources reveals a mixedsubset representing potential zoonotic pathogens. *Applied and Environmental Microbiology* , **74**:7043–7050 (2008). https://doi.org/10.1128/AEM.01395-08

8. Mellata, M. Human and avian extraintestinal pathogenic *Escherichia coli*: Infections, zoonotic risks, and antibiotic resistance trends. *Foodborne Pathogens and Disease*, **10**(11), 916-932 (2013). https://doi.org/10.1089/fpd.2013.1533

9. Cortés, P., Blanc, V., Mora, A., Dahbi, G., Blanco, J.E., Blanco, M., López, C., Andreu, A., Navarro, F., Alonso, M.P., Bou, G., Blanco, J. , and Llagostera, M. Isolation and characterization of potentially pathogenic antimicrobial-resistant *Escherichia coli* strains from chicken and pig farms in Spain. *Applied and Environmental Microbiology* , **76**:2799–2805 (2010). https://doi.org/10.1128/AEM.02421-09

10. Wang, X.M., Liao, X.P. , Zhang, W.J. , Jiang, H.X., Sun, J., Zhang, M.J., He, X.F. , Lao, D.X., and Liu, Y.H. Prevalence of serogroups, virulence genotypes, antimicrobial resistance, and phylogenetic background of avian pathogenic *Escherichia coli* in south of China. *Foodborne Pathogens and Disease*, **7**:1099–110 (2010). https://doi.org/10.1089/fpd.2010.0542

11. Hannan, H.A., Khan T.A., Khan M.N., and Ahmed Z. A study on the efficacy of inactivated avian *E. coli* vaccine in layer chicks. Internat. *International Journal of Biology and Biotechnology*, **9**(1/2): 55-58 (2012). https://www.ijbbku.com/assets/custom/journals/2012/1-2/A%20STUDY%20ON%20THE%20EFFICACY%20OF%20INACTIVATED%20AVIAN%20E.COLI%20VACCINE%20IN%20LAYER%20CHICKS.pdf

12. Zahraei Salehi, T., Tabatabaei, S., Karimi, V., Fasaei, B.N., Shandeh, A.D., and Jahrom,i O.A.N. Assessment of immunity against avian colibacillosis induced by an aroA mutant containing increased serum survival gene in broilers. *Brazilian Journal of Microbiology*, **43**(1), 363-370 (2012). https://doi.org/10.1590/S1517-838220120001000043

13. Nolan L.K., Vaillancourt J.P., Barbieri N.L., and Logue C.M. Colibacillosis. In: Swayne D.E., Boulianne M., Logue C.M., McDougald L.R., Nair V., Suarez D.L., editors. Diseases of Poultry. 14th ed. John Wiley & Sons Inc.; Hoboken, NJ, USA: pp. 770–830. (2020).

14. Hess, C., Troxler, S., Jandreski-Cvetkovic, D., Zloch, A., and Hess, M. Escherichia coli Isolated from Organic Laying Hens Reveal a High Level of Antimicrobial Resistance despite No Antimicrobial Treatments. *Antibiotics (Basel, Switzerland),* 11(4), 467 (2022). https://doi.org/10.3390/antibiotics11040467

15. Mueller M, and Tainter, C.R. *Escherichia coli* Infection. In: StatPearls [Internet]. TreasureIsland (FL): Stat Pearls Publishing; (2024). https://www.ncbi.nlm.nih.gov /books/NBK564298/

16. Bhalerao, A., Gupta, R., and Kumari, M. (). Pathological studies on natural cases of avian colibacillosis in Haryana state. Haryana Veterinarian, **52**, 118-120 (2013). https://api.semanticscholar.org/CorpusID:33692969

17. Saif, Y.M., 2008. Diseases of poultry.Blackwell Publishing. Oxford.

18. Ogunleye, A.O., Oyekunle, M.A., and Sonibare A.O. Multidrug resistant Escherichia coli isolates of poultry origin in Abeokuta, South Western Nigeria. *Veterinarski Arhiv*, **78**(6): 501-509 (2008). https://wwwi.vef.hr/vetarhiv/papers/2008-78-6-5.pdf

19. Barnes, H.J., Nolan, L., Vaillancourt, J.P.. Colibacillosis. In: Saif, Y.M., Fadly, A.A., Glisson, J.R., McDougald, L.R., Nolan, L., Swayne, D.E. [Eds.], Diseases of Poultry. ISU Press, Ames, IA, **pp**: 691–732 (2008).

20. Joseph, J., Zhang, L., Adhikari, P., Evans, J. D., and Ramachandran, R. Avian Pathogenic *Escherichia coli* (APEC) in Broiler Breeders: An Overview. *Pathogens*, **12**(11), 1280 (2023). https://doi.org/10.3390/pathogens12111280

21. Zuidhof, M.J. Lifetime productivity of conventionally and precision-fed broiler breeders. Poult. Sci. 2018, 9, 3921–3937.

22. Govindarajan, D. K., Viswalingam, N., Meganathan, Y., and Kandaswamy, K. Adherence patterns of Escherichia coli in the intestine and its role in pathogenesis. *Medicine in Microecology*, **5**, 100025 (2020). https://doi.org/10.1016/j.medmic.2020.100025

23. Pakbin, B., Brück, W. M., and A. Rossen, J. W. Virulence Factors of Enteric Pathogenic Escherichia coli: A Review. *International Journal of Molecular Sciences*, **22**(18) (2021).. https://doi.org/10.3390/ijms22189922

24. Jarocki, V.M., Reid, C.J.., Chapman, T.A., and Djordjevic, S.P. Escherichia coli ST302: Genomic Analysis of Virulence Potential and Antimicrobial Resistance Mediated by Mobile Genetic Elements. *Frontiers in Microbiology* , **10**:3098 (2020). doi: 10.3389/fmicb.2019.03098

25. Desvaux, M., Dalmasso, G., Beyrouthy, R., Barnich, N., Delmas, J., and Bonnet, R. Pathogenicity Factors of Genomic Islands in Intestinal and Extraintestinal *Escherichia coli*. *Frontiers in Microbiology*, **11**, 558927 (2020). https://doi.org/10.3389/fmicb.2020.02065

26. Dho-Moulin, M., and Fairbrother, J. M. Avian pathogenic *Escherichia coli* (APEC). *Veterinary research*, **30**(2-3), 299-316 (1999).

27. Johnson, T. J., and Nolan, L. K. Pathogenomics of the virulence plasmids of *Escherichia coli*. *Microbiology and Molecular Biology Reviews*, 73(4), 750-774 (2009). https://doi.org/10.1128/ mmbr.00015-09

28. Melton-Celsa, A. R. Shiga Toxin (Stx) Classification, Structure, and Function. *Microbiology Spectrum*, **2**(2) (2014). https://doi.org/10.1128/microbiolspec.EHEC-0024-2013

29. Karmali, M. A. 1989. Infection by verocytotoxin-producing *Escherichia coli*. *Clinical Microbiology Reviews*, 2(1), 15-38 (1988). https://doi.org/10.1128/cmr.2.1.15

30. Paton, J. C., and Paton, A. W.. Pathogenesis and diagnosis of shiga toxin-producing *Escherichia coli* infections. *Clinical Microbiology Reviews* , 11(3):450-79 (1998). https://doi:10.1128/CMR.11.3.450.

31. Blanco, M., Blanco, J. E., Mora, A., Dahbi, G., Alonso, M. P., González, E. A., Bernárdez, M. I., and Blanco, J. Serotypes, Virulence Genes, and Intimin Types of Shiga Toxin (Verotoxin)-Producing Escherichia coli Isolates from Cattle in Spain and Identification of a New Intimin Variant Gene (eae-ξ). *Journal of Clinical Microbiology*, **42**(2), 645-651(2004).. https://doi.org/10.1128/JCM.42.2.645-651.2004

32. Rodríguez-Rubio, L., Haarmann, N., Schwidder, M., Muniesa, M., and Schmidt, H. Bacteriophages of Shiga Toxin-Producing Escherichia coli and Their Contribution to Pathogenicity. *Pathogens*, **10**(4) (2021).. https://doi.org/10.3390/pathogens10040404

33. Page, M. G. The Role of Iron and Siderophores in Infection, and the Development of Siderophore Antibiotics. Clinical Infectious Diseases: An Official Publication of the Infectious *Diseases Society of America*, **69**(Suppl 7), S529 (2019).. https://doi.org/10.1093/cid/ciz825

34. Wellawa, D.H., Allan, B., White, A.P., and Köster, W. Iron-Uptake Systems of Chicken-Associated Salmonella Serovars and Their Role in Colonizing the Avian Host. *Microorganisms*. 8(8):1203 (2020). https://doi:10.3390/microorganisms8081203

35. Semenov, A. V., Costa, R., and Trevors, J. T. Survival of *Escherichia coli* in the environment: Fundamental and public health aspects. *The ISME Journal*, **5**(2), 173-183(2011).. https://doi.org/10.1038/ismej.2010.80

36. Braz, V. S., Melchior, K., and Moreira, C. G. *Escherichia coli* as a Multifaceted Pathogenic and Versatile Bacterium. *Frontiers in Cellular and Infection Microbiology*, **10** (2020). https://doi.org/10.3389/fcimb.2020.548492

37. Pokharel, P., Dhakal, S., and Dozois, C. M. The Diversity of *Escherichia coli* Pathotypes and Vaccination Strategies against This Versatile Bacterial Pathogen. *Microorganisms*, **11** (2), 344, (2023). https://doi.org/10.3390/microorganisms11020344

38. Yousef, H. M., Hashad, M. E., Osman, K. M., Alatfeehy, N. M., Hassan, W. M., Elebeedy, L. A., Salem, HM, Shami, A, Al-Saeed, FA, El-Saadony, MT, El-Tarabily, KA, and Marouf, S. Surveillance of

Escherichia coli in different types of chicken and duck hatcheries: One health outlook. Poultry Science, 103108 (2023). https://doi:10.1016/j.psj.2023.103108.

39. Sarowska, J., Futoma-Koloch, B., Jama-Kmiecik, A., Frej-Madrzak, M., Ksiazczyk, M., Bugla-Ploskonska, G., an Choroszy-Krol, I. Virulence factors, prevalence and potential transmission of extraintestinal pathogenic Escherichia coli isolated from different sources: Recent reports. *Gut Pathogens*, 11(2019).. https://doi.org/10.1186/s13099-019-0290-0

40. Johnson, J. R., Johnston, B., Kuskowski, M. A., Nougayrede, P., and Oswald, E. Molecular Epidemiology and Phylogenetic Distribution of the *Escherichia coli* pks Genomic Island. *Journal of Clinical Microbiology*, **46** (12), 3906-3911 (2008). https://doi.org/10.1128/ JCM.00949-08

41. Kathayat, D., Lokesh, D., Ranjit, S., and Rajashekara, G. Avian Pathogenic *Escherichia coli* (APEC): An Overview of Virulence and Pathogenesis Factors, Zoonotic Potential, and Control Strategies. *Pathogens*, *10*(4) (2021) . https://doi.org/10.3390/pathogens10040467

42. Rafique, M., Potter, R. F., Ferreiro, A., Wallace, M. A., Rahim, A., Malik, A. A., Siddique, N., Abbas, M. A., Burnham, A. D., Ali, N., and Dantas, G. Genomic Characterization of Antibiotic Resistant *Escherichia coli* Isolated From Domestic Chickens in Pakistan. *Frontiers in Microbiology*, **10,** 496875. (2019).. https://doi.org/10.3389/fmicb.2019.03052

43. Kalantari, M., Sharifiyazdi, H., Asasi, K., and Abdi-Hachesoo, B. High incidence of multidrug resistance and class 1 and 2 integrons in Escherichia coli isolated from broiler chickens in South of Iran. *Veterinary Research Forum*, **12** (1), 101-107 (2020) https://doi.org/10.30466/vr f.2019.96366.2309

44. Coleman, J., and Smith, C. Microbial Resistance. *Reference Module in Biomedical Sciences* (2013). https://doi.org/10.1016/B978-0-12-801238-3.05148-5

45. Hassan, E. R., Alhatami, A. O., Abdulwahab, H. M., and Schneider, B. S. Characterization of plasmid-mediated quinolone resistance genes and extended-spectrum beta-lactamases in non-typhoidal Salmonella enterica isolated from broiler chickens. *Veterinary World*, **15**(6), 1515-1522 (2022). https://doi.org/10.14202/vetworld.2022.1515-1522

46. Ma, J., Liu, J.H., Lv L., Zong, Z., Sun, Y., Zheng, H., Chen, Z., Zeng, Z.L. Characterization of extended-spectrum β-lactamase genes found among *Escherichia coli* isolates from duck and environmental samples obtained on a duck farm. *Applied and Environmental Microbiology* , **78** (10):3668-3673 (2012). https://doi.org/10.1128/AEM.07507-11

47. Wu, H., Wang, M., Liu, Y., Wang, X., Wang, Y., Lu, J., Xu, H.. Characterization of antimicrobial resistance in Klebsiella species isolated from chicken broilers. *International Journal of Food Microbiology*, **232**, 95-102 (2016). https://doi.org/10.1016/j.ijfoodmicro.2016.06.001

48. Papouskova, A., Masarikova, M., Valcek, A., Senk, D., Cejkova, D., Jahodarova, E., and Cizek, A. Genomic analysis of *Escherichia coli* strains isolated from diseased chicken in the Czech Republic. *BMC Veterinary Research*, **16** (2020). https://doi.org/10.1186/s12917-020-02407-2

49. Vilarinho Braga, J. F., Chanteloup, N. K., Trotereau, A., Baucheron, S., Guabiraba, R., Ecco, R., and Schouler, C. Diversity of Escherichia coli strains involved in vertebral osteomyelitis and arthritis in broilers in Brazil. *BMC Veterinary Research,* **12** (2016). https://doi.org/10.1186/s12917-016-0762-0

50. Darmancier, H., F. Domingues, C. P., Rebelo, J. S., Amaro, A., Dionísio, F., Pothier, J., Serra, O., and Nogueira, T. Are Virulence and Antibiotic Resistance Genes Linked? A Comprehensive Analysis of Bacterial Chromosomes and Plasmids. *Antibiotics*, 11(6) (2022). https://doi.org/10.3390/antibiotics11060706

51. Meguenni, N., Chanteloup, N., Tourtereau, A., Ahmed, C.A., Bounar-Kechih, S., and Schouler, C. Virulence and antibiotic resistance profile of avian Escherichia coli strains isolated from colibacillosis lesions in central of Algeria. *Veterenary World*, **12**(11):1840-1848 (2019). https://doi:10.14202/vetworld.2019.1840-1848.

52. Schroeder, M., Brooks, B.D., and Brooks, A.E. The Complex Relationship between Virulence and Antibiotic Resistance. *Genes (Basel)*, **8**(1):392017. https://doi.org/10.3390/genes8010039

53. Savin, M., Alexander, J., Bierbaum, G., Hammerl, J. A., Hembach, N., Schwartz, T., Schmithausen, R. M., Sib, E., Voigt, A., and Kreyenschmidt, J. Antibiotic-resistant bacteria, antibiotic resistance genes, and antibiotic residues in wastewater from a poultry slaughterhouse after conventional and advanced treatments. *Scientific Reports*, **11** (2021). https://doi.org/10.1038/s41598-021-96169-y

54. Nwobodo, D. C., Ugwu, M. C., Anie, C. O., S. Al-Ouqaili, M. T., Ikem, J. C., Chigozie, U. V., and Saki, M. Antibiotic resistance: The challenges and some emerging strategies for tackling a global menace. *Journal of Clinical Laboratory Analysis*, **36**(9), e24655m(2022). https://doi.org/10.1002/jcla.24655

55. Gambi, L., Rossini, R., Menandro, M. L., Franzo, G., Valentini, F., Tosi, G., and Fiorentini, L. Virulence Factors and Antimicrobial Resistance Profile of *Escherichia Coli* Isolated from Laying Hens in Italy. *Animals*, **12**(14) (2022). https://doi.org/10.3390/ani12141812

56. Geurtsen, J., De Been, M., Weerdenburg, E., Zomer, A., McNally, A., and Poolman, J. Genomics and pathotypes of the many faces of *Escherichia coli*. *FEMS Microbiology Reviews*, 46(6) (2022). https://doi.org/10.1093/femsre/fuac031

57. Stromberg, Z. R., Johnson, J. R., Fairbrother, J. M., Kilbourne, J., Goor, A. V., and Mellata, M. Evaluation of *Escherichia coli* isolates from healthy chickens to determine their potential risk to poultry

and human health. *PLOS ONE*, **12**(7), e0180599 (2017). https://doi.org/10.1371/journal.pone.0180599

58. Mitchell, N. M., Johnson, J. R., Johnston, B., Roy Curtiss, I., and Mellata, M. Zoonotic Potential of Escherichia coli Isolates from Retail Chicken Meat Products and Eggs. *Applied and Environmental Microbiology*, **81**(3), 1177-1187 (2015). https://doi.org/10.1128/AEM.03524-14

59. Fatima, R., and Aziz, M. Enterohemorrhagic *Escherichia coli*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, (2024). https://www.ncbi.nlm.nih.gov/books/ NBK519509/

60. Durairaj, V. and Dustan Clark, F. *E. coli* an Opportunist that Causes Enteritis. Center of Excellence for Poultry Science, University of Arkansas. Poultery Site, (2007):

61. Amare, A. , Amin, A .M , Shiferaw, A. , Nazir, S. and Negussie, H. Yolk sac infection (omphalitis) in Kombolcha Poultry Farm, Ethiopia. *American-Eurasian Journal of Scientific Research,* **8** (1)10-14 (2013). https://api.semanticscholar.org/CorpusID:21864821

62. Kogovšek, P., Ambrožic-Avguštin, J., Dovc, A., Dreo, T., Hristov, H., Krapež, U., Ravnikar, M., Slavec, B., Lotric, M., Žel, J., Zorman Rojs, O. Loop-mediated isothermal amplification: rapid molecular detection of virulence genes associated with avian pathogenic *Escherichia coli* in poultry. *Poultry Science,* **98**(3), 1500-1510. https://doi.org/10.3382/ps/pey516

63. Yadav, V., Joshi, R.K., Joshi, N., and Diwakar, R.P. Congo red binding and plasmid profile of *E. coli* isolates of poultry origin. *Journal of Animal Health and Production* , **2** (3): 31 – 32 (2014). https://doi.10.14737/journal.jahp/2014/2.3.31.32

64. Sarowska, J., Futoma-Koloch, B., Jama-Kmiecik, A., Frej-Madrzak, M., Ksiazczyk, M., Bugla-Ploskonska, G., and Choroszy-Krol, I. Virulence factors, prevalence and potential transmission of extraintestinal pathogenic Escherichia coli isolated from different sources: Recent reports. *Gut Pathogens*, **11**(2019). https://doi.org/10.1186/s13099-019-0290-0

65. Ishiguro, E.E., Ainsworth, T., Trust, T.J., Kay, W.M. Correlation between Congo red binding and pathogenicity of *E. coli*. *Journal of Bacteriology* , **164** : 1233 (1985).

66. Agarwal, R.K.., Kapoor, K.N., Verma, J.C., Bachhil, V.N., Singh, B.R., Kumar, A., Sachan, N., Singh, D.K., and Malik, S.V.S. Isolation and characterization of Salmonella Stockhalm from beef. *Indian Journal of Comparative Microbiology, Immunology and Infectious Diseases* . **20** (1):50 – 52 (1999).

67. Dubey, S., Sharda, R., Chhabra, D., Tiwari, S., and Pillai, A.G.R. Congo red colony pigmentation and haemolysin production by *E. coli* strains from diarrheic goats. *Indian Journal of Comparative Microbiology, Immunology and Infectious Diseases,* **21**(1) : 157 - 158 (2000).

68. De Carli, S., Ikuta, N., Lehmann, F. K. M., Da Silveira, V. P., De Melo Predebon, G., Fonseca, A. S. K., and Lunge, V. R. Virulence gene content in *Escherichia coli* isolates from poultry flocks with clinical signs of colibacillosis in Brazil. *Poultry Science*, **94**(11), 2635-2640 (2015). https://doi.org/10.3382/ps/pev256

69. Berkhoff, H. A., and Vinal, A. C. Congo Red Medium to Distinguish between Invasive and Non-Invasive *Escherichia coli* Pathogenic for Poultry. *Avian Diseases*, **30**(1), 117–121 (1986).. https://doi.org/10.2307/1590621

70. Saha, O., Hoque, M. N., Islam, O. K., Rahaman, M. M., Sultana, M., and Hossain, M. A. Multidrug-Resistant Avian Pathogenic Escherichia coli Strains and Association of Their Virulence Genes in Bangladesh. *Microorganisms*, 8(8), 1135 (2020). https://doi.org/10.3390/ microorganisms8081135

71. Osman, E., Osman, K., Mehmet, C. and Ersin, I. Haemagglutination, Hydrophobicity, Enterotoxigenicity and Drug-Resistance characteristics of avian *E. coli*. *Avian disease*, **33 (4)**:631-635(1989). https://doi.org/10.2307/1591136.

72. Nagwa, M. Differentiation between pathogenic and non pathogenic E. coli in apparently healthy and slaughtered poultry. M.V.Sc. Thesis (Microbiology) Fac. Vet. Med. Cairo Univ. (1995).

73. Abd El-Mongy, M. Abd-El-Moneam, G.M., Amgad Ahmed Moawad, A. A. and Mohammed, A.B. A. Serotyping and Virulence Genes Detection in *Escherichia coli* Isolated from Broiler Chickens. *Journal of Biological Sciences*, **18**: 46-50 (2018). https://scialert.net/ abstract/?doi=jbs.2018.46.50

74. Momtaz. H, Rahimi, E., and Moshkelani S. Molecular detection of antimicrobial resistance genes in *E. coli* isolated from slaughtered commercial chickens in Iran. *Veterinarni Medicina*, **57**: 193–197 (2012).

75. Hornsey M., Betts J.W., Mehat J.W., Wareham D.W., van Vliet A.H.M., Woodward M.J., and La Ragione R.M. Characterization of a colistin-resistant Avian Pathogenic *Escherichia coli ST69* isolate recovered from a broiler chicken in Germany. *Journal of Medical Microbiology* , **68** (1) (. 2018) https://doi.org/10.1099/jmm.0.000882

76. Karmy, S., Shauman, M. T., Safwat, E. E. A. and El-Danaf, N. Studies on the efficacy and levels of flumequin in healthy and experimentally infected birds with *Escherichia coli O78: K80* in vitro and vivo. *Journal of the Egyptian Veterinary Medical Association*, 47:521-536 (1987).

77. Javed, M. T., Anjum, R., Khan, M. Z., and Khan, A. Studies of the isolation, pathogenicity and sensitivity of *Escherichia coli* in layers and broilers. *Pakistan Veterinary Journal*, **11**(4):187-190 (1991):

78. Ghosh, H., Ratna, D., Batabyal, K. and Roy, J. P. Identification and pathogenicity of *Escherichia coli*

isolated from duck and hen eggs. *Journal of Interacademicia (India)*, **6**, spl., 716-717 (2002). https://agris.fao.org/search/en/providers/122648/records /64724a6753aa8c 8963055048

79. Ask, B., van der Waaij, E.H., van Eck, J.H., van Arendonk, J.A., and Stegeman, J.A. Defining susceptibility of broiler chicks to colibacillosis. *Avian Pathology*, ***35***(2):147-153 (2006). https://doi:10.1080/03079450600597998 .

80. Animesh D., Khan, M. H., Baruah, A. G., Hazarika, R. A., and Saika, G. K. Serotyping and pathogenicity of *Escherichia coli* isolates from chicken meat and meat products. *Indian Veterinary Journal,* **87**(11):1084-1086 (2010). http://www.indvetjournal.com

81. Hussein, A.H., Ghanem, I.A., Eid, A.A., Ali, M.A., Sherwood, J.S., Li, G., Nolan, L.K. and Logue, C.M. Molecular and phenotypic characterization of *Escherichia coli* isolated from broiler chicken flocks in Egypt. *Avian Disease*, **57** (3): 602–611 (2013). https://doi.org/10.1637/10503-012513-Reg.1

82. Abd El Tawab, A. A., El-Hofy, F. I.,. El-Eknawy, Kh. I., and . El-Shora, H.E. Effect of Synbiotic on immune response of experimentally infected broiler chickens with *E.coli* and salmonella. *Benha Veterinary Medical Journal*, **28**(2):188-194 (2015). https://doi:10.21608/bvmj.2015.32501

83. García-Béjar, B., Martín, B., Arévalo-Villena, M., and Pérez, A. B. High Prevalence of Antibiotic-Resistant *Escherichia coli* Isolates from Retail Poultry Products in Spain. *Animals : An Open Access Journal From MDPI*, **11**(11) (2021).. https://doi.org/10.3390/ani11113197

84. Bajwa , M. Z., Siddique, M., and Javed, M. T. Pathogenesis of *Escherichia coli* in previously *Mycoplasma gallisepticum* infected layer chicks. *Journal of Islamic Academy of Science*. **52**: 123-126 (1992). https://jag.journalagent.com/ias/pdfs/IAS_5_2_123_126.pdf

85. Hossain, M. T., Sardar, D., Afsana, S., Datta, M., and Habib, M. A. Comparative analysis between multi-strain probiotics and antibiotic as starter feed supplement of poultry on growth performance, serum metabolites and meat quality. *Veterinary and Animal Science*, **24**. (2024). https://doi.org/10.1016/j.vas.2024.100346

86. Dutta, T.K., Roychoudhury, P., Bandyopadhyay, S., Wani, S.A., and Hussain, I. Detection and characterization of shiga toxin producing *Escherichia coli* (STEC) and enteropathogenic *Escherichia coli (EPEC)* in poultry birds with diarrhoea. *The Indian Journal of Medical Research*, **133**(5):541- 545 (2011). https://www.ncbi.nlm.nih.gov /pmc/articles/PMC3121287/

87. Chaudhari, A.A. and Kariyawasam, S. An experimental infection model for *Escherichia coli* egg peritonitis in layer chickens. *Avian Diseases*, **58**(1):25-33(2014). https://doi.org/10.1637 /10536-032213-Reg.1

88. Kapakin, K. A. T., Kapakin, S., Kurt, A. , Iskender, H., Altun, S. and Celeb, D. Histopathological findings and apoptosis caused by *E. coli* in layer birds. *Pakistan Veterinary Journal,* **35**(4): 525-527 (2015). https://api.semanticscholar.org/Corpus

89. Riaz, A.M., Aslam, A,. Rehman, M., and Yaqub, T. Pathological Investigation and Molecular Detection of Avian Pathogenic *E. coli* Serogroups in Broiler Birds. *Journal of Veterinary Science & Technology*, **7**: 373 (2016). https://doi:10.4172/2157-7579

90. Nguyen, D. P., Dao Nguyen, T. A., Le, T. H., Doan Tran, N. M., Ngo, T. P., Dang, V. C., Kawai, T., Kanki, M., Kawahara, R., Jinnai, M., Yonogi, S., Hirai, Y., Yamamoto, Y., and Kumeda, Y. Dissemination of Extended-Spectrum β-Lactamase- and AmpC β-Lactamase-Producing *Escherichia coli* within the Food Distribution System of Ho Chi Minh City, Vietnam. *BioMed Research International*, **2016** (1), 8182096 (2015). https://doi.org/10.1155/2016/8182096

91. Seo, K.W., and Lee, Y.J. Characterization of plasmid mediated quinolone resistance determinants in ciprofloxacin resistant-*Escherichia coli* from chicken meat produced by integrated broiler operations in Korea. *International Journal of Food Microbiology*, **307**, 108274 (2019). https://doi.org/10.1016/j.ijfoodmicro.2019.

92. Wasyl, D., Hoszowski, A., Zając, M., and Szulowski, K. Antimicrobial resistance in commensal *Escherichia coli* isolated from animals at slaughter. *Frontiers in Microbiology*, **4**, 54851 (2013). https://doi.org/10.3389/fmicb.2013.00221

93. Koju, P., Shrestha, R., Shrestha, A., Tamrakar, S., Rai, A., Shrestha, P., Madhup, S. K., Katuwal, N., Shrestha, A., Shrestha, A., Shrestha, S., Karki, P., Tamang, P., Thekkur, P., and Shrestha, S. S. Antimicrobial Resistance in *E. Coli* Isolated from Chicken Cecum Samples and Factors Contributing to Antimicrobial Resistance in Nepal. *Tropical Medicine and Infectious Disease*, **7**(9) (2022). https://doi.org/10.3390/ tropicalmed 7090249

94. Brătfelan, D. O., Tabaran, A., Colobatiu, L., Mihaiu, R., and Mihaiu, M. Prevalence and Antimicrobial Resistance of *Escherichia coli* Isolates from Chicken Meat in Romania. *Animals,* **13**(22), 3488 (2022). https://doi.org/10.3390/ani13223488

95. Guerra, B., Soto, S. M., Arguelles, J. M., and Mendoza, M. C. Multidrug resistance plasmids carrying rmtB or qepA genes in Escherichia coli from humans and animals. *Antimicrobial Agents and Chemotherapy***, 57**(1), 559-562 (2013).

96. Ahmed, A. A., Salem, H. M., Hamoud, M. M., and Amer, M. M. Molecular Identification of Resistance and Pathogenicity Genes of *E. coli* Isolated From Broiler Chicken Farms. *Egyptian Journal of Veterinary Sciences*, **55**(7), 1787-1800 (2024. https://doi:10.21608/ejvs.2024.252030.1691

97. Racewicz, P., Majewski, M., Biesiada, H., Nowaczewski, S., Wilczyński, J., Wystalska, D., Kubiak, M., Pszczoła, M., and Madeja, Z. E. Prevalence and characterisation of antimicrobial resistance genes and class 1 and 2 integrons in multiresistant Escherichia coli isolated from poultry production. *Scientific Reports*, **12** (2022). https://doi.org/10.1038/s41598-022-09996-y.

98. Abdel-Rahman, M.A.A., Hamed, E.A., Abdelaty, M.F., Sorour, H.K., Badr, H., Hassan, W.M., Shalaby, A.G., Mohamed, A.A., Soliman, M.A., and Roshdy, H. Distribution pattern of antibiotic resistance genes in *Escherichia coli* isolated from colibacillosis cases in broiler farms of Egypt. *Veterenary World*, *16*(1):1-11 (2023). https://doi:10.14202/vetworld.2023.1-11.

99. Bhattarai, R.K., Basnet, H.B., Dhakal, I.P., and Devkota, B. Antimicrobial resistance of avian pathogenic *Escherichia coli* isolated from broiler, layer, and breeder chickens, *Veterinary World*, **17**(2): 480–499 (2024). https://www.veterinaryworld.org/Vol.17/February-2024/28.pdf

100. Van Boeckel, T. P., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., Teillant, A., and Laxminarayan, R. Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences*, *112*(18), 5649-5654 (2015). https://doi.org/10.1073/ pnas.1503141112

101 Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K. M., Wertheim, H. F. L., Sumpradit, N., Vlieghe, E., Hara, G. L., Gould, I. M., Goossens, H., Greko, C., So, A. D., Bigdeli, M., Tomson, G., Woodhouse, W., Ombaka, E., Peralta, A. Q., Qamar, F. N., Mir, F., Kariuki, S., Bhutta, Z.A., Coates, A., Bergstrom, R., Wright, G.D., Brown, E.D., and Cars, O. Antibiotic resistance- The need for global solutions. *The Lancet Infectious Diseases*, ***13***(12), 1057-1098 (2013) . https://doi.org/10.1016/S1473-3099(13)70318-9.

102. Agga, G. E., Arthur, T. M., Durso, L. M., Harhay, D. M., Schmidt, J. W., and Wasilenko, J. L. Antimicrobial-resistant bacterial populations and antimicrobial resistance genes obtained from environments impacted by livestock and municipal waste. *PLoS One*, **13**(7), e0199562 (2018). https://doi.org/10.1371/journal.pone.0132586

103. Soucy, S. M., Huang, J., ane Gogarten, J. P. Horizontal gene transfer: building the web of life. *Nature Reviews Genetics*, **16**(8), 472-482 (2015). https://doi.org/10.1038/nrg3962

104. Szmolka, A., and Nagy, B. Multidrug resistant commensal *Escherichia coli* in animals and its impact for public health. *Frontiers in Microbiology*, 4, 258 (2013). https://doi.org/10.3389/fmicb.2013.00258.

105. Michaelis, C, and Grohmann, E. Horizontal Gene Transfer of Antibiotic Resistance Genes in Biofilms. *Antibiotics (Basel)* **4**;12(2):328 (2023). https://doi:10.3390/antibiotics12020328.

106. Bello-López, J. M., Cabrero-Martínez, O. A., Ibáñez-Cervantes, G., Hernández-Cortez, C., Pelcastre-Rodríguez, L. I., Gonzalez-Avila, L. U., and Castro-Escarpulli, G. Horizontal Gene Transfer and Its Association with Antibiotic Resistance in the Genus Aeromonas spp. *Microorganisms*, **7**(9) (2019).. https://doi.org/10.3390/microorganisms 7090363

107. Johnson, T. J., Logue, C. M., Johnson, J. R., Kuskowski, M. A., Sherwood, J. S., Barnes, H. J., and Nolan, L. K. Associations between multidrug resistance, plasmid content, and virulence potential among extraintestinal pathogenic and commensal *Escherichia coli* from humans and poultry. *Foodborne Pathogens and Disease*, **13**(2), 116-124. (2016). https://doi.org/10. 1089/fpd.2011.0961

108. Hall-Stoodley, L., Costerton, J. W., and Stoodley, P. Bacterial biofilms: from the natural environment to infectious diseases. *Nature Reviews Microbiology*, **2**(2), 95-108 (2004). https://doi.org/10. 1038/nrmicro821

109. Høiby, N., Bjarnsholt, T., Givskov, M., Molin, S., and Ciofu, O. Antibiotic resistance of bacterial biofilms. *International Journal of Antimicrobial Agents*, **35**(4), 322-332 (2010). https://doi.org/ 10.1016 j.ijantimicag.2009.12.011

110. Mathew, A. G., Cissell, R., and Liamthong, S. Antibiotic resistance in bacteria associated with food animals: a United States perspective of livestock production. *Foodborne Pathogens and Disease*, **4**(2), 115-133 (2007). https://doi.org/10.1089/fpd.2006.0066

111. Berendonk, T. U., Manaia, C. M., Merlin, C., Cytryn, E., Walsh, F., Bürgmann, H., Sørum, H., Norström, M., Pons, M., Kreuzinger, N., Huovinen, P., Stefani, S., Schwartz, T., Kisand, V., Baquero, F., and Martinez, J. L. Tackling antibiotic resistance: The environmental framework. *Nature Reviews Microbiology*, **13**(5), 310-317 (2015). https://doi.org/10.1038/nrmicro3439

112. Rushton, J., Ferreira, J. P., and Stärk, K. D. Antimicrobial resistance: the use of antimicrobials in the livestock sector. *OECD Food, Agriculture and Fisheries Papers*, (68), 0_1. (2014). https://doi.org/10.1787/18156797

113. Waktole, H., Muluneh, T., Miressa, Y., Ayane, S., Berhane, G., Kabeta, T., Borena, B. M., Amenu, K., Ashenafi, H., and Antonissen, G. Quantitative Assessment of Major Biosecurity Challenges of Poultry Production in Central Ethiopia. *Animals : an open access journal from MDPI*, **13**(23), 3719 (2023). https://doi.org/10.3390/ani13233719

114. Newell, D. G., Elvers, K. T., Dopfer, D., Hansson, I., Jones, P., James, S., Gittins, J., Stern, N. J., Davies, R., Connerton, I., Pearson, D., Salvat, G., and Allen, V. M. Biosecurity-based interventions and strategies to reduce Campylobacter spp. on poultry farms. *Applied and environmental microbiology*, **77**(24), 8605–8614 (2011). https://doi.org/10.1128/AEM.01090 -10

115. Tanquilut, N., Espaldon, M., Eslava, D., Ancog, R., Medina, C., Paraso, M., Domingo, R., and Dewulf, J. (2020). Quantitative assessment of biosecurity in broiler farms using Biocheck. UGent in Central Luzon, Philippines. *Poultry Science*, **99**(6), 3047-3059. https://doi.org/10. 1016/j.psj.2020.02.004

116. Mak, P.H.W., Rehman, M.A., Kiarie, E.G. et al. Production systems and important antimicrobial resistant-pathogenic bacteria in poultry: a review. *Journal of Animal Science and Biotechnology*, **13**, 148 (2022). https://doi.org/10.1186/s40104-022-00786-0).

117. Oliveira, G. D., McManus, C., and Dos Santos, V. M. Control of *Escherichia coli* in Poultry Using the In Ovo Injection Technique. *Antibiotics*, **13**(3), 205 (2024). https://doi.org/10 .3390/antibiotics13030205

118. Paudel, S., Apostolakos, I., Ngom, R. V., Tilli, G., Ferreira, C., and Piccirillo, A. A systematic review and meta-analysis on the efficacy of vaccination against colibacillosis in broiler production. *PLOS ONE*, **19**(3) (2024). https://doi.org/10.1371/journal.pone.0301029

119. Pivnick, H., Blanch field, B. and D'aoust, J.Y. Prevention of Salmonella infection in chicks by treatment with fecal culture from mature chickens (nurmi cultures). *Journal of Food Protection*, **44**: 909-916 (1981). https://doi.org/10.4315/0362-028X-44.12.909

120. Petrariu, A., Barbu, I. C., Niculescu, G., Constantin, M., Grigore, G. A., Cristian, E., Mihaescu, G., and Vrancianu, C. O. Role of probiotics in managing various human diseases, from oral pathology to cancer and gastrointestinal diseases. *Frontiers in Microbiology*, **14**. (2023). https://doi.org/10.3389/fmicb.2023.1296447.

121. Havenaar, R. and Spanhaak, S. Probiotic from an immunological point of view. Current Opinion in Biotechnology, **5**(3), 320-325(1994). https://doi.org/10.1016/0958-1669(94)90036-1

122. Abd El-Hack, M. E., El-Saadony, M. T., Salem, H. M., El-Tahan, A. M., Soliman, M. M., Youssef, G. B., ... & Swelum, A. A. (2022). Alternatives to antibiotics for organic poultry production: types, modes of action and impacts on bird's health and production. Poultry Science, 101696.

123. Garriga M., Pascual M., Monfort J.M. and Hugas M. (1998): Selection of lactobacilli for chicken probiotic adjuncts. J. of Applied Microbiol., 84: 125–132.

124. Mack, D.R., Michail, S., Wei, S., McDougall, L. and Hollings worth, M.A. Probiotics inhibit enteropathogenic *E. coli* adherence in vitro by inducing intestinal mucin gene expression. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, **276**: 941-950 (1999). https://doi.org/1019833.

125. La Ragione, R.M., Casula, G., Cutting, S.M. and Wood ward, M.J. Bacillus subtilis spores competitively exclude *Escherichia coli O78k80* in poultry. *Veterinary Microbiology*, **79**(2), 133-142 (2001). https://doi.org/10.1016/S0378-1135(00)00350-3

126. Ahn Y.T., Lim K. L., Ryu J. C., Kang D. K., Ham J. S., Jang Y. H. and Kim H. U. Characterization of *Lactobacillus acidophilus* isolated from piglets and chicken. *Asian-australasian Journal of Animal Sciences,* **15**(12):1790-1797 (2002). https://api.semantic scholar.org/CorpusID:6456061

127. Dalloul, R. A., Lillehoj, H. S., Shellem, T. A., and Doerr J. A. Enhanced mucosal immunity against *Eimeria acervulina* in broilers fed a *Lactobacillus*-based probiotic. *Poultry Science*, **82(**1), 62-66 (2002). https://doi.org/10.1093/ps/82.1.62Poult. Sci. 82: 62-66.

128. Murry, A.C. Jr, Hinton, A. Jr and Morrison, H. Inhibition of Growth of *Escherichia coli*, *Salmonella typhimurium*, and *Clostridia perfringens* on Chicken Feed Media by *Lactobacillus salivarius* and *Lactobacillus plantarum*. *International Journal of Poultry Science* ,**3** (9) 603 – 607 (2004). https://doi:10.3923/ijps.2004.603.607

129. Ogunbanwo, S.T., Sanni, A.I. and Onilude, A.A. Influence of bacteriocin in the control of *Escherichia coli* infection of broiler chickens. *World Journal of Microbiology and Biotechnology*, **20** :51-56 (2004) https://link.springer.com/article/10.1023/B:WIBI .0000013311.43842.74

130. Ramarao, S.V., Reddy, M.R., Raju, M.V.L.N. and Panda, A.K. Growth, nutrient utilization and immune competence in b.oiler chicken fed probiotic, gut acidifier and antibacterial compounds. *Indian Journal of Poultry Science*, **39**(2): 125-130 (2004) https://www.indianjournals.com/ijor.aspx?target=ijor: ijps&volume=39&issue=2&article=004 .

131. Lonkar P. Harne S. D., Kalorey D. R. and Kurkure N. V. Isolation, in vitro antibacterial activity, bacterial sensitivity and plasmid profile of lactobacilli. *Asian-Australasian Journal of animal sciences*, **18**(9) 1336-1342 (2005). https://api.semanticscholar.org/ CorpusID:28844760

132. Hanaa, S. F. The relationship between caecal *coccidiosis* and *Escherichia coli* infection in chicken. M.V.Sc. thesis (poultry), Faculty Veterinary Medicine, Beni Suef University (2010).

133. Amer, M. M., Dahshan, A. M. H., Hassan, H. S. and Mohamed, A.A. Studies on the Prevalence of Enterobacteriaceae in Chickens and Chicken eggs. *Beni Suef Veterinary. Medical Journal* 7TH Scientific Conference, **22** (1):136-144 (2013).

134. Gao, Z., Wu, H., Shi, L., Zhang, X., Sheng, R., Yin, F., and Gooneratne, R.. Study of *Bacillus subtilis* on growth performance, nutrition metabolism and intestinal microflora of 1 to 42 d broiler chickens. *Animal Nutrition*, **3**(2): 109-113 (2017). https://doi.org/10.1016/j. aninu.2017.02.002

135. Aalaei, M., Khatibjoo, A., Zaghari, M., Taherpour, K., Akbari Gharaei, M., and Soltani, M. Comparison of single- and multi-strain probiotics effects on broiler

breeder performance, egg production, egg quality and hatchability. *British Poultry Science*, **59**(5), 531–538 (2018). https://doi.org/10.1080/00071668.2018.1496400.

136. Khalid, A. M. Studies on natural and experimental *E. coli* infection in chickens. Journal of the *Egyptian Veterinary Medical Association*, **50** (3): 379-389 (1990).

137. Char, N. L. and Rao, M. R. Zoonotically significant serotypes of *Escherichia coli* strains isolated from pathological condition of animal and poultry. *Indian Veterinary Journal* . **68** (11):1003-1006 (1991).

138. Ngeleka, M., Brereton, L., Brown, G., and Fairbrother, J. M. Pathotypes of Avian *Escherichia coli* as Related to tsh-, pap-, pil-, and iuc-DNA Sequences, and Antibiotic Sensitivity of Isolates from Internal Tissues and the Cloacae of Broilers. *Avian Diseases*, **46**:143-152 (2002). https://doi.org/10.1637/0005-2086(2002)046[0143:POAECA]2.0.CO;2

139. Huff, G. R., Huff, W. E. ,Rath, N. C., El-Gohary, F. A. ,Zhou, Z. Y. and Shini ,S. Efficacy of a novel prebiotic and a commercial probiotic in reducing mortality and production losses due to cold stress and *Escherichia coli* challenge of broiler chicks. *Poultry Science*, **94**(5):918-926 (2015). https://doi.org/10.3382/ps/pev068

140. Zhao, S., Maurerb, J.J., Hubert, S., Villena, J.F.D., Dermott, P.F.M., Meng, J., Ayersa, S., English, L. and White, D.G. Antimicrobial susceptibility and molecular characterization of avian pathogenic *Escherichia coli* isolates. *Veterinary Microbiology*, **107**(3-4), 215-224 (2005). https://doi.org/10.1016/j.vetmic.2005.01.02

141. Zhang, T., Wang, C. G., Jiang, G. E., Lv, J. C. and Zhong, X. H. Molecular epidemiological survey on aminoglycoside antibiotics-resistant genotype and phenotype of avian *Escherichia coli* in North China. *Poultry Science* , **91**(10): 2482-2486 (2012). https://doi.org/10.3382/ ps.2012-02400

142. Abd El Tawab, A. A. , Ammar, A. M., Nasef S. A., and Reda R. M. Antibacterial resistance and resistance gene detriments of *E. coli* isolated from chicken. *Benha Veterinary Medicl Journal*, **28**(2):231-240 (2014). https://doi:10.21608/bvmj.2015 .32509

143. Hiki M., Kawanishi M., Abo H., Kojima A., Koike R., Hamamoto S., and Asai,T. Decreased Resistance to Broad-Spectrum Cephalosporin in *Escherichia coli* from Healthy Broilers at Farms in Japan After Voluntary Withdrawal of Ceftiofur. *Foodborne Pathogens and Disease* , **12** (7): 639-643 (2015). https://doi.org/10.1089/fpd.2015.1960

144. Jahantigh, M., and Dizaji, R. E. Antimicrobial drug resistance pattern of *Escherichia coli* isolated from chickens farms with Colibacillosis infection. *Open Journal of Medical Microbiology* , **5**: 159-162 (2015). doi: 10.4236/ojmm.2015.54019.

145. Halfaoui, Z., Menoueri, N. M. and Bendal, L. M. Serogrouping and antibiotic resistance of *Escherichia coli* isolated from broiler chicken with colibacillosis in center of Algeria. *Veterinary World*, **10** (7): 830-835 (2017). doi: 10.14202/vetworld.2017.830-835

146. Callens B., Cargnel M., Sarrazin S., Dewulf J., Hoet B., Vermeersch K., Wattiau P., and Welby S. Associations between a decreased veterinary antimicrobial use and resistance in commensal *Escherichia coli* from Belgian livestock species (2011-2015). *Preventive Veterinary Medicine*, *157*, 50-58 (2018). https://doi.org/10.1016/j.prevetmed .2017.10.013

147. Amer M. M., Mekky, H, M., Amer, A.A., and Fedawy, H. S. Antimicrobial resistance genes in pathogenic *Escherichia coli* isolated from diseased broiler chickens in Egypt and their relationship with the phenotypic resistance characteristics. *Veterenary World*. **11**(8): 1082–1088(2018). https://doi.org/10.14202/vetworld.2018.1082-1088

148. El-Saadony, M. T., Salem, H. M., El-Tahan, A. M., Abd El-Mageed, T. A., Soliman, S. M., Khafaga, A. F., Swelum, A. A., Ahmed, A. E., Alshammari, F. A., and Abd El-Hack, M. E. . The control of poultry salmonellosis using organic agents: an updated overview. *Poultry Science*, **101**(4), 101716 (2022). https://doi.org/10.1016/j.psj.2022.101716

149. Żbikowska, K., Michalczuk, M., and Dolka, B. The Use of Bacteriophages in the Poultry Industry. *Animals (Basel)*, 10(5):872 (2020). doi:10.3390/ani10050872.

150. Kulkarni, R.R., Gaghan, C., Gorrell, K., Sharif, S., Taha-Abdelaziz, K. Probiotics as Alternatives to Antibiotics for the Prevention and Control of Necrotic Enteritis in Chickens. *Pathogens*, *11*(6):692 (2022). https://doi.org/10.3390/pathogens11060692

151. Krysiak, K., Konkol, D., and Korczyński, M. Overview of the Use of Probiotics in Poultry Production. *Animals (Basel)*,**11**(6):1620 (2021). https://doi.org/10.3390/ani11061620

152. Salem, H. M., Alqhtani, A. H., Swelum, A. A., Babalghith, A. O., Melebary, S. J., Soliman, S. M., Khafaga, A. F., Selim, S., El-Saadony, M. T., El-Tarabily, K. A., and Abd El-Hack, M. E. Heat stress in poultry with particular reference to the role of probiotics in its amelioration: An updated review. *Journal of Thermal Biology*, **108**, 103302 (2022). https://doi.org/10.1016/j.jtherbio.2022.103302

153, Salem, H. M., Saad, A. M., Soliman, S. M., Selim, S., Mosa, W. F., Ahmed, A. E., Al Jaouni, S. K., Almuhayawi, M. S., Abd El-Hack, M. E., El-Tarabily, K. A., and El-Saadony, M. T. Ameliorative avian gut environment and bird productivity through the application of safe antibiotics alternatives: A comprehensive review. *Poultry Science*, **102**(9), 102840 (2023). https://doi.org/10.1016/j.psj.2023.102840

154. Plaza-Diaz, J., Ruiz-Ojeda, F. J., Gil-Campos, M., & Gil, A. (2018). Mechanisms of Action of Probiotics. *Advances in Nutrition*, **10**(Suppl 1), S49. https://doi.org/10.1093/advanc es/nmy063

155. Awad, N. F., Hashem, Y. M., Erfan, A. M., Abdelrahman, B. A., and Mahmoud, H. I. Impact of single and mixed infections with *Escherichia coli* and *Mycoplasma gallisepticum* on Newcastle disease virus

vaccine performance in broiler chickens: An in vivo perspective. *Journal of Applied Microbiology*, **127**(2), 396-405 (2019). https://doi.org/10.1111/jam.14303

156. Mazmanian, S.K. Round, J.L. and Kasper, D.L. A microbial symbiosis factor prevents inflammatory disease. *Nature*, **453**: 620– 625 (2008). https://doi.org/10.1038/nature 07008

157. Spring, P., Wenk, C., Dawson, K.A., and Newman, K.E. The effects of dietary mannanoligosaccharides on cecal parameters and the concentrations of enteric bacteria in the ceca of salmonella challenged broiler chicks. *Poultry Science*, **79**(2), 205-211 (2000). https://doi.org/10.1093/ps/79.2.205

158. Elijah, I.O., and Ruth, T.S.O. The effect of probiotic and prebiotic feed supplementation on chicken health and gut microflora: A review. *International Journal of Animal and Veterinary Advances*, **4**(2):135- 143 (2012). https://api.semanticscholar.org/Corpus ID:37347102

159. Mahmoud, S. I., Zyan, K. A., Hamoud, M. M., Khalifa, E., Dardir, S., Khalifa, R., Kilany, W. H., and Elfeil, W. K. Effect of Co-infection of Low Pathogenic Avian Influenza H9N2 Virus and Avian Pathogenic *E. Coli* on H9N2-Vaccinated Commercial Broiler Chickens. *Frontiers in Veterinary Science*, **9**, 918440 (2022).

160. Ahmed, I., Li, Z., Shahzad, S., Naveed, S., Khan, A. K., Ahmed, A., Kamran, Z., Yousaf, M., Ahmad, S., Afzal, G., Ahmad, H. I., Yasin, N. A., Jia, J., Hussain, M., and Munir, S. Potential Probiotics Role in Excluding Antibiotic Resistance. *Journal of Food Quality*, **2022**(1), 5590004 (2021). https://doi.org/10.1155/2022/5590004

161. Fair . J. and Y. Tor, Antibiotics and bacterial resistance in the 21st century. *Perspectives In Medicinal Chemistry*, **6**, S14459 (2014.). https://doi.org/10.4137/PMC.S14459

162. Ventola C. L. The antibiotic resistance crisis: part 1: causes and threats, Part 1: *Causes and Threats. Pharmacy and Therapeutics,* **40**(4), 277-283 (2015).. https://www.ncbi.nlm.nih. gov/pmc/articles/PMC4378521/

163. Davies, J. and Davies, D. Origins and evolution of antibiotic resistance. *Microbiology and Molecular Biology Reviews*, *MMBR*, **74 (**3); 417-433 (2010). https://doi.org/10.1128/ .00016-10

164. Bagal V. L., Khatta, V. K., Tewatia, B. S., Sangwan, S. K., and Raut, S. S. Relative efficacy of organic acids and antibiotics as growth promoters in broiler chicken. *Veterinary World*,. **9**, (4): 377–382 (2016) .. https://doi.org/10.14202/vetworld .2016.377-382

165. Solis-Cruz B. Hernandez-Patlan, D., Hargis, B. M., and Tellez, G. Use of prebiotics as an alternative to antibiotic growth promoters in the poultry industry in prebiotics and probiotics-potential benefits in human nutrition and health. *IntechOpen* (2020) https://doi:10.5772/intec hopen.89053

166. van Dijk, A., Veldhuizen, E.J., Kalkhove, S.I., Tjeerdsma-van Bokhoven, J.L., Romijn, R.A., and Haagsman, H.P. The beta-defensin gallinacin-6 is expressed in the chicken digestive tract and has antimicrobial activity against food-borne pathogens. *Antimicrob Agents Chemother*. , **51**(3):912-922 (2007). https://doi:10.1128/AAC.00568-06

.

167. Nazeer, N., Uribe-Diaz, S., Rodriguez-Lecompte, J. C., and Ahmed, M. Antimicrobial peptides as an alternative to relieve antimicrobial growth promoters in poultry. *British Poultry Science*, **62**(5), 672–685 (2021). https://doi.org/10.1080/00071668 .2021.1919993

168. Mountzouris, K. C., Tsitrsikos, P., Palamidi, I., Arvaniti, A., Mohnl, M., and Schatzmayr, G. Effects of probiotic inclusion levels in broiler nutrition on growth performance, nutrient digestibility, plasma immunoglobulins, and cecal microflora composition. *Poultry Science*, **89**(1), 58-67 (2010). https://doi.org/10.3382/ps.2009-00308

169. Nath, S. K., Hossain, M. T., Ferdous, M., Siddika, M. A., Hossain, A., Maruf, A. A., Chowdhory, A. T., and Nath, T. C. Effects of antibiotic, acidifier, and probiotic supplementation on mortality rates, lipoprotein profile, and carcass traits of broiler chickens. *Veterinary and Animal Science*, **22**, 100325 (2023). https://doi.org/10.1016/j.vas.2023.100325

170. Awad, W. A., Ghareeb, K., Abdel-Raheem, S., and Böhm, J. Effects of dietary inclusion of probiotic and synbiotic on growth performance, organ weights, and intestinal histomorphology of broiler chickens. *Poultry Science*, **88**(1), 49-56. https://doi.org/10.3382/ps.2008-00244.

171. Lin, D.M., Koskella, B., and Lin, H.C. Phage therapy: An alternative to antibiotics in the age of multi-drug resistance. *World Journal of Gastrointestinal Pharmacology and Therapeutics*, **8**(3):162-173 (2017). https://doi:10.4292/wjgpt.v8.i3.162.

172. Loc-Carrillo, C., and Abedon, S. T. Pros and cons of phage therapy. *Bacteriophage*, **1**(2), 111-114 (2011). https://doi.org/10.4161/bact.1.2.14590

173. Eid, S., Tolba, H. M., Hamed, R. I., and Al-Atfeehy, N. M. Bacteriophage therapy as an alternative biocontrol against emerging multidrug resistant *E. coli* in broilers. *Saudi Journal of Biological Sciences*, **29**(5), 3380-3389 (2022).

174. Torres-Barceló, C., Arias-Sánchez, F. I., Vasse, M., Ramsayer, J., Kaltz, O., and Hochberg, M. E. A window of opportunity to control the bacterial pathogen *Pseudomonas aeruginosa* combining antibiotics and phages. *PLoS Pathogens*, 14(1), e1006879 (2018). https://doi.org/10.1371/journal.pone.0106628

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

أحمد علي أحمد[1،2]، هبة محمد سالم[3]*، محمد ممدوح حمود[3،4] و محمد محروس عامر[3]

[1] طالب ماجستير- قسم أمراض الدواجن - كلية الطب البيطري - جامعة القاهرة - ص.ب. 12211- الجيزة - مصر.
[2] ضمان الجودة - شركة القاهرة للدواجن - مصر.
[3] قسم أمراض الدواجن - كلية الطب البيطري - جامعة القاهرة - ص.ب. 12211 – الجيزة - مصر.
[4] مدير 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 (معقد 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 الإدانات 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؛ بكتريا قولونية؛ الجينات. البروبيوتيك. الأنماط المصلية.