

A Review of the Presence of Antibiotic Resistance Problems on *Klebsiella Pneumoniae* Acquired from Pigs: Public Health Importance

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ABSTRACT

Antibiotic resistance is a global public health problem. Antibiotic resistant bacteria such as *Klebsiella pneumoniae* is bacteria that is common in the digestive tract and upper respiratory tract of animals and humans. Several studies have shown that this bacterium is not only found in humans but also in animals, one of which is pigs which are known to be a reservoir for the spread of this bacteria. There are several strains, resistant antibiotics, antibiotic resistance genes and virulence genes of the *Klebsiella pneumoniae* bacteria in pigs which were summarized in this article. Not only in pigs, but this antibiotic resistant bacterium is also known to be found in other food-producing animals, such as cows, chickens and sheep. Many cases of *Klebsiella pneumoniae* in humans have been reported, but cases of *Klebsiella pneumoniae* in humans related to animals or strains related to animals and humans were also summarized in this article. Control and prevention are needed to prevent the spread of antibiotic resistant bacteria from animal to animal, animal to human and vice versa as well as to the surrounding environment.

Keywords: Antibiotic Resistance, *Klebsiella pneumoniae*, Pigs, Public Health
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INTRODUCTION

One of the most important issues for healthcare societies in the world today is the issue of antibiotic resistance (1). Antimicrobials are commonly used for the treatment and prevention of animal diseases in veterinary medication. In addition, they are also applied as an antimicrobe growth promoter (AGP) to feed ingredients in many countries to improve productivity (2). Over time, there has been much evidence that the use of antimicrobials in animals is helping to establish antimicrobial resistance (AMR) (3,4). The antibiotic resistance is a problem of the use of antibiotics in medicine and its diffusion in environments that encourage the development and propagation of antibiotic resistant bacteria (5). Nine important bacteria are involved in antibiotic resistance and *Klebsiella pneumoniae* is one of the main bacteria (1). In hog farming, pig farmers use antibiotics, metaphylaxis, prophylaxis, and growth promotion in their livestock (7). Antibiotics primarily are used in hog farming. Various studies were documented with the discovery of antibiotic resistant *Klebsiella pneumoniae* bacteria in pigs (8,9). Antibiotics used in pigs are classified into all major antibiotic classes used in clinical practise. Pigs are also known to transmit pneumoniae bacteria of *Klebsiella* to the environment and humans. The disposal of antibiotics with agricultural waste affects the spread, primarily from agricultural fertiliser application and/or irrigation of polluted water supplies to nearby communities, of the antibiotic resistance generation and of resistant bacteria by contaminated soil, land and surface water, atmosphere and plants (10); Horizontactous genes may be transmitted to other bacteria of the *Klebsiella pneumoniae* and other

bacterias within an Enterobacteriaceae family through horizontal gene transmission (11). *Klebsiella pneumoniae* *Klebsiella pneumoniae* is a gram-negative bacterium commonly found in the animals' atmosphere and digestive tract within the enterobacteriaceae family. The *Klebsiella*-General causes carnivorous and ungulated pneumonia and urogenital infections, ruminant and pig mastitis, rabbit enterocolitis, and sporadic septicemia for many species (12). The discovery of several *Klebsiella pneumoniae* which are antibiotic resistant to animals has a detrimental effect on public health and an influence on a country's economy, and thus monitoring or prevention needs to take place, in order to address this problem (13). The research was thus conducted to establish *Klebsiella pneumoniae* antibiotic resistance profile, in particular in pigs, focusing on the resistance of *Klebsiella pneumonye* in pigs, virulence genes, genes mediating resistance to antibiotics, cases in other animals and the relationship between *Klebsiella pneumoniae* in humans and pigs. and monitoring and preventive strategies to resolve these issues. both.

Strain of *Klebsiella pneumoniae* on pigs

Pigs are livestock that are consumed by some people in the world. These food-producing animals may play an important role as transfer of antibacterial resistance among farmers, livestock and the agricultural environment, in fact some studies have focused on the possibility of this transmission (14). As in the research conducted by Kieffer, the strains of *Klebsiella pneumoniae* in pigs that were found were STs, ST45 and ST1563 (15). In the study conducted by Founou, the *Klebsiella pneumoniae* strains were ST14, ST39, ST2958 and ST2959

(16). The bacteria developed by the ESBL-enzyme have been reported to different levels in a clinical sample in Ivory Coast, Morocco, Cameroon and Madagascar (11). Even the community-acquired urinary tract infections in the city of Cameroon have an incidence of 16.4 percent). (18. The ESBL-producing strains of KI have been reported by Founou. (18)

Research conducted by Mobasser (19) in Malaysia also stated that there was a link between *Klebsiella pneumoniae* strains in pigs and in humans, *Klebsiella pneumoniae* strains in their research, namely: KP2013Z05, KP2013Z12, KP2013Z13, KP2013Z14, KP2013Z15, KP2013Z17, KP2013Z18, KP2013Z22, KP2013Z24, KP2013Z26, KP2013Z27, KP2013Z28, KP2013Z30, KP2013Z31, KP2013Z33, KP2013Z38, KP2013Z39, KP2013Z44, KP2013Z48, KP2015Z01, KP2015Z02, KP2015Z03, PIG201504, KP2015Z05, KP2015Z06, KP2015Z07, KP2015Z08, KP2015Z09, KP2015Z10, KP2015Z11, KP2015Z12, KP2015Z13, KP2015Z14, KP2015Z15, KP2015Z16, KP2015Z17. Transmission of antibiotic-resistant strains from animals to humans can occur through direct such as direct contact with farmers and veterinarians or indirectly such as through consumption of contaminated animal feed, contaminated ground or surface water and animal waste

handling routes (20). *Klebsiella pneumoniae* is an important opportunistic bacterial pathogen that causes infectious diseases in animals, including pigs (8,9,21). This occurs due to the widespread use of antibiotics and the misuse of antibiotics as growth enhancers and treatment of diseases in animals. In research conducted by Yang in Henan Province, China. It has been reported that 47 isolates from the pigs studied were almost all of the isolates resistant to several classes of antibiotics tested. *Klebsiella pneumoniae* strains in studies conducted using multilocus sequence type (MLST) have been reported, namely ST11, ST106, ST235, ST258, ST263, ST270, ST1102, ST1863. ST *Klebsiella pneumoniae* which is most often found is ST11 in pig isolates. ST235 and ST258 are also common ST strains of *Klebsiella pneumoniae* isolated in pigs (13).

The finding of *Klebsiella pneumoniae* strains in food-producing animals, namely pigs, is of course very important and needs to be known as an indication of whether these strains are related to one another. The following is a summary of the strains of *Klebsiella pneumoniae* bacteria in pigs from several studies that have been carried out from various countries which are summarized in Table 1.

Table 1. *Klebsiella pneumoniae* strains in pigs

Year	Strain <i>Klebsiella pneumoniae</i>	References
2015	KP2013Z05, KP2013Z12, KP2013Z13, KP2013Z14, KP2013Z15, KP2013Z17, KP2013Z18, KP2013Z20, KP2013Z21, KP2013Z22, KP2013Z24, KP2013Z26, KP2013Z27, KP2013Z28, KP2013Z30, KP2013Z31, KP2013Z33, KP2013Z38, KP2013Z39, KP2013Z44, KP2013Z48, KP2015Z01, KP2015Z02, KP2015Z03, PIG201504, KP2015Z05, KP2015Z06, KP2015Z07, KP2015Z08, KP2015Z09, KP2015Z10, KP2015Z11, KP2015Z12, KP2015Z13, KP2015Z14, KP2015Z15, KP2015Z16, KP2015Z17	19
2016	STs, ST45, ST1563	15
2016	ST14, ST39, ST2958, ST2959	16
2017	ST11, ST106, ST235, ST258, ST263, ST270, ST1102, ST1863	13

Antibiotic Resistant of *Klebsiella pneumoniae* on pigs

Many antibiotics are typically overused and unreasonable for multi-infection (22) care clinics, raising the antibiotic resistance and multi-pharmaceutical resistance selectives. Antimicrobial drugs are widely used to treat diseases and to promote animal growth in modern livestock systems, which has led to a climate that increases antibiotic resistance. In large pig farms in China, widespread use and misuse of antimicrobials, which explains the greater prevalence of antibiotic resistance in the strain of *pneumoniae* isolated from pigs, are popular. Some newly synthesised costly antibiotics in animal husbands are seldom used and therefore bacteria are less drug resistant than conventional antibiotics. The treatment of animal infections is rarely used, for instance, with GAT, IMP or MEM (23).

Study conducted by Yang, the highest multi-drug resistance (MDR) rates were found among the *Klebsiella pneumoniae* strains from swine (47 isolates), reaching a value of 93.6%, *Klebsiella pneumoniae* in pigs was resistant to the AK antibiotic class 76.6%, AMP 85.1%, AMC 63.8%, AZM 44.7%, CAZ 53.2%, CTX 55.3%, CLI 74.5%, CIP 87.2%, ERY 66.0%, GAT 23.4%, IMP 4.3%, KAN 78.7%, MEM 2.1%, TCY 74.5%, VAN 10.6%, and MDR 93.6%, Yang found that most of the *Klebsiella pneumoniae*

isolates from animals were susceptible to GAT, IMP and MEM, and similar findings revealed that all *Klebsiella pneumoniae* isolates from food animals were susceptible to IMP and MEM (13, 24). In addition, multiresistant strains increase the risk of infection caused by treatment failure in humans and animals. Multiresistant *Klebsiella pneumoniae* isolates have emerged in many countries, including Northwestern Iran, Turkey, Australia and China (25-27). In Founou's study, ESBL-producing *Klebsiella pneumoniae* taken from pig isolates in Cameroon were resistant to AMP, CXM, CTX, CAZ, GEN, TMP / SXT antibiotics. *Klebsiella pneumoniae* isolate was found to be resistant to ampicillin, cefuroxime, cefuroxime-axetil, cefotaxime, ceftazidime and trimethoprim-sulfamethoxazole and not resistant to the antibiotic fosfomycin. This Cameroonian study also reported that all *Klebsiella pneumoniae* isolated from pigs and humans showed reduced susceptibility to amino penicillin, cephalosporins and trimethoprim (16).

Founou studies of the *fosA* chromosome gene have been reported to have shown several gram-negative studies that are widely used in Europe and Africa for the uncomplicated treatment of the urinary tract infection (28). This provides new knowledge globally as a therapeutic option for treating infection caused by

carbapenem-resistant enterobacteriaceae. The Kieffers analysis showed 17 isolates of the 100 Swab rectal isolates on Portuguese farms were positive and were immune to various antibiotics, including colistin and penicillin, for the use of *Klebsiella pneumoniae*. Amoxicillin (AMX) and tetracycline (TET) were resistant to sulfamethoxazole / trimethoprim (SXT), tobramycin (TMN), chloramphenicol (CHL) and sulfonamide (SUL) (15).

The results of research in Malaysia on *Klebsiella pneumoniae* in pigs were found to be resistant to several antibiotics including: ciprofloxacin, aztreonam, ampicillin, tazobactam, amikacin, nalidixic acid, imipenem, ceftazidime, colistin, tetracycline, cefotaxime, amoxicillin-clavulanate, cefixime. In that study, the highest level of antimicrobial resistance to tetracycline antibiotics. *Klebsiella pneumoniae* species are intrinsically resistant to penicillin and can acquire resistance to third and fourth generation cephalosporins by producing ESBLs. Most strains of both isolates from swine and humans were resistant to at least one non- β -lactam antibiotic (tetracycline and gentamicin), which is used for the treatment of prophylactic disease and therapy in food-producing animals. There were found 22 MDR strains which showed resistance to more than three categories of antibiotics (19). All strains from the agricultural environment and pigs show resistance to tetracyclines, which are widely used in feed supplements (30).

***Klebsiella pneumoniae* virulence genes on pigs**

Klebsiella pneumoniae has a pathogenicity due to a variety of virulence factors (including the development of capsule, hypermucoviscosity, lipopolysaccharide, iron acquisition system) all of which contribute to the overcoming of the mammalian hosts' innate immunity and the maintenance of infection in this host (31). The hypermucoviscous strain of *Klebsiella pneumoniae* is considered to be a hypervirulent strain. This strain's molecular identity is correlated with the existence of RmpA and MagA genes. RmpA is a mucoid phenotype A gene plasmid controlling gene, a regulator of polysaccharide extracapsular synthesis (32). MagA is a gene encoded in chromosomal hypermucoviscosity, encoded with the K1 serotype. While most of the *Klebsiella pneumoniae* strains have magA, some MagA negative strains that carry the RmpA gene also have this phenotype. HMV (31.9%) were *Klebsiella pneumoniae* (33). In Yang's research, 47 pig isolates, namely magA (6.4%), rmpA (12.8%), mrkD, fimH-1, were taken from the virulence gene ownership of *Klebsiella pneumoniae* (89.0%) (95%), inB (100%) (13).

Genes mediated the antibiotic resistance of *Klebsiella pneumoniae* in pigs

Klebsiella pneumoniae is a bacterium that produces ESBL (34). This enzyme can hydrolyze the β -lactam ring from antibiotics so that antibiotic resistance can occur (35). *Klebsiella pneumoniae* has been confirmed to be able to fight many antibiotics, especially the third generation cephalosporins such as Cefotaxim, Ceftriaxone and Ceftazidime (36). Commonly used treatments for *Klebsiella pneumoniae* infection include β -lactam antibiotics such as cephalosporins and carbapenems, aminoglycosides such as Gentamicin and Quinolones. However, this therapy was not effective against *Klebsiella pneumoniae*, which has a resistance gene to this antibiotic (37). *Klebsiella pneumoniae* is highly resistant to many antibiotics and has many determinants of resistance such as β -lactamase or ESBL, including TEM, SHV, CTX-M and type GES (19).

In Yang's study, 21 isolates from pigs (44.7%) strains of *Klebsiella pneumoniae* produced ESBL and resistance genes *Klebsiella pneumoniae* blaKPC (51.1%), blaNDM (2.1%), blaSHV (14.9%), blaTEM (29.8%), qnrA (61.7%), qnrB (40.4%), tolC (74.5%) (13). Study conducted by Fonou et al., in Cameroon with porcine isolates, it was obtained ESBL-producing *Klebsiella pneumoniae* with resistance genes: strA, strB, blaTEM-116, blaSHV-28, blaCTX-M-15, oqxA, oqxB, QnrB1, fosA, sul1, sul2, tet (A), dfrA15, aac 3-IIa, aadA1, blaTEM-1B, blaSHV-27, blaSCO-1, fosA, mph (A), catA113 (16). All isolates contained genes that were resistant to sulfonamides (sul1), fosfomycin (fosA) and quinolones (oqxA and oqxB). Various determinants of β -lactamase coding were detected with blaCTX-M-15, blaTEM-1B and blaSCO-1 being the most common. Likewise, the dfrA15 gene which is responsible for trimethoprim resistance, encodes strA and strB for aminoglycoside resistance, as does the tet (A) gene which is responsible for tetracycline resistance. None of the *Klebsiella pneumoniae* isolates contained the virulence gene (16).

This resistance phenotype was confirmed by the identification of the CTX-M-15, SHV-28, and TEM-116 genes by WGS which was also explained by various determinants of resistance to non- β -lactam antibiotics, especially aminoglycoside resistant genes (strA, strB), genes plasmid-mediated quinolone resistance (QnrB1, oqxA, oqxB), phosphomycin (fosA) resistance genes and sulfonamide resistance genes (sul1 and sul2) which were not phenotypically proven. Detection of CTX-M-15 is consistent with multicentre studies conducted in five African and two Vietnamese cities where it was detected in 74% of isolates and was the dominant ESBL among African isolates. This study further reports the predominance of the determinant QnrB among African strains (17). The CTX-M-15 gene is currently the most widely distributed CTX-M enzyme worldwide (16).

Furthermore, the wide-ranging distributions of the fosA gene in Fonou's analysis indicate that the gene can be used as a reservoir for this gene and can easily be transmitted to phosphA-depleted organisms such as *E. Coli* (16). Although it is difficult to bring these results into perspective because of molecular epidemiological studies scarce in Africa, these findings are consistent in several studies from Asia (38-40) and European countries showing several ESBL-*E. coli*-production fosA lines (41). The interest in the reuse of old antibiotics must therefore be carefully taken into consideration and given current genes of ambient resistance (16).

Research conducted by Kieffer was stated that out of 100 swab rectal isolates in Portuguese farms, 17 isolates tested positive for *Klebsiella pneumoniae* which had the mcr-1 gene. Among these positive isolates, 10 exhibited the ESBL phenotype. Sequencing revealed that all mcr-positive isolates had genes that were 100% identical to mcr-1. All MCR-1 producing isolates had the blaTEM-1 gene and all ESBL producers had the blaCTX-M-2 gene. Among the chloramphenicol resistant isolates, positive for the floR resistance gene (15).

In Malaysia, research on the *Klebsiella pneumoniae* bacteria was also carried out in pigs that have antibiotic-resistant genes, including: SHV-61, SHV-12, SHV-11, TEM-1, CTXM-15, CTX-M-2 and CTX-M-1. In this study, TEM was the most common β -lactamase enzyme detected on 15/18 ESBL producing strains of *Klebsiella pneumoniae*, all of which were identified as TEM-119. TEM-1 hydrolyzes penicillin and initial cephalosporins and is known as class

2b b-lactamase but is unable to significantly hydrolyze broad-spectrum cephalosporins or aztreonam (42). Members of the betalactamase family of TEM, SHV and CTX-M are found in Enterobacteriaceae; MDR *Klebsiella pneumoniae*, which produces ESBL, contains mostly TEM, SHV and types CTX-M (43). beta-lactamase type CTX-M has been reported as the dominant gene coding for ESBL, and other ESBLs such as SHV and TEM have also been reported in many countries (44). Study done by Mobasser found that SHV was a common ESBL enzyme among *Klebsiella pneumoniae* strains, detected in 15/18 ESBL-producing *K. pneumoniae* strains and identified as SHV-11, SHV-12, and SHV-61. SHV-11 and SHV-61 are known as class 2b blactamases, whereas SHV-12 is known as ESBL (class 2b b-lactamase) enzymes (19, 42).

The CTX-M-1 group was detected in 7/18 of the ESBL-producing strains, which were identified as CTX-M-1 and CTX-M-15. The CTX-M-2 group was found in two strains of *Klebsiella pneumoniae* isolated from pigs and the environment. CTX-M-1, CTX-M-3, CTX-M-14, CTX-M-24 and CTX-M-32 are the most common CTX-M type ESBLs in pigs (19). CTX-M appears to be the dominant ESBL enzyme worldwide (42). The CTX-M-15 gene is one of the most common ESBL CTX-M types among the Enterobacteriaceae family. Nosocomial infections caused by *Klebsiella pneumoniae* producing CTX-M-15 have dramatically increased in recent years (45). In Asian countries, CTX-M-15 is the main ESBL enzyme reported (46). Carbapenemase-producing *Klebsiella pneumoniae* strains are reported in pig farms in Germany and elsewhere around the world (47-49).

Case of antibiotic resistant *Klebsiella pneumoniae* in another animal

Yang's studies find that resistant isolates of pigs and chickens have a greater prevalence of than resistant isolates of cattle and sheep among animal isolates. Ciprofloxacin (13) has been found to be of highest resistance among chicken and pig isolates (82.2 and 87.2 per cent). Quinolones are commonly available antimicrobial agents which have been commonly used in food processing in China, including chicken and pork (50). There are some data showing that 80.0 percent of chicken isolates are ciprofloxacin resistant (51). In *Klebsiella pneumoniae*, the most frequent ST was ST11, which was commonly found in isolates from five hosts, one of which was pigs in people (34.6%), pigs (36.2%), chickens (15.6%), bovine (28.0%) and sheep (30.0%). Also common STs of *K* are ST235 and ST258. *Pneumoniae* isolated from humans (46.2%), pigs (42.6%) and chicken (57.8%) (13%). Effendi has researched to find 10 positive isolates of *Klebsiella pneumoniae* from rectal swabs of milk cows, beef cattle, broiler chickens and tilapia for *Klebsiella pneumoniae*, and has found positive Bacteria from *Klebsiella pneumoniae* in 45 animals. The rectal swab samples showed 20% (4/20) of *Klebsiella pneumoniae* bacterial animal beef, 40% (2/5), 10% (1/10) of broiler chicken and 30% (3/10) of tilapia in the rectal Swab. The resistance to LMA was present in 90 percent (9/10) and sensibility to other antibiotics was shown for all *Klebsiella pneumoniae* isolates. The results of the examination of DNA extraction of samples using an electrophoresis of agarosis gel have revealed that the BlaTEM-F and blaTEM-R primers have been successfully amplified. Nine (90 per cent) samples from the 10 PCR samples tested for the blaTEM gene (52).

Study conducted by Ahmed and Shimamoto, the blaTEM gene as the coding for antimicrobial resistance was found

as many as 23 isolates (20.5%) from 34 isolates of gram-negative bacteria, including mastitis cases in cattle in Egypt and *Klebsiella pneumoniae* bacteria found as many as 7 blaTEM genes. isolates or 6.3% of the total sample obtained. Most of the ESBL originates from the TEM type enzyme encoded by the blaTEM gene. The blaTEM gene is the most frequently detected gene for antibiotic resistance in plasmids in the clinical population of gram-negative microorganisms (53).

Relation to strains of *Klebsiella pneumoniae* in humans and animals

Klebsiella pneumoniae, provided by ESBL, goes beyond health to a broad range of ecological niches, including poultry, food products, soils and wastewater. ESBL-produced *Klebsiella pneumoniae* can in reality be colonised or infected by human beings when in contact with ESBL-carrying ELD blood, saliva, faeces and urine or if contaminated water or food products are consumed (54). In *Klebsiella pneumoniae*, the most frequent ST was ST11, which was commonly found in isolates from five hosts, one of which was pigs in people (34.6%), pigs (36.2%), chickens (15.6%), bovine (28.0%) and sheep (30.0%). ST235, ST258 and *Klebsiella pneumoniae* were typical human isolated ST strains (46.2%), pigs (42.6%) and chicken strains (57.8%) (16). (16).

The numbers of studies have isolated MDR *Klebsiella pneumoniae* from a range of animals and people (24,55) but few studies have assessed the molecular relationship of livestock infected *Klebsiella pneumoniae* isolates (49). Research carried out by Yang raises the likelihood of this multiresistant strain being transmitted between humans and animals. The survey also documented the molecular characterization and antimicrobially resistant *Klebsiella pneumoniae* strain in Henan, China. Resulted from his study, many strains of *Klebsiella pneumoniae* of different origin had the same molecule type and similar phenotypes, with high incidences of multiresistant pneumonia between humans and various animals. These strains may possibly have been transmitted between humans and animals (13).

A common ST MDR mainly found in Asia and South American 56, the *Klebsiella pneumoniae* strain ST11, is the primary ST in hospitals and veterinarian clinics in China (57). 56 These findings are consistent with Yang's survey showing that ST11 is a human and cattle isolate for *Klebsiella pneumoniae* that indicates that Str11 can spread between humans and livestock. ST11 *Klebsiella pneumoniae* in addition, ST235 and ST258 were identified in human isolates, pigs and chickens, suggesting that these STs can be associated with transmission from humans to animals. Correlation study of the STs, genes for pharmaceutical resistance, virulence genes and phenotypic features showed a large correlation between different types of molecules with multiple resistance or virulence genes (13).

In a study in Cameroon with pig and human isolates, it was shown that the *Klebsiella pneumoniae* strains were overlapping and interrelated between pig and human sources in and across the abattoir (Figure 1). Specifically, the *Klebsiella pneumoniae* ST14 strain colonized human and swine nares located at two different slaughterhouses (SH001 and SH003) whereas *Klebsiella pneumoniae* ST39 was detected in the nose of the pigs and hands of workers present in the same abattoir, SH002 (Figure 1). This can be related to neglected hygiene and sanitation practices that apply during the production, transportation, storage and / or retail stages. Fonou also reported that *Klebsiella*

pneumoniae isolated from humans has also shown reduced susceptibility to amino penicillin, cephalosporins and trimethoprim (16).

The ST14 and ST39 clonal lineages are the leading causes of nosocomial infection and outbreak situations worldwide, although their evolutionary emergence is somewhat less documented in developing countries. In fact, *Klebsiella pneumoniae* ST14 producing OXA-181 was detected in South Africa where it was responsible for outbreaks among tertiary hospital-treated patients (58), whereas *Klebsiella pneumoniae* was multi-drug resistance biofilm that was resistant to multiple drugs and biofilms. The *Klebsiella pneumoniae* strain belonging to ST14 was detected in India also in tertiary care (59). Likewise,

Klebsiella pneumoniae ST39 was responsible for the outbreak in a children's hospital in Algeria (60).

The emergence of this ESBL-producing *Klebsiella pneumoniae* in exposed pigs and workers in and between slaughterhouses in Cameroon is particularly important as it confirms the spread of their active clones by direct contact, and indicates their indirect spread across the food chain in the country. These findings further demonstrate that pigs, pigs and slaughterhouse workers represent a potential reservoir and source of ESBL-producing *Klebsiella pneumoniae* infection in Cameroon and reinforce the importance of implementing appropriate food safety measures and promoting rational antibiotic use (16).

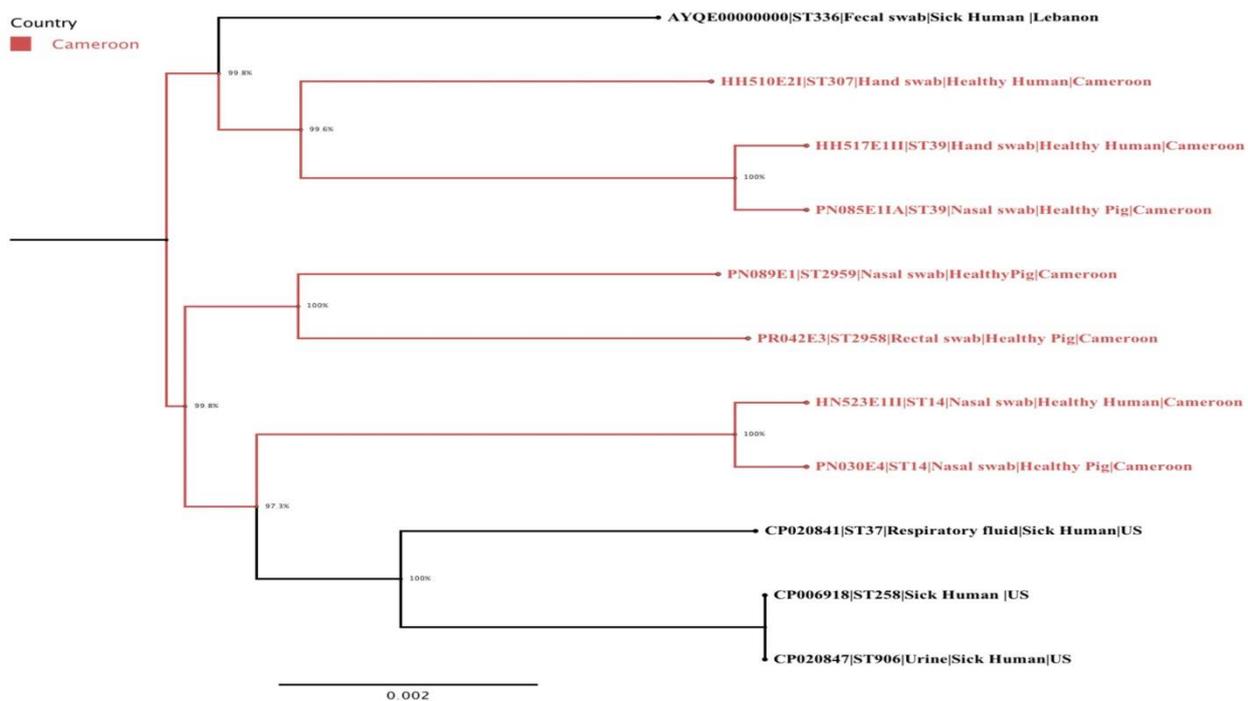


Figure 1. Overlapping and interrelated *Klebsiella pneumoniae* between pig and human sources in and across slaughterhouses in Cameroon (16).

In 2017, it was also reported that *Klebsiella pneumoniae* was found in pigs that have strains similar to *Klebsiella pneumoniae* in humans, namely in a study conducted by Kieffer, *Klebsiella pneumoniae* strains in pigs were found, namely STs, ST45 and ST1563 where The strain is the same as the *Klebsiella pneumoniae* strain in humans (15). In the Mobaseri study also stated that there was an association between *Klebsiella pneumoniae* isolates in pigs and *Klebsiella pneumoniae* isolates in humans, most of the strains of both isolates from pigs and humans were resistant to at least one non-b-lactam antibiotic such as tetracycline and gentamicin, which were used for treatment prophylactic disease and therapy in food-producing animals. There were 22 MDR strains in this study, which showed resistance to more than three categories of antibiotics (19).

Control and Prevention

Basic indications for the use of antibiotics can be classified into antibiotics for definitive therapy, empirical therapy and prophylactic therapy. Therapy is definitively only used to treat bacterial infections. To find out whether the infection is caused by bacteria, you can do a bacterial culture, sensitivity test, serological test, or other test.

Based on available reports, an antibiotic with a narrow spectrum, low toxicity, affordable price and highest effectiveness should be prescribed in definitive therapy. In empirical therapy, antibiotics are given in cases of infection with unknown germs such as in emergency cases due to sepsis, immunocompromised patients and so on. Antibiotic therapy in this case was given based on existing germ epidemiological data. While prophylactic therapy is antibiotic therapy that is given for prevention in patients who are prone to infection. The antibiotics given are narrow spectrum and specific (61). Antibiotic resistance occurs when microorganisms undergo changes causing the drugs given with the aim of curing infections by microorganisms to become ineffective. This is a serious concern because it can cause death, spread, and impose huge costs on individuals and society (62).

The use of antibiotics wisely is closely related to the use of narrow spectrum antibiotics with the right indication, adequate doses, and not longer than needed. Many studies have reported the occurrence of antibiotic resistance problems due to inaccurate use of antibiotics in the veterinary field, such as in livestock (63-68), pets (69-73), poultry (74-76), and fisheries (77-79), as well as those

isolated from animal products (80, 81). Therefore, to prevent further transmission of *Klebsiella pneumoniae* between humans and animals, strict infection control measures, such as the rational application of antibiotics in clinical and livestock settings, routine disinfection of the livestock environment, reduction of human-animal contact and screening of drugs are necessary. more effective, must be implemented. Prudent use of antimicrobials in human and livestock clinical therapy as well as control measures for transmission of *Klebsiella pneumoniae* between humans and animals is also needed (13), as well as increasing public awareness of the dangers of AMR transmission (82).

The isolation of this *Klebsiella pneumoniae* strain always urges the adoption of strict infection and control measures and constant surveillance of antibiotic resistance in the hospital. Similar rigorous interventions must be made in the food production industry if we are to successfully contain the spread of their clones in the food chain (16).

CONCLUSION

ESBL-producing *Klebsiella pneumoniae* can actively spread to pigs, other animals and humans worldwide and may be underestimated given the absence of molecular epidemiological studies. This underscores the potential negligible food safety and public health threats associated with resistant strains in various countries especially if they spread to susceptible persons such as immunocompromised. In general, *Klebsiella pneumoniae* producing MDR and ESBL is becoming a serious problem in humans and animals, increasing resistance to most of the available antibiotics. *Klebsiella pneumoniae* is a bacterium that is commonly found as multidrug resistant and several strains of *Klebsiella pneumoniae* are ESBL producers. All ESBL producers carry ESBL coding genes such as blaSHV, blaCTX-M, blaTEM as well as other antibiotic coding genes that have been summarized in this journal. This ESBL-producing *Klebsiella pneumoniae* strain causes resistance to several antibiotics such as aminoglycosides and trimethoprim and various other antibiotics that have been described in this journal.

Control and prevention are needed to prevent further transmission of *Klebsiella pneumoniae* between humans and animals, strict infection control measures, such as the rational application of antibiotics in clinical and livestock settings, routine disinfection of the farm environment, reduced human-animal contact and drug screening which is more effective, must be implemented. Therefore, the prudent use of antimicrobials in human clinical therapy and animal production as well as control measures for transmission of *Klebsiella pneumoniae* between humans and animals is also needed.

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