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# DETECTION OF MULTIDRUG-RESISTANT *Klebsiella pneumoniae* IN THE UPPER RESPIRATORY TRACT OF BROILERS AND LAYER CHICKENS FROM COMMUNITY FARM IN ACEH BESAR, INDONESIA

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## ABSTRACT

This study aimed to investigate the presence of multidrug-resistant (MDR) *Klebsiella pneumoniae* in upper respiratory tract of broiler chickens and laying hens from community farms in Aceh Besar. Tracheal swab samples were collected and cultured on eosin methylene blue agar for bacterial isolation. Suspected isolates were identified through biochemical testing and confirmed via PCR targeting the *rpoB* gene. Identified isolates were tested for antibiotic susceptibility against ciprofloxacin, tetracycline, gentamicin, erythromycin, and chloramphenicol, using the disc diffusion method. The results revealed *K. pneumoniae* in 6% of broiler and 14% of laying hens, with widespread multidrug resistance. All isolates were resistant to erythromycin (100%), gentamicin (100%), tetracycline (85%), ciprofloxacin (40%), and chloramphenicol (15%). These findings concluded that there has been the spread of MDR of *K. pneumoniae* in broiler chickens and laying hens within Aceh Besar's community farms in Aceh Besar, Indonesia.

Key words: antibiotics, broiler chickens, *Klebsiella pneumoniae*, laying hens, multidrug-resistance

## *ABSTRAK*

*Penelitian ini bertujuan mendeteksi keberadaan multidrugs-resistant (MDR) Klebsiella pneumoniae pada saluran pernafasan bagian atas ayam petelur dan ayam pedaging. Penelitian ini menggunakan sampel swab trakhea dari ayam pedaging dan ayam petelur yang dikoleksi dari peternakan rakyat. Sampel swab trakhea dikultur pada media Eosin Methylene Blue Agar untuk mengisolasi bakteri. Isolat yang dicurigai kemudian diidentifikasi melalui uji biokimia dan dikonfirmasi melalui polymerase chain reaction (PCR) yang menargetkan gen* rpo*B. Isolat yang telah teridentifikasi selanjutnya diuji kerentanannya terhadap beberapa antibiotik, yaitu siprofloksasin, tetrasiklin, gentamisin, eritromisin, dan kloramfenikol, dengan metode disc diffusion. Hasil penelitian menunjukkan K. pneumoniae ditemukan pada 6% ayam pedaging dan 14% ayam petelur, dengan sebaran MDR yang meluas. Hasil uji sensitivitas antibiotika menunjukkan bahwa isolat K. pneumoniae telah resisten terhadap eritromisin (100%), gentamisin (100%), tetrasiklin (85%), siprofloksasin (40%), dan kloramfenikol (15%). Berdasarkan temuan ini dapat disimpulkan bahwa telah terjadi penyebaran multidrug-resistance K. pneumoniae pada peternakan rakyat di Kabupaten Aceh Besar, Indonesia.*

*Kata kunci: antibiotik, ayam pedaging, Klebsiella pneumoniae, ayam petelur, multidrug-resistance*

## INTRODUCTION

Broiler chickens and laying hens are often reared in intensive farming systems to fulfill the growing consumer demand for animal protein. Statistical data from the National Statistics Agency (BPS 2024) indicate that Aceh Province maintains a poultry population of 676,886 layer chickens and 35,891,791 broilers. Farmers frequently utilize vitamins, vaccines, and antibiotics to enhance livestock productivity and immunity (Bahri *et al*. 2005; Denli and Demirel 2018; Widhi and Saputra 2021). While vitamins and vaccines enhance immune function, antibiotics have traditionally been incorporated into feed as growth promoters. However, the Indonesian government prohibiting the use of antibiotics for growth promotion in livestock under regulation number 14/PERMENTAN/PK.350/ 5/2017.

Antibiotics are antimicrobial agents that require precise dosing and treatment duration to maintain efficacy. Inappropriate use can induce bacterial genetic mutations and accelerating the development of antimicrobial resistance (Navon-Venezia *et al*. 2017). Antimicrobial resistance (AMR) occurs when bacterial pathogens evolve mechanisms to survive antibiotic exposure, leading to ineffective treatment (Yaddi *et al*. 2020). This phenomenon has been particularly amplified in agricultural settings through the historical practice of incorporating antibiotics as growth promoters in livestock feed (Indana *et al*. 2020). *Klebsiella pneumoniae* (*K. pneumoniae)* is a pathogen known for antibiotic resistance worldwide (Opoku-Temeng *et al*. 2019). It resides on mucosal surfaces in mammals and exists in environmental reservoirs (Shon *et al*. 2013). While typically causing severe multisystem infections in immunocompromised individuals (Paczosa and Mecsas 2016), the recent emergence of hypervirulent and multidrug-resistant (MDR) strains has resulted in treatment challenges even in immunocompetent hosts (Effah *et al*. 2020).

Resistance in *K. pneumoniae* is attributed to its thick capsule and expression of resistance genes (Jamal *et al*. 2018; Ramirez *et al*. 1999). The resistance trait of *K. pneumoniae* is also encoded in plasmid DNA which acts as a carrier of resistance genes. Bacterial plasmids can spread in the environment and affect the resistance of various other microbes (Marr and Russo 2019). Multidrug-resistance *K. pneumoniae* cases in humans in Indonesia have been documented (Afifah *et al*. 2017; Khasanah *et al*. 2019; Suhartono *et al*. 2024), but reports in animals remain limited. This study investigates MDR *K. pneumoniae* in broilers and layers, potential reservoirs and transmitters of resistance.

## MATERIALS AND METHODS

### Sample Collection

A total of 200 tracheal swab samples (100 from broiler chickens and 100 from laying hens) were randomly collected from community farms across Aceh Besar District. All specimens were immediately transferred in sterile tubes containing Nutrient Broth and maintained in a cold chain during transportation to the laboratory.

### Bacteria Cultivation

Samples were incubated in Nutrient Broth (OXOID) at 37° C for 24 hours. Cultures were streaked on EMB agar (OXOID). Colony morphology, Gram staining, carbohydrate fermentation, IMViC tests, TSIA, and catalase tests were performed.

### Molecular Identification

PCR amplification of the *rpo*B gene (RNA polymerase β subunit) was conducted using primers F-CAACGGTGTGGTTACTGACG and R-TCTACGA AGTGGCCGTTTTC. DNA was extracted via the boiling method. PCR (Bio-Rad Laboratories, Inc., Hercules, CA, USA) conditions included initial denaturation at 95° C for 3 minutes, followed by 30 cycles (95° C for 30 s, 55° C for 90 s, 72° C for 90 s) and a final elongation at 72° C for 10 minutes. Products were visualized on 1.5% agarose gel for 30 min at 120 V and visualized using a UV-transilluminator.

### Antibiotic Susceptibility Test

Antibiotic resistance profiles were determined according to Clinical and Laboratory Standards Institute (CLSI, 2018) standards using the Kirby-Bauer disk diffusion method. The test antibiotic included ciprofloxacin (5 µg), tetracycline (30 µg), erythromycin (15 µg), gentamicin (10 µg), and chloramphenicol (30 µg). Bacterial suspensions were adjusted to 0.5 McFarland (1.5 x $10^8$ CFU/mL) and spread on MHA plates. Zones of inhibition were measured and categorized as sensitive, intermediate, or resistant.

### Data Analysis

Data were analyzed descriptively and presented in tables and figures.

## RESULTS AND DISCUSSION

Phenotypic characterization revealed *K. pneumoniae* in 14% (14/100) of laying hen samples and 6% (6/100) of broiler chicken samples obtained from tracheal swabs (Table 1). *K. pneumoniae* identified with dome-shaped mucoid colonies on agar medium (Figure 1). *K. pneumoniae* showed circular, showed pink-purple, and large colonies with a diameter of 2-5 mm on EMB agar (Bolla *et al*. 2021). Based on the biochemical tests, all isolates exhibited non-motility, tested negative for indole production and methyl red, positive for the Voges-Proskauer and citrate utilization tests, produced an acid/acid reaction with gas in TSIA, and demonstrated the ability to ferment glucose, lactose, sucrose, maltose, and mannitol.

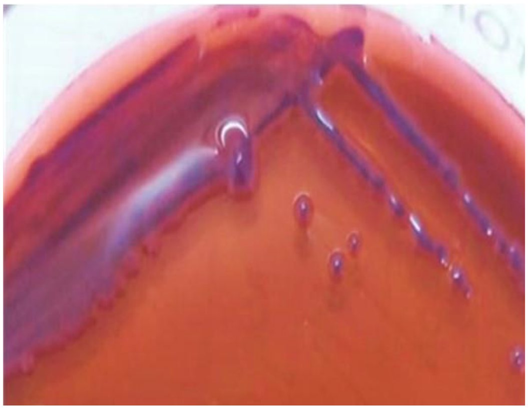

**Figure 1**. Pink-purple colony *K. pneumoniae* on Eosin methylene blue agar medium

### Molecular identification Using Polymerase Chain Reaction

Molecular detection showed all phenotypically identified isolates display a similar single band at an approximate 108 bp DNA fragment in agar gel electrophoresis (Figure 2). Thus, the 20 isolates were classified as *K. pneumoniae* according to amplification of the *rpo*B gene.

The detection of *K. pneumoniae* in both broiler chickens and laying hens underscores the expanding ecological niche of this opportunistic pathogen beyond clinical and hospital settings into animal husbandry and the food production chain. In this study, the prevalence of *K. pneumoniae* in upper respiratory was observed in 6% of broiler chickens phenotypically, and confirmed genetically using PCR. In comparison, a higher prevalence of *K. pneumoniae* (14%) was observed in upper respiratory of laying hens. This result aligning with previous findings reported by Alchalaby *et al*. (2024) in Nineveh Governorate, iraq (30%), and Popy *et al.* (2011) in Bangladesh (6%). Notably, a study by Franklin-Alming *et al.* (2021) found a significantly higher prevalence in turkeys (74.2%) compared to broilers (25.8%) in Norway, suggesting species-specific differences in colonization rates.

The presence of *K. pneumoniae* in broiler chickens, which are typically raised in high-density and high-turnover systems, may be attributed to environmental contamination, close animal contact, and frequent antibiotic exposure, all of which create favorable conditions for the colonization and persistence of bacteria (Ewers *et al*. 2012). The elevated prevalence in laying hens may be attributed to their longer lifespan and prolonged exposure to environmental contaminants, as well as differences in husbandry practices compared to broiler chickens. Laying hens typically managed under different housing systems, may serve as long-term carriers of *K. pneumoniae*. The pathogen's ability to colonize the gastrointestinal and respiratory tracts asymptomatically enables persistence and intermittent shedding, thus maintaining its presence in the farm environment (Lepuschitz *et al*. 2020).

**Antimicrobial Testing**

The prevalence of antimicrobial resistant *K. pneumoniae* in poultry has been a public concern. Antimicrobial resistance occurs when germs defeat the antibiotic or antifungal drugs designed to kill them. Multidrug-resistance occurs when an organism becomes resistant to at least one agent in three or more chemical classes of antibiotic**.** In this study, three isolates showed resistant to macrolides (erytromycin) and amino-glycosides (gentamicin), while still sensitive to quinolones (ciprofloxacin), tetracycline, and chloramphenicol. According to these data, the overall prevalence of multidrug-resistant *K. pneumoniae* isolates was 85% (17/20) in both broiler chickens and laying hens This result was nearby to the study by Tongkamsai *et al*. (2024) were obtained 89.65 % MDR *K. pneumoniae* isolates from broiler chickens in Thailand. However, this study significantly higher than in a study conducted in Permatasari *et al*. (2020), where the MDR prevalence of broilers and layers was 53.57% (15/63) in Blitar, Indonesia.

The *K. pneumoniae* isolates showed differences in resistance against the different antimicrobial used in this research. Overall, the isolates from broiler chickens exhibited highest resistance (100%) to erythromycin and gentamicin, 85% to tetracycline, 40% ciprofloxacin, and 15% to chloramphenicol (Table 2). In the previous study, 42 isolates of *K. pneumoniae* from broiler chicken in west java showed resistance to erythromycin, 95% to tetracycline, 75% ciprofloxacin, 45% to gentamicin, and 25% to chloramphenicol (Safika *et al*. 2022). Furthermore, *K. pneumoniae* isolates from laying hens in exhibited completely (100%) resistant to ampicillin, 90.91% to sulfisoxazole, 54.55 to ciprofloxacin, and 72,73% to both gentamycin and tetracycline (Hou *et al*. 2024). Erythromycin is one of the most widely used antibiotics in food animals, which might result in antimicrobial resistance among the isolates.

The lowest resistance level of broiler chickens and laying hens isolates was observed in chloramphenicol. This finding is in line with Safika *et al.* (2022) which conveys that there is a possibility that *K. pneumoniae* isolates resistant still carry the gene that codes for chloramphenicol resistance although this antibiotic has been banned in Indonesia. According to decree of the Minister of Agriculture number: 806/Kpts/TN.260/ 12/1994 concerning classification of animal drugs, chloramphenicol is included among the harsh medications not permitted for animal use. Additionally, according to regulation of Minister of Health number 722/Menkes/per/ix/1988 concerning food additives, number: 1168/Menkes/PER/X/1999, chloramphenicol is one of the nine prohibited food additives.

In the current study, differences in resistance were observed between isolates of *K. pneumoniae* from broiler chickens and laying hens. Differences in antibiotic resistance levels between broiler chickens and layer chickens can be influenced by varying antibiotic usage patterns, farming practices, and the specific

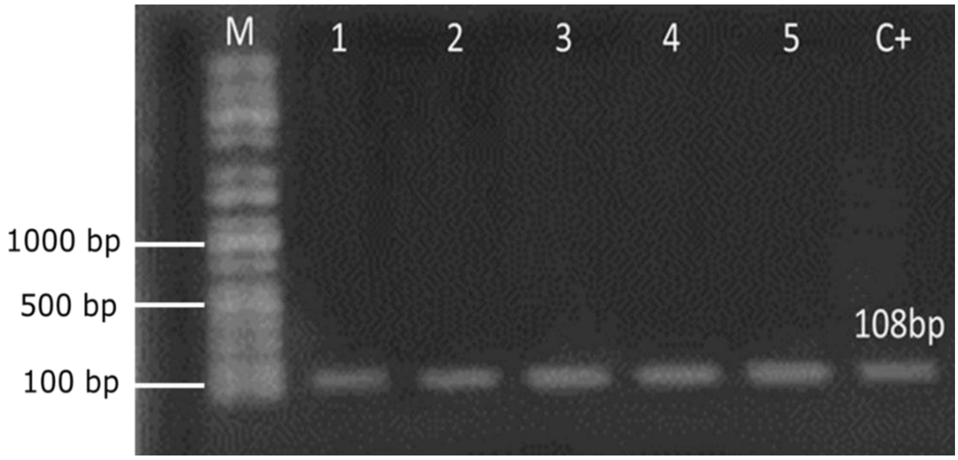


**Figure 2**. Visualization of DNA bands in the 108 bp *rpo*B gene of *K. pneumoniae*. M= Marker, 1-5= Isolates that were PCR tested, C+= Positive control

**Table 1**. Prevalence *Klebsiella pneumoniae* isolated from upper respiratory tract of broiler chickens and laying hens

| Sample | Total sample | Positive sample (%) |
|---|---|---|
| Broiler | 100 | 6 |
| Layer | 100 | 14 |

**Table 2**. Antibiotic resistance pattern of *K. pneumoniae* isolated from broiler chickens and laying hens

| Antibiotics | Broiler | Layer | % of total isolates resistant |
|---|---|---|---|
| | % of resistant isolates (n= 6) | % of resistant isolates (n= 14) | |
| Ciprofloxacin | 33,3 | 28,5 | 40 |
| Tetracycline | 100 | 78.5 | 85 |
| Erytromycin | 100 | 100 | 100 |
| Gentamicin | 100 | 100 | 100 |
| Cloramphenicol | 16.6 | 14.3 | 15 |

pathogens present in each environment. Broiler chickens as a meat producer are often given antibiotics in feed to promote growth and prevent disease, while antibiotic use in layers is more restricted, especially during the laying period (Singer 2023; Singh *et al*. 2025). Additionally, the types of antibiotics used and their concentrations can differ between the two groups, impacting the development of antibiotic resistance. The spread of resistance features between bacteria is a significant contributor to the development and spread of MDR infections (Widhi and Saputra 2021). The rise of MDR *K. pneumoniae* in poultry poses a serious public health risk, especially for individuals in close contact with infected birds. A recent Pakistani study identified six MDR *K. pneumoniae* strains in broiler chickens, all of which carried numerous resistance genes, including those linked to aminoglycoside, β-lactam, and fluoroquinolone resistance. In addition, research in Egypt reported that humans were found to be infected by MDR *K. pneumoniae* strains, which reflected resistance profiles similar to those of strains isolated from chickens (Khalifa *et al*. 2021).

Multidrug-resistant *K. pneumoniae* represents a critical public health threat worldwide due to its ability to cause severe infections that are increasingly difficult to treat. *K. pneumoniae* naturally resides in the human gastrointestinal tract but can become pathogenic under certain conditions, leading to illnesses such as pneumonia, bloodstream infections, wound infections, and urinary tract infections (Podschun and Ullmann 1998). The emergence of MDR strains, particularly those resistant to carbapenems, further complicates treatment and significantly increases morbidity, mortality, and healthcare costs (WHO 2017).

One major impact of MDR *K. pneumoniae* is the limited availability of effective antibiotics. Resistance to multiple drug classes, including β-lactams, aminoglycosides, and fluoroquinolones, restricts therapeutic options to last-resort agents like colistin, which itself is associated with considerable toxicity (van Duin and Doi 2017). Infections caused by MDR strains have been associated with prolonged hospital stays, increased need for intensive care, and higher mortality rates compared to infections by susceptible strains (Munoz-Price *et al*. 2013). According to a study by Giannella *et al*. (2014), the mortality rate of patients with bloodstream infections due to carbapenem-resistant *K. pneumoniae* can exceed 50%.

Another critical consequence is the potential for nosocomial (hospital-acquired) outbreaks. Multidrug-resistance *K. pneumoniae* is notorious for its ability to spread rapidly in healthcare settings, facilitated by factors such as antibiotic misuse, invasive procedures, and poor infection control practices (Logan and Weinstein 2017). Its ability to form biofilms on medical devices further enhances persistence and resistance to treatment, contributing to recurrent infections (Li *et al*. 2018).

Furthermore, the genetic plasticity of *K. pneumoniae* enables the acquisition and dissemination of resistance genes through mobile genetic elements such as plasmids and transposons (Navon-Venezia *et al*. 2017). This not only exacerbates the resistance problem within *K. pneumoniae* populations but also poses a risk for horizontal gene transfer to other pathogenic bacteria, broadening the spectrum of antimicrobial resistance in clinical settings. From a public health perspective, the rise of MDR *K. pneumoniae* necessitates urgent interventions including enhanced surveillance, strict infection control measures, prudent antibiotic stewardship, and the development of novel antimicrobial agents (WHO 2017). Without coordinated global efforts, the burden of MDR bacterial infections, including those caused by *K. pneumoniae*, is expected to escalate, posing a formidable challenge to modern medicine. To routinely monitor antimicrobial resistance, genotypic methods involving the detection of specific resistance genes or mutations through molecular techniques are essential. These methods offer rapid and specific identification of resistance determinants and can detect resistance even before phenotypically apparent (Ellington *et al*., 2017; Boolchandani *et al*., 2019). However, genotypic assays are limited to detecting only known genes included in the test panel, and the presence of resistance genes does not always equate to phenotypic resistance due to factors such as lack of expression, gene silencing or posttranscriptional regulation (van Belkum *et al*., 2019).

## CONCLUSION

The study revealed multidrug-resistant *K. pneumoniae* in 6% of broiler and 14% of layer chicken. The isolates demonstrated alarming resistance patterns, with complete resistance to both erythromycin and gentamicin (100%), followed by high resistance to tetracycline (85%), moderate resistance to ciprofloxacin (40%), and lower but notable resistance to chloramphenicol (15%). These finding provide compelling evidence of MDR *K. pneumoniae* colonization in poultry populations within community farms in Aceh Besar, Indonesia.

## REFERENCES


Afifah A, Purwonegoro TA, Peramiarti ID. Resistensi *Klebsiella* sp terhadap meropenem di RSUD Prof. Dr. Margono Soekarjo Purwokerto. *Scripta Biologica*, 4(2):135-137.

Alchalaby AY, Al-Abedi SF, Al-Aalim AM. 2024. Isolation and identification of *Klebsiella pneumoniae* from respiratory disease in chicken. *Iraqi Journal of Veterinary Sciences*, 38(3):583-588.

Bahri S, Masbulan E, Kusumaningsih A. 2005. Proses praproduksi sebagai faktor penting dalam menghasilkan produk ternak yang aman untuk manusia. *Jurnal Litbang Pertanian*, 24(1):27-35.

Bolla NE, Suarjana IGK, Gelgel KTP. 2021. Isolasi dan identifikasi *Klebsiella* sp. Asal rongga hidung babi penderita Porcine *Respiratory Disease Complex*. *Indonesia Medicus Veterinus*, 10(6):917-925.

Boolchandani M, D'Souza AW, Dantas G. 2019. Sequencing-based methods and resources to study antimicrobial resistance. *Nature Reviews Genetics*, 20(6):356-370.

BPS [Badan Pusat Statsitik] Propinsi Jawa Barat. 2024. Produksi Daging Ayam Ras Pedaging dan Ayam Petelur Menurut Provinsi. *www.bps.go.id.*

Denli M, Demirel R. 2018. Replacement of antibiotics in poultry diets. *CABI Reviews*, 13(035):1-9.

Effah CY, Sun T, Liu S, Wu Y. 2020. *Klebsiella pneumoniae*: An increasing threat to public health. *Annals of Clinical Microbiology and Antimicrobials*, 19(1):1-9.

Ellington MJ, Ekelund O, Aarestrup FM, Canton R, Doumith M, Giske C, Grundman H, Hasman H, Holden MTG, Hopkins KL, Iredell J. 2017. The role of whole genome sequencing in antimicrobial susceptibility testing of bacteria: report from the EUCAST Subcommittee. *Clinical microbiology and infection*, 23(1):2-22.

Ewers C, Bethe A, Semmler T, Guenther S, Wieler LH. 2012. Extended-spectrum β-lactamase-producing and AmpC-producing *Escherichia coli* from livestock and companion animals, and their putative impact on public health: A global perspective. *Journal Clinical Microbiology and Infection*, 18(7):646-655.

Franklin-Alming FV, Kaspersen H, Hetland MA, Bakksjø RJ, Nesse LL, Leangapichart T, Löhr IH, Telke AA, Sunde M. 2021. Exploring *Klebsiella pneumoniae* in healthy poultry reveals high genetic diversity, good biofilm-forming abilities and higher prevalence in Turkeys than broilers. *Journal Frontiers in Microbiology*, 7(12):1-11

Giannella M, Trecarichi EM, De Rosa FG, Del Bono V, Bassetti M, Lewis RE, Losito AR, Corcione S, Saffioti C, Bartoletti M, Maiuro G. 2014. Risk factors for carbapenem-resistant *Klebsiella pneumoniae* bloodstream infection among rectal carriers: A prospective observational multicentre study. *Journal Clinical Microbiology and Infection*, 20(12):1357-1362.

Hou G, Ahmad S, Li Y, Yan D, Yang S, Chen S, Qiu Z, Yu X, Li N, Li Y, Liang Y. 2024. Epidemiological, virulence, and antibiotic resistance analysis of *Klebsiella pneumoniae*, a major source of threat to livestock and poultry in some regions of Xinjiang, China. *Journal Animals*, 14(10):1-19.

Indana, K, Effendi M. H. dan Soeharsono. 2020. Uji resistensi antibiotik ampicilin pada bakteri *Escherichia coli* yang di isolasi dari beberapa peternakan di Surabaya. *Jurnal Peternakan Lingkungan Tropis*, 3(1):37-43.

Jamal M, Ahmad W, Andleeb S, Jalil F, Imran M, Nawaz MA, Hussain T, Ali M, Rafiq M, Kamil MA. 2018. Bacterial biofilm and associated infections. *Journal Chinese Medical Association*, 81(1):7-11.

Khalifa SM, Abd El-Aziz AM, Hassan R, Abdelmegeed ES. 2021. β-lactam resistance associated with β-lactamase production and porin alteration in clinical isolates of *E. coli* and *K. pneumoniae*. *PLoS One*, 16(5):1-22.

Khasanah RN, Puspitasari I, Nuryastuti T, Yuniarti N. 2020. Prevalensi multidrug-resistant *Klebsiella pneumoniae* dan evaluasi kesesuaian antibiotik empiris berdasarkan nilai prediksi farmakokinetik terhadap outcome klinis di RSUP Dr Soeradji Tirtonegoro Klaten. *Majalah Farmaseutik*, 16(1):27-33.

Lepuschitz S, Hauser K, Schriebl A, Schlagenhaufen C, Stöger A, Chakeri A, Vötsch K, Pekard-Amenitsch S, Springer B, Allerberge, F, Ruppitsch W. 2020. Fecal *Klebsiella pneumoniae* carriage is intermittent and of high clonal diversity. *Journal Frontiers in Microbiology*, 11(581081):1-17.

Li Y, Zhang L, Zhou Y, Zhang Z, Zhang X. 2018. Survival of bactericidal antibiotic treatment by tolerant persister cells of *Klebsiella pneumoniae*. *Journal of Medical Microbiology*, 67(3):273-281.

Logan LK, Weinstein RA. 2017. The epidemiology of carbapenem-resistant Enterobacteriaceae: the impact and evolution of a global menace. *The Journal of Infectious Diseases*, 215(1):S28-S36.

Marr CM, Russo TA. 2019. Hypervirulent Klebsiella pneumoniae: A new public health threat. *Expert Review of Anti-infective Therapy*, 17(2):71-73.

Munoz-Price, LS, Poirel L, Bonomo RA, Schwaber MJ, Daikos GL, Cormican M, Cornaglia G, Garau J, Gniadkowski M, Hayden MK, Kumarasamy K. 2013. Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases. *Journal the Lancet Infectious Diseases*, 13(9):785-796.

Navon-Venezia S, Kondratyeva K, Carattoli A. 2017. *Klebsiella pneumoniae*: A major worldwide source and shuttle for antibiotic resistance. *Journal FEMS Microbiology Reviews*, 41(3):252-275

Opoku-Temeng C, Kobayashi SD, DeLeo FR. 2019. *Klebsiella pneumoniae* capsule polysaccharide as a target for therapeutics and vaccines. *Computational Structural Biotechnology Journal*, 17:1360-1366.

Paczosa M, Mecsas J. 2016. *Klebsiella pneumoniae*: Going on the offense with a strong defense. *Journal Microbiology and Molecular Biology Reviews*, 80(3):629-661.

Permatasari DA, Witaningrum AM, Wibisono FJ, Effendi MH. 2020. Detection and prevalence of multidrug-resistant *Klebsiella pneumoniae* strains isolated from poultry farms in Blitar, Indonesia. *Biodiversitas Journal of Biological Diversity*, 21(10):4642-4647.

Podschun R, Ullmann U. 1998. *Klebsiella spp*. as nosocomial pathogens: Epidemiology, taxonomy, typing methods, and pathogenicity factors. *Journal Clinical Microbiology Reviews*, 11(4):589-603.

Popy N, Asaduzzaman M, Miah MS, Siddika A, Sufian MA, Hossain MM. 2011. Pathological study on the upper respiratory tract infection of chickens and isolation, identification of causal bacteria, *Journal Bangladesh Veterinarian*, 28(2): 60-69.

Ramirez JA, Vargas S, Ritter GW, Brier ME, Wright A, Smith S, Newman D, Burke J, Mushtaq M, Huang A. 1999. Early switch from intravenous to oral antibiotics and early hospital discharge: a prospective observational study of 200 consecutive patients with community-acquired pneumonia. *Journal Archives of Internal Medicine*, 159(20): 2449-2454.

Safika S, Nilasari Z, Pasaribu FH. 2022. Detection of antibiotic resistance coding gene in Klebsiella pneumoniae bacteria isolated from broiler chickens in West Java, Indonesia. *Journal of Applied Pharmaceutical Science*, 12(7):190-198.

Shon AS, Bajwa RPS, Russo TA. 2013. Hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*: A new and dangerous breed. *Journal Virulence*, 4(2):107-118.

Singer RS. 2023. Estimates of on-farm antimicrobial usage in egg production in the United States, 2016-221. *Journal Frontiers in Veterinary Science*, 10(1135377):1-8.

Singh S, Kriti M, Sharma P, Pal N, Sarma DK, Tiwari R, Kumar M. 2025. A One Health Approach Addressing Poultry-Associated Antimicrobial Resistance: Human, Animal and Environmental Perspectives. *The Microbe*, 7(100309):1-17.

Suhartono S, Hayati Z, Mahdani W, Andini F. 2024. Distribution of ESBL-producing and non-ESBL-producing *Klebsiella pneumoniae* isolated from sputum specimens in the Zainoel Abidin General Hospital, Banda Aceh, Indonesia. *Biodiversitas Journal of Biological Diversity*, 25(7):3247-3254.

Tongkamsai S, Chatmontee W, Nakbubpa K. 2024. Multidrug-resistance in *Escherichia coli* and *Klebsiella pneumoniae* isolated from broiler chickens in Eastern Thailand. *Thai Journal of Veterinary Medicine*, 54(3):1-6.

van Belkum A, Bachmann TT, Lüdke G, Lisby JG, Kahlmeter G, Mohess A, Becker K, Hays JP, Woodford N, Mitsakakis K, Moran-Gilad J. 2019. Developmental roadmap for antimicrobial susceptibility testing systems. *Nature Reviews Microbiology*, 17(1):51-62.

van Duin D, Doi Y. 2017. The global epidemiology of carbapenemase-producing Enterobacteriaceae. *Journal Virulence*, 8(4):460-469.

WHO [World Health Organization]. 2017. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and evelopment of new antibiotics. *https://www.who.int/medicines/publications/WHO-PPL-Short_Summary*.

Widhi APKN, Saputra INY. 2021. Residu antibiotik serta keberadaan *Escherichia coli* penghasil ESBL pada daging ayam broiler di Pasar Kota Purwokerto. *Jurnal Kesehatan Lingkungan Indonesia*, 20(2):137-142.

Yaddi Y, Safika, Pasaribu FH. 2020. Uji resistensi terhadap beberapa antibiotika pada *Escherichia coli* yang di isolasi dari kucing di klinik hewan kota bogor. *Jurnal Ilmu dan Teknologi Peternakan Tropis*, 7(3):203-210.