



# Development of Antimicrobial Resistance in Layer Chicken Farms in Indonesia: A Review

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## ABSTRACT

Layer farming plays a vital role in providing animal-derived food products. Increased production raises concern about antimicrobial resistance (AMR), mainly due to widespread and indiscriminate use of antibiotics as growth promoters and prophylactic therapeutics. The present study aimed to investigate the development and risk factors associated with AMR in layer farms across Indonesia. Antimicrobial resistance represented a significant global threat to both human and animal health, leading to treatment failures, rising healthcare costs, and the spread of resistant pathogens through the food chain. Bacterial resistance mechanisms, including antibiotic inactivation, modifications of antimicrobial target sites, and reduced cellular permeability, particularly in Gram-negative bacteria further exacerbated AMR problem. Globally, regulations on antibiotic use in livestock farming differed significantly, with some countries implementing stringent bans while others continued to permit their use. In Indonesia, the use of antibiotics as growth promoters has been officially prohibited; however, enforcement remained inconsistent due to limited access to veterinary services, inadequate monitoring systems, and insufficient awareness among farmers. Effective AMR management depended on a one health framework that integrates human, animal, and environmental health. To promote responsible antimicrobial use and strengthen veterinary services, cross-sectoral coordination was vital for advancing training, infrastructure, and diagnostics. These efforts enabled the development of evidence-based policies, including regulations on the use of antibiotics in livestock and national action plans supported by robust surveillance systems. By adopting systemic approaches and innovative farm management practices, the risks associated with AMR can be effectively mitigated, ensuring the sustainability of the livestock sector and safeguarding global health.

**Keywords:** Antibiotic residue, Antibiotic use, Antimicrobial resistance, Layer farming, One health

## INTRODUCTION

Indonesia has a large and diverse livestock population, with layer chickens among the most prominent livestock species. As demand for eggs continues to increase, farming practices have become more intensive and increasingly rely on antibiotics to maintain productivity and control disease (BPPSDMP, 2025). Furthermore, this phenomenon has been observed in Southeast Asia, including Indonesia. Antimicrobial medicines are highly effective in treating infectious diseases caused by pathogenic bacteria, which often adversely affect egg production (Wall, 2019). However, the escalating use of antimicrobials for disease prevention and treatment, driven by the need to maintain high egg production levels, is a

major contributor to the emergence and spread of antimicrobial resistance (AMR; Salam et al., 2023). Antimicrobial resistance represented a persistent and critical global health challenge, with profound negative implications for both human and animal health (Gray et al., 2021). The intensive farming model, in response to rising egg demand, exerted strong selective pressure, facilitating the emergence and spread of resistant bacteria from farms to humans through the food chain, the environment, and direct contact, ultimately causing treatment failures. If AMR is not properly managed, it could cause more than 10 million deaths per year by 2050 (de Kraker et al., 2016). Raising awareness among layer farmers about AMR is essential to mitigating this global issue. However, studies indicated that many farmers lack a

comprehensive understanding of AMR and the factors that contribute to its development (Mudenda et al., 2022). Addressing this knowledge gap is critical to implementing effective strategies to reduce antimicrobial misuse and combat the spread of bacterial resistance (Salam et al., 2023).

Many poultry farmers in lower- to middle-income countries, such as Indonesia, have unrestricted access to antibiotics without a veterinary prescription (Coyne et al., 2020; BPPSDMP, 2025). This unrestricted access facilitated the purchase and administration of antibiotics to poultry without veterinary professional oversight. Consequently, farmers often fail to adhere to recommended antibiotic dosages or comply with required withdrawal periods before marketing poultry products (Manyi-Loh et al., 2018). Scientific evidence demonstrated a direct correlation between antibiotic consumption and the development of AMR (Medic et al., 2023). This highlighted that inappropriate use of antimicrobials, including excessive and improper use, plays a central role in the development and dissemination of AMR (Salam et al., 2023). Furthermore, antimicrobials have been widely misused in poultry production systems, including their incorporation into poultry feed and drinking water. These practices commonly focus on promoting growth, increasing egg production, preventing disease (prophylaxis), and providing empirical treatment when a definitive diagnosis is unavailable (Abreu et al., 2023). The inappropriate use of antimicrobials significantly increases the risk of AMR development in poultry flocks and their associated products, posing a serious threat to both animal and public health (Abreu et al., 2023; Azizi et al., 2024).

Humans can be exposed to antimicrobial-resistant microorganisms from animals through contaminated food (Almansour et al., 2023). Conversely, humans can act as vectors, transmitting these resistant microorganisms back to animals and the surrounding environment (Graham et al., 2019). Currently, numerous microorganisms have developed resistance to antimicrobials that are widely used in the livestock industry (Manyi-Loh et al., 2018). *Escherichia coli* (*E. coli*) is a prominent pathogen that has exhibited high levels of AMR in livestock settings (Lv et al., 2024). Additionally, other antimicrobial-resistant microorganisms, such as *Enterococcus* spp. and *Salmonella* spp., have been frequently identified in livestock production systems (Abreu et al., 2023). Moreover, species such as *Staphylococcus aureus* (*S. aureus*) and *Listeria* spp. have demonstrated resistance to antimicrobials commonly used in poultry and human

medicines (Ayoub et al., 2025). The transmission of resistant microorganisms to humans via the food chain poses a significant public health threat, leading to infections that are challenging to treat (Uddin et al., 2021).

In response, many countries have implemented regulations to reduce antibiotic use in livestock (Lindmeier, 2017). Antibiotic growth promoters (AGPs) were first introduced in 1951 when the U.S. Food and Drug Administration approved their use without requiring a veterinary prescription (Ma et al., 2021). A worldwide regulatory change started when Sweden banned AGPs in 1986. This policy was further expanded by the European Union's comprehensive ban in 2006, thereby motivating countries such as Mexico, New Zealand, and South Korea to adopt similar measures (McEwen et al., 2018). In Indonesia, a similar policy was established in 2018 under the minister of agriculture regulation, which regulated the classification and usage of veterinary medicines (Ministry of Agriculture, 2017). The responsible use of antibiotics is critical for ensuring animal welfare and reducing the risk of zoonotic disease transmission to humans (Sattar et al., 2023).

Limited global awareness of AMR among poultry farmers is a key driver of resistance issue, leading to the nonprescription purchase and misuse of antimicrobials and neglect of biosecurity (Kramer et al., 2017; Hassan et al., 2021). Additionally, in Africa, farmers often obtain antibiotics from unregulated suppliers for growth promotion and disease prevention, which exacerbates AMR (Mudenda et al., 2022).

Numerous studies have highlighted the bacterial resistance issue, supporting the implementation of a one health approach to address AMR effectively worldwide (Rousham et al., 2018). The present study aimed to evaluate the effects of antibiotic use in layer farming, assess the potential for AMR development, and explore its implications for animal, human, and environmental health, thereby informing strategies to mitigate AMR and promote sustainable practices in Indonesian layer chicken farms.

## MATERIALS AND METHODS

The data for the present study were collected through a comprehensive literature review of scientific articles. The literature search was conducted over a ten-year period from 2015 to 2025. However, only studies reporting bacterial AMR in layer chickens and published in the past five years (2020-2025) were included in the analysis. Investigations were performed using major academic databases, including Google Scholar, Research Gate,

ScienceDirect, PubMed, Web of Science, Scopus, and NCBI. The search strategy employed specific keywords, including antibiotic use in layer chicken farms, awareness of AMR and associated factors among layer farmers in Indonesia, and AMR as a one health issue in layer chickens. These keywords were selected to ensure the retrieval of relevant studies addressing antibiotic use, AMR, and related factors within the layer poultry production system.

## **LAYER FARMING INTENSIFICATION AND ANTIMICROBIAL RESISTANCE DYNAMICS**

The global intensification of layer farming, driven by a rising demand for animal protein, has significant implications for antimicrobial use (AMU) and the development of AMR. Intensive, high-density poultry production systems increase the risk of disease stressors, leading farmers to depend on antibiotics for prevention and treatment. This reliance created selective pressure for resistant bacteria (Grzanic *et al.*, 2023; Horvat and Kovacevic, 2025). This strong link between AMU in livestock and the emergence of AMR poses a critical public health challenge, as resistance originating in farms can spread to clinical settings (Bist *et al.*, 2024). The situation is particularly critical in resource-limited regions adopting intensive practices, underscoring a global risk that requires immediate evaluation of AMR trends associated with poultry production (Hedman *et al.*, 2020).

In Indonesia, where egg production and consumption were steadily increasing, this dynamic was particularly evident. From 2017 to 2022, national egg production grew at an annual rate of 3.80%, with East Java accounting for 27.80% of total output. At the same time, per capita egg consumption increased from 17.69 kg to 20.02 kg annually and was expected to keep growing (BPS, 2024). This growing poultry sector is vital to national food security and heightens AMR risks. Therefore, the Indonesian government has created a regulatory framework via the National Action Plan for Antimicrobial Resistance Control (2020-2024) to encourage prudent AMU and reduce the spread of resistance in the food production system.

## **MECHANISMS OF DISSEMINATION AND EVOLUTION OF ANTIMICROBIAL RESISTANCE**

Numerous antibiotics are derived from natural compounds used by microbes to combat one another. Since these chemicals naturally exist in environments like soil, bacteria have had enough time to develop resistance.

Consequently, many bacteria in the environment are already resistant to current medicines. This includes intrinsic resistance, a permanent, inherited characteristic that renders an entire bacterial species unaffected by a specific medicine, such as *E. coli*, which is resistant to macrolide antibiotics (Reygaert, 2018). Historically, bacteria have always found ways to resist new antibiotics. This pattern has followed the release of almost every antimicrobial medicine. While the development of antibiotics typically requires at least 10 years before they are approved for general use, bacteria can develop resistance mechanisms within hours, creating a highly unbalanced evolutionary race (Uddin *et al.*, 2021; Muteeb *et al.*, 2023). Acquired bacterial resistance is driven through four primary mechanisms, including antibiotic inactivation, target modification, reduced permeability, and increased efflux (Banin *et al.*, 2017). One major resistance mechanism involves modifications of antimicrobial target sites, most commonly resulting from spontaneous genetic mutations selected under antibiotic pressure. For instance, mutations in genes encoding RNA polymerase and DNA gyrase led to resistance against rifamycins and quinolones, respectively (Belay *et al.*, 2024). Another mechanism entails the enzymatic inactivation or chemical modification of antimicrobial agents, whereby bacterial enzymes neutralize the medicine's efficacy; this process is frequently implicated in resistance to aminoglycosides, chloramphenicol, and  $\beta$ -lactam antibiotics (Singh and Kim, 2025). A third mechanism is reduced cellular permeability, particularly in Gram-negative bacteria, which limits antibiotic entry by restricting transmembrane transport across the cell envelope. The fourth mechanism involves efflux systems that actively expel antibiotics and other toxic compounds from bacterial cells. Collectively, these mechanisms allow bacteria to persist and multiply despite exposure to antimicrobial agents (Peterson and Kaur, 2018; Reygaert, 2018).

## **CHALLENGES AND MANAGEMENT OF ANTIMICROBIAL USE IN LAYER FARMING**

Bacterial diseases, including salmonellosis, colibacillosis, mycoplasmosis, and necrotic enteritis, constitute major health constraints in layer chicken production systems. From 2002 to 2018, these infections consistently ranked among the most commonly documented diseases affecting the layer industry (Redweik *et al.*, 2020). Some farmers employed antimicrobials to improve growth efficiency and feed conversion rates (Miyakawa *et al.*, 2024). Although

antimicrobials play an important role in reducing disease incidence and mortality in poultry, their inappropriate use poses serious risks to public health. Antimicrobial resistance leads to prolonged illness, increased medical expenditures, and the spread of drug-resistant pathogens within healthcare settings, thereby imposing considerable economic pressures on individuals and families (Dadgostar, 2019).

In Indonesia, evidence of AMR in poultry production systems has been increasingly documented. Studies have reported high levels of antibiotic resistance among *E. coli* and *Salmonella* spp. isolated from chickens and chicken products (Ramdani et al., 2024; Wibisono et al., 2025). *Escherichia coli* isolates from chicken meat in East Java, Indonesia, demonstrated resistance rates of 75% to amoxicillin and ampicillin and 59% to oxytetracycline, while *Salmonella* spp. exhibited 84% resistance to oxytetracycline, with multidrug resistance detected in 42–43% of isolates, indicating widespread resistant bacteria in the poultry food chain (Gresik District, East Java; Wibisono et al., 2025). Additionally, *E. coli* from cloacal swabs of layer chickens in Indonesia exhibited high resistance to quinolone antibiotics, including ciprofloxacin (45%) and enrofloxacin (44.7%), with 44.4% of isolates classified as multidrug-resistant, highlighting significant AMR challenges within layer farms (Hidayah et al., 2024).

The majority of layer farmers utilized antimicrobials primarily for prophylactic purposes, often in response to inadequate farm management, to prevent common diseases, or due to a lack of vaccination programs (Kisoo et al., 2023). Furthermore, the high cost of veterinary services drove farmers to rely on antimicrobials as a preventive measure against severe diseases (Dadgostar, 2019). Consequently, farmers often rely on their personal experience or subjective perceptions of disease risk when administering antimicrobials, often without proper diagnostic confirmation (Toghroli et al., 2024). Additionally, the use of antimicrobials in layer farming is heavily influenced by recommendations from suppliers, such as feed vendors and day-old chicken providers, who often collaborate with pharmaceutical companies to achieve sales targets. This dynamic greatly influenced farmers' decisions to use antimicrobials, thereby prolonging this cycle. In Indonesia, livestock producers frequently rely on external technical advice and supplied inputs when deciding which antibiotics to use, and many farmers obtain antimicrobial products through non-veterinary channels with limited professional oversight, contributing to the widespread and routine use of antibiotics in poultry production. Surveys in major

poultry-producing regions such as West Java, East Java, and South Sulawesi, Indonesia, found that over 80% of farmers regularly used antibiotics to prevent disease, and a substantial portion used antibiotics for treatment, despite the national policies prohibiting the use of AGPs since 2018 (FAO, 2018). Furthermore, since poultry accounts for the majority of AMU in livestock, choices made by suppliers and integrators significantly influence overall usage trends. These practices not only influenced on-farm antibiotic use but also contributed to the high levels of AMU observed in Indonesian poultry production, reinforcing dependence on these medicines (Imam et al., 2020; KSI, 2025).

## RISKS AND REGULATIONS OF ANTIMICROBIAL USE IN LAYER FARMING

The affordability and efficacy of antibiotics have led to their widespread use (Rodrigues et al., 2022). The European Union adopted similar regulations but later banned 25 types of AGPs in 2006. Other countries, such as Mexico, South Korea, and New Zealand, have implemented bans on AGP use, while nations such as Japan and several non-OECD countries, including China, Brazil, and India, have continued to permit their use (Krysiak et al., 2021). In Indonesia, the use of AGPs was prohibited in 2018 under the Minister of Agriculture Regulation (Widyatmanti et al., 2022). Despite the ban on AGPs, antibiotics remain essential for preventing and treating bacterial infections, supporting animal welfare, and mitigating the risk of zoonotic diseases (Sattar et al., 2023).

The widespread use of antibiotics in animal farming for growth promotion, disease prevention, and treatment, despite ongoing global regulatory gaps for AGPs, has directly promoted the development and emergence of AMR, even though regions such as the European Union have implemented bans (Hedman et al., 2020). The economic impact of banning AGPs was relatively limited in countries with advanced production systems but was substantial in low-income countries where poor sanitation and biosecurity measures are common (Coyne et al., 2020). Certain antibiotics, including tetracyclines, aminoglycosides, and  $\beta$ -lactams, remain critical for maintaining animal health (Matheou et al., 2025). Consequently, a careful and logical evaluation of antibiotic use in layer farming is essential to strike a balance between the demands of animal production and the global imperative to manage AMR effectively (Abreu et al., 2023).

## ANTIBIOTIC RESIDUES FOUND IN EGGS IN INDONESIA

Several studies in Indonesia have reported the presence of antibiotic residues in eggs available in the market, indicating widespread and insufficiently controlled antibiotic use in layer production systems and underscoring the need for stricter regulatory oversight and enforcement in the livestock sector (BPPSDMP, 2025; Nur et al., 2025). A recent report focused on identifying bacterial contamination and antibiotic residues in animal products such as meat and eggs from Bali, West Nusa Tenggara, and East Nusa Tenggara, Indonesia, in accordance with Indonesian Law No. 7 of 1996. These regulations indicated that animal products should adhere to the standards of being Safe, Healthy, Whole, and Halal. The bacterial targets of the study conducted by Tenaya et al. (2024), namely *E. coli*, *Streptococcus aureus*, *Salmonella* spp., and *Campylobacter* spp., were all of critical importance to public health as common agents of foodborne illness in Bali and Nusa Tenggara of Indonesia (Tenaya et al., 2024). Additionally, in several locations of Indonesia, antibiotic residues, including penicillin, tetracycline, aminoglycosides, and macrolides, were detected in animal product samples, such as eggs, raising concerns about their potential contribution to AMR (Bura et al., 2024). Of 601 poultry product samples collected from Bali and Nusa Tenggara, Indonesia, 213 (35.44%) contained antibiotic residues (Tenaya et al., 2024). All chicken meat, quail egg, and liver samples collected from the study regions contained detectable levels of antibiotic residues, indicating widespread and insufficiently regulated antibiotic use. The distribution of residues showed the highest prevalence for penicillins (13%), followed by aminoglycosides (9%), macrolides (8%), and tetracyclines (5.5%; Tenaya et al., 2024).

Meanwhile, a 2020 study conducted in East Jakarta, Indonesia, focused on detecting antibiotic residues from the aminoglycoside group, specifically kanamycin, and on assessing the microbiological quality of chicken eggs sold in traditional markets and supermarkets. The study analyzed 100 egg samples and found that 27% contained kanamycin residues, indicating substantial consumer exposure to antibiotic residues in commercially available eggs. Furthermore, eggs purchased from traditional markets had higher levels of contamination than those from supermarkets. These findings suggest that non-compliant practices, such as the use of antibiotics without adhering to proper withdrawal periods before egg

collection, persist in the poultry industry in Indonesia. Such practices pose potential risks to consumer health and highlight the need for stricter adherence to food safety standards (Anton et al., 2020).

In 2019, a study was conducted to detect antibiotic residues in chicken eggs obtained from both farmers and distributors in Denpasar, Bali, Indonesia (Witoko et al., 2019). A total of 24 egg samples were randomly collected and analyzed using a bioassay. The results showed that 13 out of 18 samples from farmers and 1 out of 6 samples from distributors tested positive for antibiotic residues. Among the positive samples, aminoglycoside residues were the most common, detected in 66.7% of the eggs from farmers. Tetracycline residues were found in 44.4% of the farmers' eggs and 16.7% of the distributors' eggs, while macrolide residues were present in 16.7% of the farmers' eggs. These findings highlight the prevalence of antibiotic residues in eggs and emphasize the need for enhanced monitoring and regulation of antibiotic use in poultry farming (Witoko et al., 2019).

A study conducted in Yogyakarta, Indonesia, in May 2018 found that 100% (24 out of 24) of the tested egg samples contained antibiotic residues, with 75% (18 out of 24) testing positive for penicillin residues, 12.5% (3 out of 24) for aminoglycoside residues, and another 12.5% (3 out of 24) for oxytetracycline residues (Sivalingam, 2019). Similarly, a study in Semarang Regency focusing on tetracycline residues in chicken eggs sourced directly from farms revealed that 3.3% of the tested samples contained tetracycline residues, with an inhibition zone of 27 mm, indicating significant residue levels. Although the proportion of contaminated samples was relatively low, the detected concentrations raised concerns about potential long-term health risks for consumers, particularly with prolonged exposure through regular consumption (Sa'adah, 2017).

Utari et al. (2018) reported the results of antibiotic residue testing conducted at the BPMSPH Laboratory in Bogor, Indonesia (2017). The study revealed that no penicillin residues were detected in chicken egg samples over three consecutive years (2015-2017), indicating controlled usage. In contrast, macrolide residues showed a fluctuating trend, with a positive detection rate of 1.25% in 2015, dropping to 0% in 2016, and slightly increasing to 0.13% in 2017. Similarly, aminoglycoside and tetracycline residues declined significantly, from 46.25% in 2015 to 2.06% in 2016, and then to 0.13% in 2017. These trends suggest improvements in the regulation of antibiotic use within Indonesia's layer sector, although continued efforts are necessary to ensure food safety and mitigate the risk of

AMR at the national level (Utari et al., 2018). Another study conducted in 2015 analyzed 1,300 egg samples collected from 13 provinces across Indonesia. The results revealed antibiotic residues in the sampled eggs, with 0.77% beta-lactam residues and 0.62% tetracycline residues (Nurhidayah et al., 2015).

**ANTIBIOTIC-RESISTANT BACTERIA IN LAYER CHICKEN FARMS IN INDONESIA**

Several studies have investigated bacterial resistance in layer farms across Indonesia (Table 1). Table 1 summarizes the antibiotic susceptibility profiles of bacterial isolates recovered from layer chickens in several

regions of Indonesia over a five-year period (2020-2024). The majority of studies focused on *E. coli*, although other clinically relevant pathogens, including *Salmonella* spp., *S. aureus*, *Pasteurella multocida*, *Proteus* spp., and *Klebsiella pneumoniae*, were reported. The recent findings demonstrated substantial heterogeneity in resistance patterns across bacterial species, geographic locations, and antibiotic classes. These findings indicated widespread and persistent AMR among bacterial pathogens isolated from layer chickens in Indonesia. The frequent detection of resistance to critical antimicrobials highlighted the urgent need for improved antimicrobial stewardship, biosecurity, and surveillance in poultry to prevent AMR transmission to humans' environment.

**Table 1.** Reports on antibiotic resistance in bacterial isolates from layer chickens in Indonesia, from 2020-2024.

Location	Microbes	Number of samples	Antibiotic class	Antibiotic	Percentage (%)			Source
					S	I	R	
Blitar, East Java	<i>E. coli</i>	34	Cephalosporin	Cephazolin	97	0	3	Witaningrum et al. (2020)
				Ceftazidime	94	0	6	
				Cefepime	94	0	6	
			Beta lactam	Amoxiclav	100	0	0	
				Ampicillin Sulbactam	100	0	0	
				Ampicillin	38	0	62	
				Meropenem	100	0	0	
			Aminoglycosides	Gentamycin	82	0	18	
				Amikacin	100	0	0	
			Tetracycline	Tetracycline	32	15	53	
			Quinolone	Ciprofloxacin	35	9	56	
				Levofloxacin	47	18	35	
Amphenicol	Chloramphenicol	97	0	3				
Sulfonamida and combination	Trimethrophi-sulfamethoxazole	47	0	53				
Tabanan, Bali	<i>E. coli</i>	44 samples, less than seven-day-old chickens	Cyclic polypeptide	Bacitracin	93.02	2.33	4.65	Besung et al. (2024)
			Tetracycline	Oxytetracycline	90.7	9.3	0	
			Linkosamida	Clindamycin	95.35	0	4.65	
			Sulfonamida and combination	Trimethrophi-sulfamethoxazole	69.77	0	30.23	
				Streptomycin	88.37	0	11.63	
			Aminoglycosides	Kanamycin	34.88	2.33	62.79	
				Beta lactam	Ampicillin	90.7	0	
			Quinolone	Enrofloxacin	46.51	16.28	37.21	
		41 samples, 8-	Cyclic polypeptide	Bacitracin	97.56	2.44	0	

		30-day-old chickens	Tetracycline	Oxytetracycline	95.12	4.88	0	
			Linkosamida	Clindamycin	97.56	0	2.44	
			Sulfonamida and combination	Trimethrophi-sulfamethoxazole	70.73	0	29.27	
			Aminoglycosides	Streptomycin	29.27	26.83	43.9	
				Kanamycin	14.63	0	85.37	
			Beta lactam	Ampicillin	75.61	0	24.39	
		Quinolone	Enrofloxacin	85.37	0	14.63		
		49 samples, over 30- day-old chickens	Cyclic polypeptide	Bacitracin	100	0	0	
			Tetracycline	Oxytetracycline	100	0	0	
			Linkosamida	Clindamycin	100	0	0	
			Sulfonamida and combination	Trimethrophi-sulfamethoxazole	14.29	0	85.71	
			Aminoglycosides	Streptomycin	48.98	10.2	40.82	
				Kanamycin	18.37	0	81.63	
Beta lactam	Ampicillin		18.37	20.41	61.22			
Quinolone	Enrofloxacin	12.24	30.61	57.15				
Tabanan, Bali	<i>E. coli</i>	12	Sulfonamida and combination	Trimethrophi-sulfamethoxazole	100	0	0	Ashley et al. (2024)
			Aminoglycosides	Kanamycin	50	0	50	
			Quinolone	Enrofloxacin	83	17	0	
Jember, East java	<i>E. coli</i>	4	Macrolide	Azithromycin	50	0	50	Suswati et al. (2023)
			Sulfonamida	Sulfametoxazole	0	0	100	
			Quinolone	Ciprofloxacin	0	0	100	
			Cephalosporin	Cefixime	0	0	100	
				Ceftriaxone	0	0	100	
			Beta lactam	Amoxiclav	0	0	100	
			Tetracycline	Tetracycline	0	0	100	
Amphenicol	Chloramphenicol	0	0	100				
Medan, North Sumatera	<i>E. coli</i>	7	Beta lactam	Ampicillin	0	0	100	Audiya et al. (2023)
			Tetracycline	Tetracycline	29	0	71	
			Quinolone	Ciprofloxacin	60	26	14	
			Amphenicol	Chloramphenicol	100	0	0	
			Aminoglycosides	Gentamycin	76	24	0	
Blitar, East Java	<i>E. coli</i>	27	Beta lactam	Ampicillin	22.2	0	77.8	Wibisono et al. (2020)
			Aminoglycosides	Streptomycin	18.5	14.3	66.7	
			Macrolide	Erythromycin	0	3.7	96.3	
			Tetracycline	Tetracycline	40.7	14.8	44.4	
			Sulfonamida and combination	Trimethrophi-sulfamethoxazole	40.7	0	59.3	
Sesaot, West Lombok	<i>Salmonella sp.</i>	8	Beta lactam	Penicillin	25	0	75	April et al. (2022)
			Tetracycline	Oxytetracycline	12.5	12.5	75	
				Tetracycline	12.5	50	37.5	

Kediri, West Lombok	<i>Salmonella</i> <i>sp.</i>	10	Beta lactam	Aztreonam	90	10	0	Ramdani et al. (2024)
			Tetracycline	Tetracycline	10	40	50	
			Aminoglycosides	Streptomycin	40	10	50	
			Amphenicol	Chloramphenicol	100	0	0	
			Quinolone	Ciprofloxacin	10	80	10	
Bogor, West Java	<i>Staphyloco</i> <i>ccus aureus</i>	15	Tetracycline	Tetracycline	0	0	100	Hermana et al. (2021)
				Oxytetracycline	0	0	100	
			Beta lactam	Ampicillin	0	0	100	
			Aminoglycosides	Gentamycin	100	0	0	
			Quinolone	Nalidixic acid	0	0	100	
				Enrofloxacin	27	0	73	
				Ciprofloxacin	27	33	40	
Macrolide	Erythromycin	0	0	100				
Amphenicol	Chloramphenicol	87	0	13				
West Java	<i>Pasteurella</i> <i>multocida</i>	9	Beta lactam	Amoxicillin	66.7	0	33.3	Sunartatie et al. (2024)
			Tetracycline	Tetracycline	88.9	0	11.1	
			Quinolone	Ciprofloxacin	66.7	0	33.3	
				Enrofloxacin	88.9	0	11.1	
			Polymyxins	Colistin	0	0	100	
			Sulfonamida	Sulfamethoxazole	100	0	0	
Jember, East java	<i>Proteus spp</i>	3	Macrolide	Azithromycin	66.7	0	33.3	Suswati et al. (2023)
			Sulfonamida	Sulfametoxazole	0	0	100	
			Quinolone	Ciprofloxacin	0	0	100	
			Cephalosporin	Cefixime	0	0	100	
				Ceftriaxone	0	0	100	
			Beta lactam	Amoxiclav	0	0	100	
			Tetracycline	Tetracycline	0	0	100	
Amphenicol	Chloramphenicol	0	0	100				
Blitar, East Java	<i>Klebsiella</i> <i>pneumoniae</i>	6	Beta lactam	Ampicillin	33.3	0	66.7	Permatasari et al. (2020)
			Aminoglycosides	Streptomycin	66.7	0	33.3	
			Macrolide	Erythromycin	0	50	50	
			Tetracycline	Tetracycline	50	0	50	
			Sulfonamida	Sulfametoxazole	50	0	50	

S: Sensitive; I: Intermediate; R: Resistant

Among *E. coli* isolates, high levels of resistance were consistently observed against commonly used antibiotics, particularly tetracyclines, sulfonamides, quinolones, and  $\beta$ -lactams (Niasono et al., 2019). In Blitar, East Java, Indonesia, *E. coli* isolates exhibited high resistance rates of 62-77.8% to ampicillin, 44.4-53% to tetracycline, 56% to ciprofloxacin, and 53-59.3% to trimethoprim-

sulfamethoxazole, suggesting multidrug resistance. Similar trends were observed in Medan, North Sumatra, Indonesia, where *E. coli* isolates demonstrated high resistance to tetracycline (71%) and complete resistance to ampicillin (100%). In contrast, susceptibility to carbapenems (meropenem) and certain aminoglycosides (amikacin) remained high in several locations (Wibisono

et al., 2020; Audiya et al., 2023; Suswati et al., 2023; Ashley et al., 2024).

Age-related differences in resistance profiles were evident in *E. coli* isolates from Tabanan, Bali, Indonesia. Isolates from younger chickens (less than seven days old) indicated relatively high susceptibility to oxytetracycline, ampicillin, and bacitracin, whereas increased resistance to kanamycin, enrofloxacin, and trimethoprim-sulfamethoxazole was observed in older age groups (older than 30 days old). Notably, resistance to sulfonamides and aminoglycosides increased markedly with age, suggesting the cumulative exposure to antimicrobial agents during the production cycle (Besung et al., 2024).

Extremely high resistance levels were reported in small sample studies from Jember, East Java, Indonesia, where *E. coli* and *Proteus* spp. isolates exhibited 100% resistance to multiple antibiotic classes, including quinolones, cephalosporins, tetracyclines,  $\beta$ -lactams, and amphenicols. Although the sample sizes were limited, these findings highlighted the potential presence of extensively drug-resistant strains in poultry production systems (Suswati et al., 2023; 2025).

Non-*E. coli* pathogens also demonstrated concerning resistance patterns. *Salmonella* spp. isolates from West Lombok and Kediri, Indonesia, exhibited high resistance to tetracyclines (50-75%) and  $\beta$ -lactams (up to 75%), while maintaining susceptibility to chloramphenicol in some studies. *Staphylococcus aureus* isolates from Bogor, West Java, Indonesia, were uniformly resistant (100%) to tetracyclines, ampicillin, erythromycin, nalidixic acid, and enrofloxacin, indicating a high burden of multidrug resistance. Similarly, *Pasteurella multocida* isolates were completely resistant to colistin, raising significant public health concerns.

#### **POTENTIAL RISK OF ANTIMICROBIAL RESISTANCE EXPOSURE IN HUMANS ASSOCIATED WITH THE DEVELOPMENT OF LAYER FARMING**

The poultry sector faces several threats, including predation and subpar feed quality, structural weaknesses such as inadequate infrastructure and limited financial resources, and systemic gaps in policy, training, and biosecurity that pose serious public health risks (Wong et al., 2017). Intensive poultry farming systems, particularly in resource-limited settings, can worsen existing public health problems. Without appropriate oversight, the growth of layer farming could unintentionally worsen poverty and food insecurity (Boeckel et al., 2019). Many

development programs sourced poultry stock from large-scale commercial farms, which increased the risk of exposing households and communities to AMR bacteria and zoonotic diseases (Hedman et al., 2020).

The proximity of layer farms to human residences in resource-limited areas has increased the risk of AMR transmission, driven by insufficient sanitation, substandard hygiene, and frequent human-animal contact (Struik and Kuyper, 2017). Additionally, this proximity increased the likelihood of anthro-zoonotic transmission, in which resistant *E. coli* from humans spread to animals (Olaru et al., 2023). This can lead to resistance against antibiotics such as fluoroquinolones and colistin, which are rarely used in poultry farming in low- and middle-income countries (Monte et al., 2017).

Live animal markets further contributed to the spread of AMR and infectious diseases in layer farming. In live markets, animals from different geographic locations are sold, creating opportunities for pathogens to cross species barriers and infect humans (Hedman et al., 2020). Poultry sold in these markets often originates from intensive farms with high AMU, resulting in day-old chickens frequently harboring multidrug-resistant bacteria (Okorafor et al., 2019).

#### **A MULTIDISCIPLINARY APPROACH TO TACKLING ANTIMICROBIAL RESISTANCE IN LAYER FARMING**

The growing global challenge of AMR has led experts to develop innovative interventions to properly understand and address the complex social and ecological factors that influence the evolution, spread, and persistence of AMR (Salam et al., 2023). Guided by the multidisciplinary principles of Boulding's Skeleton of Science, a framework previously applied to emerging infectious diseases, the present study analyzed AMR in layer farming using a systems-based approach. Specifically, the framework was used to examine AMR as a complex phenomenon shaped by interactions across multiple levels, including microbial dynamics, farm management practices, AMU patterns, and broader human-animal-environment interfaces. By integrating ecological and epidemiological perspectives, this approach enabled a more comprehensive understanding of how AMR emerges, persists, and spreads within layer production systems (Coque et al., 2023).

The AMR determinants significantly influence bacterial resistance patterns in layer farming. It is important to note that the selective pressures leading to resistance are significantly affected by differences in

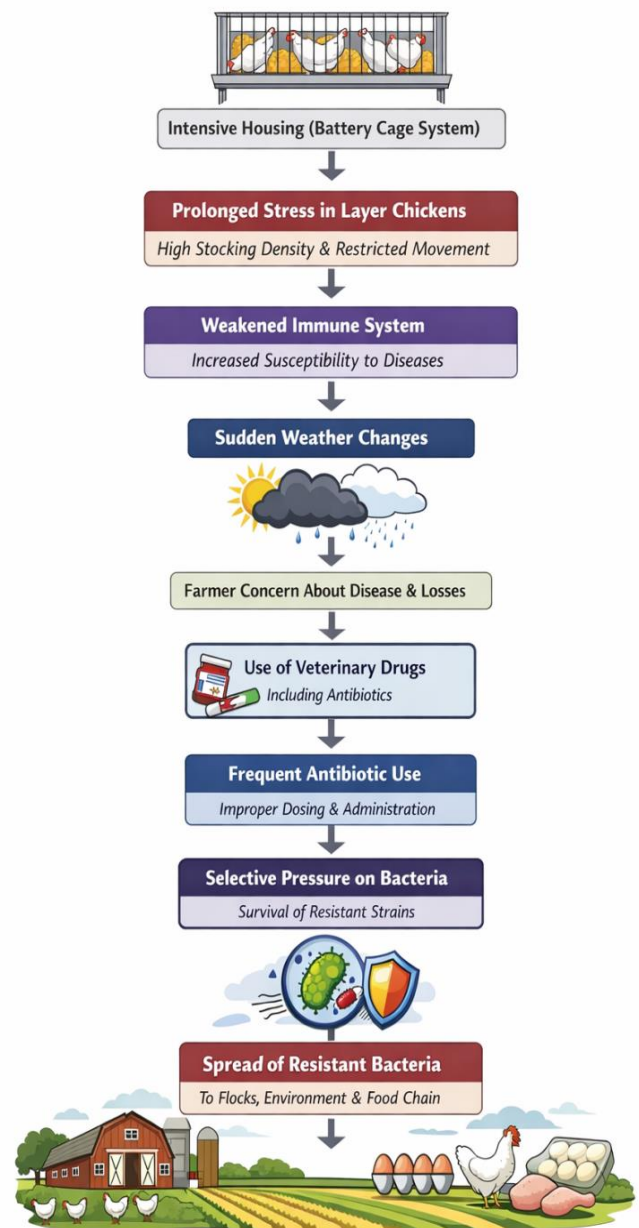
AMU, such as the types of antimicrobials administered, the duration of treatment, and the defined daily dose (Morrow, 2024). Studying ecological indicator species within poultry microbiota can provide valuable insights into bacterial populations that respond to changes in AMU patterns (Bennani et al., 2020).

While existing studies on poultry AMR have predominantly examined foodborne pathogens such as *E. coli*, *Salmonella*, and *Campylobacter* spp. for their clinical relevance (Shang et al., 2023), the threat posed by commensal bacteria and other opportunistic pathogens is significant. Commensals can act as reservoirs of resistance genes, facilitating their transfer to human pathogens and thereby posing a major public health risk. Monitoring poultry microbiomes and resistomes can provide a more detailed understanding of ecological diversity and host-microbe interactions related to AMR (Kilonzo-Nthenge et al., 2024). The factors leading to resistance to poultry-derived foods, such as eggs, differ by farming methods (Samtiya et al., 2022). Products such as meat and eggs from farms that regularly use antimicrobials are more likely to contain AMR bacteria than products from antimicrobial-free farms. In many developing countries, the need to feed growing cities and the continued use of older farming techniques combined to create a wide gap in antibiotic use (Mottet and Tempio, 2017).

Many international development projects promoted small-scale intensive poultry farming to reduce poverty. However, without adequate biosecurity measures and ongoing financial support, these initiatives can unintentionally raise the risk of zoonotic diseases and AMR, placing additional stress on farming households. (Hedman et al., 2021). The intensification of poultry production may have broader socio-economic impacts, including changes in gender roles in poultry management and shifts in local markets driven by cultural preferences for poultry products such as eggs (Struik and Kuyper, 2017).

Figure 1 illustrates a conceptual pathway explaining how intensive battery cage systems in layer chicken production can contribute to the development of AMR. Prolonged limitations at high stocking density induce chronic physiological stress that suppresses the immune system and increases susceptibility to infectious diseases. Environmental stressors, such as sudden weather changes, further exacerbate health risks and heighten farmers' concern over disease outbreaks and productivity losses (Abo-Al-Ela et al., 2021). Therefore, veterinary medicines, including antibiotics, are frequently used, often empirically or prophylactically, to manage stress-related

diseases. Repeated and inappropriate antibiotic exposure creates selective pressure on bacterial populations, enabling the survival and proliferation of resistant strains. These resistant bacteria may subsequently spread within poultry flocks, contaminate the farm environment, and enter the food chain, posing significant risks to animal health, public health, and the broader One Health system (Abo-Al-Ela et al., 2021; Niu et al., 2022; Grzinic et al., 2023).



**Figure 1.** Conceptual pathway linking intensive battery cage systems, antibiotic use, and the emergence of antimicrobial resistance in layer chickens (Figure produced by Canva software)

## VETERINARY MANAGEMENT AND THE ONE HEALTH APPROACH TO COMBAT ANTIMICROBIAL RESISTANCE

Effective control of the growing threat of bacterial resistance depends heavily on well-functioning veterinary services. Nevertheless, assessments by the World Organization for Animal Health (WOAH) indicated that, in many countries, these services have not yet met internationally recommended performance levels. This posed significant biosafety risks not only for food production in low- and middle-income countries but also for their international trading counterparts (WOAH, 2024).

International support for veterinary services remains inadequate. Further complicating the matter, profit-driven motives might cause some veterinarians to overprescribe antibiotics. In many countries, particularly low- and middle-income regions such as Indonesia, animal health agendas reflect an incomplete approach to disease management by focusing narrowly on a limited set of pathogens. Furthermore, the lack of comprehensive veterinary education programs in many regions continues to hinder progress (Odoi et al., 2021). Political commitment is often insufficient, with outdated or nonexistent policies regulating AMU. Moreover, post-market surveillance of veterinary antimicrobial products is rare, allowing counterfeit medicines to enter the market and undermine treatment efficacy. Effective, transparent, and well-managed veterinary services are critical to reducing the spread of AMR. Achieving effective AMR control requires an integrated approach that includes education, surveillance, and policy reform (WBG, 2017).

Reducing the risks of AMR linked to AMU in livestock requires an integrated One Health approach that acknowledges the interrelation of human, animal, and environmental health and promotes coordinated efforts among these sectors (Cella et al., 2023). Key components of this strategy include governance, surveillance systems, educational initiatives, investigation, preventive measures, and public awareness campaigns. Additionally, alternatives to antibiotics, such as probiotics, prebiotics, enzymes, and essential oils, were increasingly being explored to reduce reliance on antibiotics in livestock production (Muteeb et al., 2023). Scientific studies from Indonesia demonstrated that probiotics and herbal feed additives can serve as effective alternatives to traditional antibiotics in poultry farming, offering potential benefits for reducing AMR. A recent study demonstrated that supplementing layer hen diets with probiotics such as *Lactobacillus plantarum* can enhance intestinal health,

improve immune function, and reduce the load of *E. coli* in the small intestine, indicating the capacity to suppress pathogenic bacterial populations without antibiotic use (Agpretasia et al., 2024). Additionally, experimental studies on herbal probiotic combinations suggested that these probiotics can modulate gut microbial resistance traits and improve host performance. This finding indicated the role of herbal probiotics in promoting a healthier gut microbiome and reducing selection pressure that drives the emergence of AMR (Sabdoningrum et al., 2020). These findings suggested that probiotics and herbal interventions play important roles in a sustainable One Health-based strategy to mitigate AMR in Indonesia. (Dharmayanti et al., 2025).

In layer farming, the One Health approach is particularly vital for combating AMR, as it integrates surveillance, policy development, and investigations to address antibiotic overuse. The One Health approach promotes sustainable practices, improves biosecurity, and educates farmers, which helps prevent resistant bacteria from spreading to humans and the environment. Additionally, this approach ensures safer food production and protects public health (Zhang et al., 2024). Ultimately, the one health strategy can provide a comprehensive framework for tackling AMR through coordinated, proactive interventions.

## CONCLUSION

The present findings demonstrated that AMR among bacterial isolates from layer chickens in Indonesia is widespread, multifaceted, and geographically diverse. High levels of resistance were consistently observed across major bacterial pathogens, particularly *E. coli*, *Salmonella* spp., *S. aureus*, and other opportunistic organisms, against commonly used antibiotic classes such as  $\beta$ -lactams, tetracyclines, sulfonamides, quinolones, and, in some cases, critically important antimicrobials. These resistance patterns strongly reflected the intensive and often inappropriate use of antibiotics in layer farming for therapeutic, prophylactic, and growth-promotion purposes. During disease outbreaks, high levels of AMU exerted selective pressure, allowing resistant strains to proliferate and survive in poultry populations and on farms, including in manure, drinking water, and feed.

The current study indicated that poor biosecurity, inaccurate diagnoses and prescription-based treatments, lack of antibiotic rotation, and mixing chickens of different ages or sources significantly promoted the growth and spread of resistant bacteria. The persistence of

antibiotic residues within poultry farming systems has intensified this selective pressure, thereby expediting the emergence of resistant strains and promoting horizontal gene transfer among bacterial populations. These conditions had severe impacts on poultry health and productivity, leading to greater economic losses from decreased egg production and rising treatment costs. Additionally, significant public health risks were associated with increasing the spread of resistant bacteria through eggs, poultry products, and environmental pathways.

Future studies should focus on longitudinal and farm-level investigations to clarify how antibiotic use influences AMR development and resistance patterns in layer farms. Molecular characterization of resistance genes, including plasmid-mediated and mobile genetic elements, is essential for understanding their transmission within farms, between farms, and across the human-animal-environment interface. Additionally, integrated One Health approaches linking poultry-derived AMR to human clinical isolates and environmental reservoirs would provide critical evidence for risk assessment. Assessments of alternative disease management strategies, including enhanced biosecurity, vaccination, probiotics, and antimicrobial stewardship, are crucial for guiding evidence-based policies and supporting sustainable layer farming in Indonesia.

## DECLARATIONS

### Availability of data and materials

The data supporting the findings of the present study are available from the corresponding author upon reasonable request.

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### Authors' contribution

I Made Mahaputera conducted data collection, performed data analysis, and prepared the initial

manuscript draft. I Nengah Kerta Besung was responsible for study design, data analysis, and manuscript writing. Kadek Karang Agustina contributed to the study design, conducted the scientific literature search, and participated in manuscript writing. All authors read and approved the final edition of the manuscript.

### Competing interests

The authors declared that there are no conflicts of interest regarding the data, interpretation, or ownership of this manuscript.

### Ethical considerations

All data and information used were obtained from publicly available scientific publications, such as journals, books, and academic articles. The authors ensured academic integrity by properly citing all references and avoiding plagiarism, thereby upholding the principles of academic ethics. Grammarly software was used exclusively for language editing and grammar checking, and then the manuscript was reviewed and revised by the authors before submission. The authors also take full responsibility for using AI for language editing, grammar checking. The figure was created by Deepseek software.

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