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Review

Mobile Colistin Resistance Genes in Africa: A One Health Narrative Review of Reservoirs, Drivers, Transmission Pathways, and Knowledge Gaps

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Abstract

Background/Objectives: Colistin has re-emerged as a critical last-resort antimicrobial for treating infections caused by multidrug-resistant Gram-negative bacteria. The discovery of plasmid-mediated mobile colistin resistance (mcr) genes in 2015 fundamentally changed the understanding of colistin resistance by demonstrating its capacity for horizontal transfer across bacterial species, hosts, and environments. Since then, increasing evidence has documented the widespread occurrence of mcr genes across Africa, threatening the long-term effectiveness of colistin. Earlier reviews have largely addressed single sectors or regions; here, we integrate all sectors, distinguish direct detection from inferred transmission, and propose prioritised actions. **Methods:** This narrative review synthesises current evidence on mobile colistin resistance in Africa through a One Health lens, integrating findings from human, animal, food, wildlife, and environmental sectors. **Results:** We provide a comprehensive overview of the molecular mechanisms, epidemiology, transmission pathways, and drivers of *mcr* dissemination across the continent. Available evidence indicates that *mcr* genes, particularly mcr-1, are distributed among clinical isolates, livestock, retail food products, wastewater, surface waters, agricultural soils, and wild birds, which is consistent with connected transmission across sectors. Key drivers include inappropriate antimicrobial use, livestock intensification, inadequate wastewater treatment, environmental contamination, climate change, and human and animal mobility. **Conclusions:** The frequent association of mcr genes with mobile genetic elements and other antimicrobial resistance

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determinants facilitates their persistence through horizontal gene transfer and co-selection. Despite increasing recognition of this threat, major gaps remain in surveillance, genomic characterisation, environmental monitoring, and understanding of transmission dynamics. Addressing these challenges will require stronger One Health surveillance, antimicrobial stewardship, genomic monitoring, improved environmental management, and coordinated policy interventions to mitigate the spread of mobile colistin resistance and preserve the clinical utility of colistin across Africa.

Keywords: Public health; *mcr* genes; antimicrobial resistance; One Health; low- and middle-income countries; plasmid-mediated resistance; environmental reservoirs; antimicrobial stewardship

1. Introduction

Colistin (polymyxin E) has re-emerged as a critical last-resort antimicrobial for treating infections caused by multidrug-resistant Gram-negative bacteria. For decades, its clinical utility was limited by nephrotoxicity and neurotoxicity [1,2], and its use was largely abandoned in favour of safer antibiotics. However, the late 1990s and early 2000s saw a rise and global spread of multidrug-resistant Gram-negative bacteria, especially carbapenem-resistant Enterobacterales (such as *Klebsiella pneumoniae* [3]) and non-fermenting Gram-negative bacilli of the order Pseudomonadales, namely *Acinetobacter baumannii* (family Moraxellaceae) [4] and *Pseudomonas aeruginosa* (family Pseudomonadaceae), prompting the restoration of colistin in human medicine as a last-resort treatment option [5,6]. Following its reintroduction, colistin resistance was thought to be mediated only by chromosomal mutations, which were passed down vertically (from parent cell to daughter cells), until 2015, when the *mcr-1* gene was identified during a routine surveillance project on antimicrobial resistance in commensal *E. coli* from food animals (pigs and chickens), as well as from human patients, in China [7]. Identifying *mcr-1* on a plasmid fundamentally changed our understanding of colistin resistance, clarifying its horizontal transfer between bacterial species, hosts, and ecosystems and enabling its rapid global spread.

In Africa, the emergence of mobile colistin resistance presents a particularly complex challenge, making the continent a unique and understudied hotspot. Most African countries are characterised by heterogeneous antimicrobial-use practices, limited regulatory enforcement, expanding food-animal production systems, and widespread environmental contamination arising from inadequate wastewater and waste management infrastructure [8]. These conditions create favourable ecological conditions for the selection, persistence and dissemination of *mcr*-harbouring bacteria. Thus, evidence increasingly shows that mobile colistin resistance in Africa is not confined to clinical settings but spans human [9], animal, and food [10] environments, with the environment playing a significant role as a reservoir and transmission route [9].

Several reviews have addressed colistin resistance and *mcr* genes. Global syntheses describe the molecular epidemiology of *mcr-1* to *mcr-9* [11], the global burden of mobilised colistin resistance [12], and the genomic distribution of *mcr*-carrying bacteria [13], while mechanism-focused reviews cover polymyxin resistance encoded by plasmids and chromosomes [14–16]. Africa-focused syntheses include systematic or scoping reviews of the molecular mechanisms of colistin resistance on the continent [17,18], of colistin-resistant Enterobacteriaceae and *K. pneumoniae* in clinical samples [19,20], and of colistin resistance in Egypt [21], as well as sector-specific reviews of *mcr* in African livestock and poultry [22,23] and of environmental mediation of colistin resistance [9], and One Health reviews of antimicrobial resistance in Africa [24] and of plasmid-mediated *mcr-1* across clinical, agricultural

and environmental ecosystems [25]. Most of these works focus on one sector (clinical, livestock or environmental), one country or one methodological lens. The present review differs in four ways: (i) it integrates human, food-animal, food-chain, environmental and wildlife evidence for Africa in a single framework; (ii) it separates direct detections of *mcr* from transmission links that are only inferred, and words each claim accordingly; (iii) it defines the terms used to describe reservoirs, drivers and transmission pathways and includes the most recently described variants (*mcr-9* to *mcr-12*); and (iv) it converts the knowledge gaps into prioritised, pathway-linked intervention actions Table 2, recognising that evidence for the effectiveness of interventions in Africa is still limited.

This review synthesises current evidence on mobile colistin resistance in Africa through a One Health lens, integrating data from human health, food-animal production, and environmental studies. By examining molecular mechanisms, epidemiology, transmission pathways, and drivers of emergence, we highlight critical knowledge gaps and propose surveillance, policy, and intervention priorities to preserve colistin's efficacy and mitigate the broader antimicrobial resistance crisis within and beyond the continent.

To avoid ambiguity, the following terms are used consistently. *mcr* (italic) denotes the genes, and MCR-1 to MCR-10 the phosphoethanolamine transferases they encode (not to be confused with methyl-coenzyme M reductase); "mobile colistin resistance" denotes the resistance phenomenon mediated by these genes. A reservoir is a host or habitat (humans, food-producing animals, food products, the environment, wild birds) in which *mcr*-bearing bacteria have been detected. A driver is a factor that promotes the emergence, selection or spread of *mcr*-bearing bacteria (for example, antimicrobial use, co-selection, weak infrastructure, climate change, or mobility). Amplification means an increase in the abundance of *mcr*-bearing bacteria or plasmids within a reservoir, and selection is the antimicrobial pressure that favours them. A transmission pathway is a route by which *mcr*-bearing bacteria or plasmids move between reservoirs, and an interface is a point at which two sectors come into contact. We avoid the terms node, hub and engine. Claims are worded as "detected" when an *mcr* gene or protein has been identified in the sector in question, and as "may", "plausible" or "probable" when a link is inferred from co-occurrence, shared mobile elements or ecological reasoning.

2. Molecular Basis of Mobile Colistin Resistance

2.1. General Mode of Action

Colistin, a polypeptide antibiotic from the polymyxin class (specifically polymyxin E), was first isolated in 1947 by Koyama from cultures of *Paenibacillus polymyxa* subsp.colistinus [10]. It acts as a narrow-spectrum bactericidal agent that targets most Gram-negative bacteria. However, it is ineffective against Gram-positive bacteria, anaerobes, and mycoplasmas [14]. Polymyxins primarily target lipopolysaccharide (LPS) in the outer membrane of Gram-negative bacteria [15]. The lipid A portion of LPS is negatively charged and stabilised by divalent cations, mainly Mg^{2+} and Ca^{2+}, which help maintain membrane integrity [26]. As a positively charged molecule, colistin binds to LPS and displaces these cations, destabilising the outer membrane and promoting LPS release. Colistin enters the outer membrane via its lipophilic fatty-acyl chain, increasing membrane permeability and enabling insertion toward the inner membrane. It then disrupts the inner membrane by compromising the phospholipid bilayer, leading to membrane lysis, leakage of intracellular contents, and bacterial death [27]. This mechanism is widely regarded as the primary explanation for colistin's antibacterial activity; however, the exact processes that ultimately lead to bacterial cell death remain incompletely understood. Figure 1 presents a schematic overview of the sequential steps involved in colistin-mediated membrane disruption. Additional mechanisms have also been proposed, including vesicle-to-vesicle contact. Once colistin

passes through the outer membrane, lipids can be exchanged between the inner and outer membranes, triggering membrane remodelling and phospholipid loss. These changes create an osmotic imbalance that ultimately lyses the bacterial cell [28].

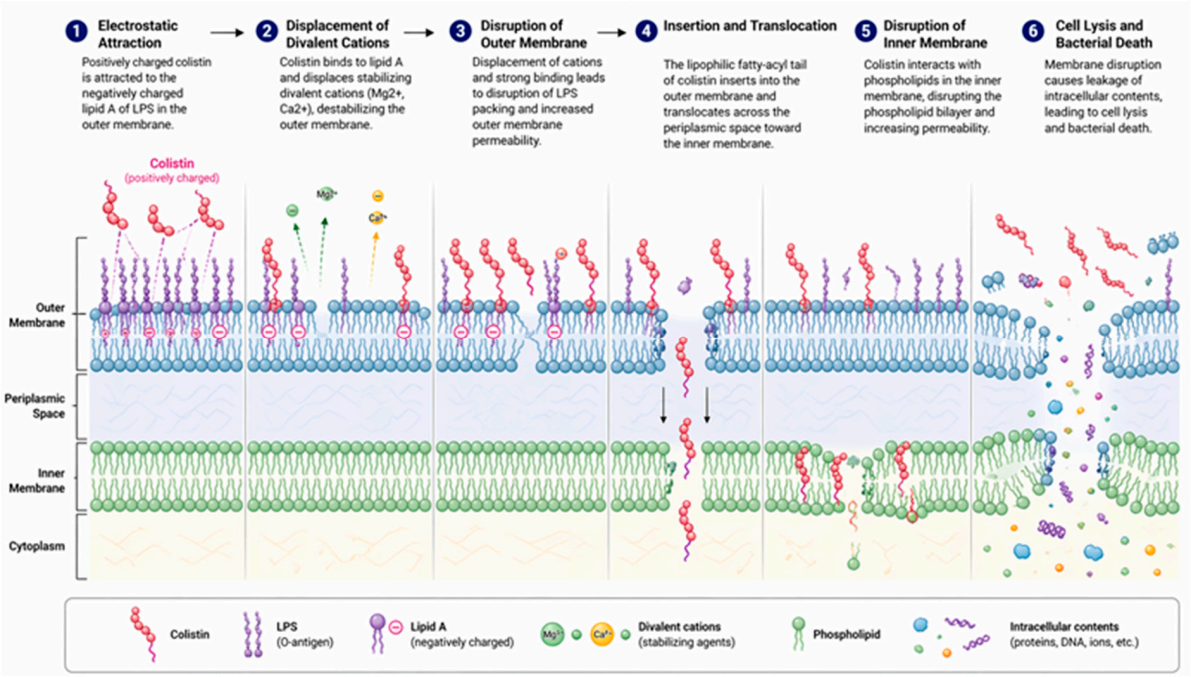


Figure 1. Schematic representation of the general mode of action of colistin (polymyxin E) against Gram-negative bacteria.

Despite colistin's potent membrane-disrupting activity, resistance has emerged as a significant global concern. Colistin resistance can arise through chromosomal mutations and horizontally acquired mobile genetic elements (MGEs) carrying colistin resistance genes, with the latter posing a greater threat because they can disseminate rapidly [14,16,29]. The primary mechanism underlying resistance involves modification of the lipid A component of LPS, which reduces its net negative charge and consequently diminishes the electrostatic interaction with colistin [15,30].

2.2. Chromosomal Mechanisms of Resistance

Chromosomal resistance to colistin is primarily mediated by mutations in two-component regulatory systems, notably PmrA/PmrB and PhoP/PhoQ, which regulate genes involved in LPS modification [31]. These systems are activated by environmental stimuli, such as low Mg^{2+} concentrations, acidic pH, or exposure to antimicrobial peptides, upregulating operons including pmrCAB and arnBCADTEF, which are responsible for lipid A remodelling. Upregulation of these operons adds phosphoethanolamine (pEtN) and 4-amino-4-deoxy-L-arabinose (L-Ara4N) to lipid A, thereby reducing its net negative charge and weakening colistin binding affinity [32,33].

Additionally, cross-regulation between PhoP/PhoQ and PmrA/PmrB via connector proteins such as PmrD further enhances lipid A modification pathways, amplifying resistance phenotypes. Recent genomic and experimental studies show that mutations in these regulatory systems, along with alterations in genes such as mgrB, are central to the development of colistin resistance in clinical isolates [34,35]. In particular, the arnBCADTEF operon has been shown to be essential for the synthesis and transfer of L-Ara4N to lipid A, and these regulatory networks tightly control its expression. Notably, this pathway is not universal: *Acinetobacter baumannii* lacks the arnBCADTEF operon and cannot synthesise

L-Ara4N, so colistin resistance in this species depends exclusively on the addition of pEtN to lipid A (through chromosomal PmrA/PmrB-mediated modification or acquired *mcr* genes) or on complete loss of LPS [33].

In *Klebsiella pneumoniae*, inactivation or mutation of the MgrB protein, a key negative regulator of the PhoP/PhoQ system, is one of the most common mechanisms of chromosomal colistin resistance. Loss-of-function mutations in *mgrB*, frequently caused by insertion sequences, lead to constitutive activation of PhoP/PhoQ signalling and sustained expression of lipid A modification genes [36]. Studies have reported that *mgrB* mutations occur in up to ~65% of colistin-resistant *K. pneumoniae* isolates, highlighting their clinical significance.

Moreover, recent investigations have revealed that chromosomal resistance may also involve mutations affecting lipid A biosynthesis pathways, alterations in membrane composition, and adaptive responses that can impose fitness costs but enhance survival under antibiotic pressure [37]. Unlike plasmid-mediated resistance, these chromosomal mechanisms are generally stable and heritable, but remain restricted to vertical transmission and rarely disseminate beyond clonal expansion, making mcr-mediated resistance substantially more important from a One Health perspective. Nevertheless, their rapid emergence during therapy and frequent association with multidrug-resistant phenotypes underscore their critical clinical importance.

2.3. Mobile Colistin Resistance (mcr) Genes

A breakthrough in understanding colistin resistance was the 2015 discovery of the mobilised colistin resistance (*mcr-1*) gene, the first report of plasmid-mediated colistin resistance, which highlighted the potential for horizontal dissemination of resistance to a last-resort antibiotic [29]. Since this initial report, multiple homologous variants (*mcr-1* to *mcr-10*) have been identified in a wide range of Gram-negative bacteria, including *Escherichia coli*, *K. pneumoniae*, *Salmonella enterica*, and *Acinetobacter* spp., particularly on conjugative plasmids such as IncI2, IncX4, and IncHI2, and often associated with insertion sequences like ISApl1 that facilitate their mobilisation and genetic rearrangement [11,14] (Figure 2(1)). Ongoing genomic surveillance has identified novel variants, including from environmental bacteria outside the Gammaproteobacteria. Recent studies have reported *mcr-11* [38] and *mcr-12* [39] as the latest variants, demonstrating the continuous evolution of mobile colistin resistance. For example, *mcr-12* was first identified in *Pigmentiphaga litoralis*, an environmental betaproteobacterium, illustrating an expanded host range beyond the Gammaproteobacteria; its transfer to *Pseudomonas* spp. and *A. baumannii* (both Gammaproteobacteria) underscores the risk of dissemination back into major clinical pathogens [39].

The *mcr* genes encode membrane-associated phosphoethanolamine transferases, which catalyse the addition of pEtN to the phosphate groups of lipid A, a key component of LPS [15] (Figure 2(2)). Structurally, MCR-1 and related phosphoethanolamine transferases are composed of an N-terminal transmembrane domain (five helices) anchoring the enzyme to the inner membrane and a periplasmic catalytic domain responsible for substrate modification. In the catalytic domain, a Zn^{2+}-dependent active site containing a nucleophilic threonine (Thr285 in MCR-1) transfers pEtN from phosphatidylethanolamine (PE) to lipid A, forming a covalent phosphodiester bond (Figure 2(2,3)). The enzymatic addition of pEtN reduces the net negative charge of lipid A, thereby weakening electrostatic interactions between colistin and the bacterial outer membrane (Figure 2(3)). This mechanism closely mirrors chromosomal resistance pathways but is particularly concerning because it is transferable [14,16].

Importantly, *mcr* genes are predominantly located on conjugative plasmids, which facilitate efficient horizontal gene transfer (HGT) via bacterial conjugation. These plasmids are often associated with insertion sequences, particularly ISApl1, which play a crucial role

in the mobilisation, recombination, and stabilisation of *mcr* genes within diverse genetic contexts [29,40]. In some cases, ISApl1 elements flank the *mcr-1* gene, forming composite transposons that enhance its mobility across plasmids and chromosomes. Conjugation involves plasmid transfer from donor to recipient cells through a conjugative pilus, facilitating spread across species and ecological niches, including clinical, agricultural, and environmental settings (Figure 2(4)).

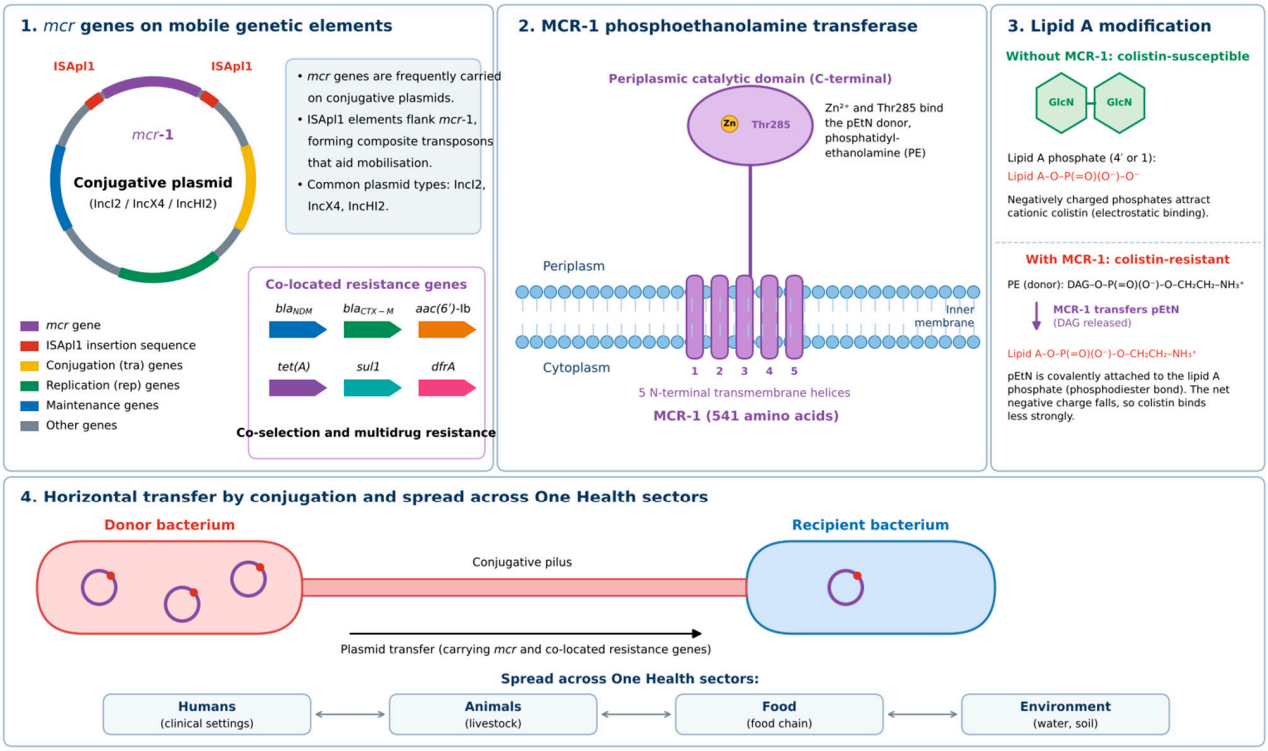


Figure 2. Schematic representation of *mcr*-mediated colistin resistance showing (**1**) plasmid localisation and mobilisation of *mcr* genes, (**2**) domain organisation of the MCR-1 phosphoethanolamine transferase, (**3**) transfer of pEtN from phosphatidylethanolamine (PE) to lipid A, forming a covalent phosphodiester bond that reduces colistin binding, and (**4**) horizontal transfer by conjugation and spread across One Health sectors. DAG, diacylglycerol; GlcN, glucosamine; pEtN, phosphoethanolamine.

Recent genomic surveillance studies show that *mcr* genes frequently coexist with other clinically relevant resistance determinants, including extended-spectrum β-lactamase (ESBL) and carbapenemase genes (e.g., bla_{NDM}, bla_{KPC}), leading to the emergence of multidrug-resistant and potentially pan-drug-resistant strains [12,22]. A critical consequence is that this genetic arrangement creates co-selection, whereby exposure to one antimicrobial class simultaneously selects for resistance to multiple unrelated antibiotics because the resistance genes reside on the same mobile genetic element. Consequently, even if colistin use is substantially reduced or prohibited, continued use of β-lactams, tetracyclines, sulfonamides, fluoroquinolones, or other commonly used antimicrobials can maintain selective pressure favouring the persistence and dissemination of *mcr*-bearing plasmids. In many African settings, where these antimicrobial classes remain widely used in both human medicine and livestock production, co-selection may sustain mobile colistin resistance despite restrictions on colistin itself. Co-selection illustrates why interventions targeting a single antimicrobial are unlikely to eliminate *mcr* genes once they have become established. Instead, containment is likely to require comprehensive antimicrobial stewardship (AMS) that reduces unnecessary use across multiple antibiotic classes, complemented

by integrated surveillance, infection prevention, and environmental management within a One Health framework. Section 6 (Table 2) outlines specific priorities.

From ecological and epidemiological perspectives, the widespread use of colistin in livestock and agriculture has been strongly implicated in the selection and global dissemination of *mcr*-bearing plasmids. These resistance elements have been detected in diverse niches, including food-producing animals, wastewater, soil, and clinical isolates, underscoring the interconnected nature of resistance spread within a One Health framework [11,41]. Furthermore, the widespread distribution and co-localisation of *mcr* genes with other resistance determinants significantly contribute to the emergence of multidrug-resistant strains and pose a major threat to public health. Figure 2 summarises the molecular mechanism and horizontal transfer of mcr-mediated resistance, and Table 1 summarises its distribution in Africa.

Table 1. Decadal summary of mobile colistin resistance reports in Africa across One Health sectors.

Decade	Key Developments	*mcr* Variants Reported	Primary Reservoirs	Country	Key References
2015–2016	First documented cases of chromosomal resistance to colistin	None	Humans (*A. baumannii*)	Algeria	[42,43]
	Emergence of first *mcr-1* in the region (animals, humans, environment); dissemination via IncHI2, IncFIB plasmids	*mcr-1*	Animals (*E. coli*), humans, environment	Tunisia, Algeria, Egypt	[44]
	First report of *mcr-1* in a clinical *E. coli* isolate	*mcr-1*	Humans	Algeria	[45]
	Early detection of *mcr-1* in chickens and humans in North and Southern Africa	*mcr-1*, *mcr-2*	Chickens, cattle, pigs, humans	Algeria, Tunisia, Egypt, South Africa	[26,46,47]
	Travellers carrying *mcr* (Egypt)	*mcr-1*, *mcr-8*	Travelers	Egypt	[48]
2017–2018	One Health stewardship framework for colistin as an antibiotic of last resort in human health (policy response; no *mcr* data)	-	Humans, animals (policy)	South Africa	[49]
	Detection of *mcr-1* in clinical *E. coli* and *K. pneumoniae* from Sudan; comparison of *mcr-1* in human and animal Enterobacteriaceae across countries	*mcr-1*, *mcr-2*	Chickens, cattle, pigs, humans	Algeria, South Africa, Sudan	[50,51]
	Expansion of *mcr-1* in animals and environment; emergence of *mcr-2* and *mcr-8* in *K. pneumoniae*; chromosomal mutations (*mgrB, pmrA/B*)	*mcr-1*, *mcr-2*, *mcr-8*	Animals, humans (*K. pneumoniae, E. coli*), environment	Tunisia, Algeria, Egypt, Libya	[1,52,53]
	mcr-1 and *mcr-3* in soils and waters; *mcr-8* in *K. pneumoniae*	*mcr-1*, *mcr-3*, *mcr-8*	Soils, waters, humans	Algeria, Kenya	[54]
	Detection of *mcr-1* in broiler chickens	*mcr-1*	Chickens	Morocco	[55]

Table 1. *Cont.*

Decade	Key Developments	*mcr* Variants Reported	Primary Reservoirs	Country	Key References
2019–2020	Colistin resistance and *mcr-1*/*mcr-2* screening in ESBL/AmpC-producing *E. coli* from chickens	-	Chickens	Senegal	[56]
	Community transmission (Tanzania, Zanzibar)	*mcr-1*, *mcr-8*	Travelers	Tanzania	[57]
	Increase in human and animal cases; coexistence of plasmid-mediated (*mcr-1, mcr-3, mcr-8*) and chromosomal (*mgrB, pmrA/B*) mechanisms; clonal diversity (ST11, ST405, ST101, etc.)	*mcr-1*, *mcr-3*, *mcr-8*	Humans, animals, environment, food; soils, waters	Algeria, Tunisia, Egypt, Libya, South Africa, Kenya	[26,58–61]
	Diversity of *mcr* (*mcr-1, mcr-5, mcr-8*) in Nigeria; circulation in meat and cheese	*mcr-1*, *mcr-2*, *mcr-5*, *mcr-8*, *mcr-9*	Chickens, pigs, meat, cheese, birds	Nigeria, Egypt, Congo-Brazzaville, Tunisia	[27,62–64]
	New *mcr-3.33–3.37* variants in *Aeromonas*; circulation in wastewater	*mcr-3*, *mcr-5*	Aquatic	South Africa	[65]
	Detection of *mcr-9* in *Enterobacter* in South Africa and Egypt	*mcr-9*	Humans, food	South Africa, Egypt	[66,67]
	Travel and the international food trade identified as routes for the global dissemination of *mcr* genes	*mcr-1* to *mcr-9*	Animals, food, environment, humans, travellers	Africa (North, West, East, South)	[68]
2021–2022	Continental synthesis of the prevalence and traits of *mcr*-harbouring isolates across African ecosystems (systematic review)	*mcr-1* (mainly), *mcr-2*, *mcr-3*, *mcr-5*, *mcr-8*, *mcr-9*	Humans, animals, environment	Africa (North, West, South), global analyses	[69]
	Colistin-resistant *E. coli* harbouring *mcr-1* in raw beef and ready-to-eat beef products	*mcr-1*	Meat	Egypt	[70]
2023–present	Silent (phenotypically undetected) *mcr-9* in ESBL-producing clinical Enterobacteriaceae	*mcr-9*	Humans	Ethiopia	[71]
	Sporadic but persistent reports; growing importance of environments as reservoirs; documentation of new variants (*mcr-3, mcr-5*); integration into One Health surveillance programs	*mcr-1*, *mcr-3*, *mcr-5*	Environment (waters, soils), animals, humans	Algeria, Tunisia, Egypt, Libya, South Africa, Côte d'Ivoire	[32]
	Genomic evidence of *mcr-9* and *mcr-10* in clinical Enterobacterales; *mcr-10.1* among the most frequently deposited African subvariants	*mcr-9*, *mcr-10*	Humans	South Africa, Egypt	[13]

Note: Only variants with published African detections are listed; *mcr*-11 and *mcr*-12, described very recently [38,39], have, to our knowledge, not yet been reported from African isolates, unlike *mcr*-9 and *mcr*-10 (listed in the 2023–present rows).

Although *mcr*-mediated resistance typically confers only moderate increases in colistin minimum inhibitory concentrations, its clinical impact is substantial because it can spread rapidly across bacterial populations. Furthermore, although *mcr-1* remains globally dominant, the emergence of additional variants (e.g., *mcr-3*, *mcr-9*) that differ in expression, regulation, and fitness costs demonstrates ongoing evolutionary diversification and adaptation to different ecological niches. Despite significant advances, research on the regulation, structural diversity, and ecological drivers of *mcr* dissemination remains active.

3. Epidemiology of mcr in Africa: A One Health Overview

3.1. Historical Overview of Colistin Use and the Emergence of Resistance in Africa

Colistin was introduced into clinical practice in the late 1950s and was initially valued for its potent activity against Gram-negative bacteria [14]. However, concerns regarding nephrotoxicity and neurotoxicity led to a marked decline in its use in human medicine by the 1970s, particularly in high-income countries where safer alternatives became available [14]. Consequently, colistin resistance was considered rare and of limited clinical significance, with resistance largely attributed to chromosomal mutations rather than transferable genetic mechanisms [16,72]. However, since the 1990s, colistin use expanded substantially across Africa in food-animal production systems. Intensification of poultry, pig, and cattle farming, often without robust biosecurity and AMS frameworks, was accompanied by increased antimicrobial use (AMU) for therapeutic, metaphylactic, and prophylactic purposes. Thus, although many high-income countries have banned its non-therapeutic use, colistin remained particularly attractive in food animal production and veterinary practice because of its low cost, broad antimicrobial spectrum, and widespread availability, frequently without prescription or regulatory oversight [8,73]. During this period, researchers still widely regarded colistin resistance as non-mobile and underestimated its broader epidemiological implications.

A major paradigm shift occurred in 2015 with the discovery of plasmid-mediated colistin resistance, mediated by the *mcr-1* gene [7]. Importantly, the absence of previously recognised transferable resistance mechanisms had contributed to a false sense of security regarding the long-term sustainability of colistin efficacy. Subsequent investigations revealed that *mcr* genes likely circulated within African ecosystems before their formal identification. Early reports documented *E. coli* harbouring the *mcr-1* gene in food-producing animals, retail meat, and human clinical isolates in countries including South Africa [72], Egypt [70], Tunisia, and Algeria [74]. These findings suggest that prolonged, largely unregulated colistin use in animal agriculture exerted sustained selective pressure, enabling the emergence and silent dissemination of mobile colistin resistance across interconnected reservoirs.

In the years following this discovery, surveillance studies across Africa identified an expanding diversity of *mcr* determinants, including *mcr-1*, *mcr-3*, *mcr-5*, *mcr-8*, and *mcr-9*, in isolates derived from humans, livestock, food products, and environmental sources [9,75]. Of particular concern is the frequent co-localisation of *mcr* genes with ESBL and carbapenemase genes on conjugative plasmids [66]. Co-localisation of *mcr* with these genes facilitates co-selection under antimicrobial pressure and significantly increases the risk of dissemination of multidrug-resistant pathogens.

Environmental investigations have further reshaped understanding of colistin resistance dynamics on the continent. The detection of *mcr* genes in surface waters, wastewater effluents, agricultural soils, and manure-amended fields indicates that environmental matrices are reservoirs of mcr-positive bacteria and plausible routes linking human and animal systems [46,76,77]. In many African settings, inadequate wastewater treatment infrastructure, informal slaughter practices, and the reuse of untreated waste in agriculture may

contribute to the persistence and movement of mobile colistin resistance across interconnected One Health interfaces, although longitudinal evidence is lacking.

In response to these developments and the alarming rise in pan-drug-resistant and extensively drug-resistant bacterial strains, colistin was reclassified as a critically important antimicrobial for human medicine, prompting global calls to restrict its use in animal agriculture [42,78]. However, the recent medically important antimicrobials list has authorised its use in humans and animals [79]. Although several African countries have adopted national action plans aligned with One Health principles, implementation, enforcement, and surveillance coverage remain uneven and often limited in scope [49,80]. The trajectory of colistin resistance in Africa, therefore, reflects not only delayed recognition of mobile resistance mechanisms but also systemic challenges, including weak regulatory frameworks, fragmented surveillance systems, and under-resourced environmental monitoring. Such delayed recognition reflects a broader underestimation of mobile resistance dynamics in low-resource settings, where surveillance gaps allowed critical resistance determinants to disseminate undetected across human, animal, and environmental interfaces. Section 6 (Table 2) sets out the priority interventions that follow from this history.

These developments provide context for the contemporary epidemiology discussed below.

3.2. Human Clinical Settings

Human clinical settings constitute the most extensively investigated reservoir of mobile colistin resistance in Africa, accounting for more than half of the available continental evidence on *mcr* genes [69]. Overall, the prevalence of *mcr* genes among clinical *Enterobacterales* isolates remains relatively low, typically ranging from 1% to 5% in routine hospital surveillance [19,81,82]. However, prevalence increases markedly when investigations focus on phenotypically colistin-resistant isolates, where *mcr* genes have been reported in approximately 31- 45% of isolates [83]. These findings suggest that while plasmid-mediated colistin resistance is not yet widespread across all clinical Gram-negative pathogens, it is strongly associated with established colistin-resistant populations and represents an increasingly important mechanism underlying treatment failure in healthcare settings. Furthermore, the predominance of human-derived reports, which account for more than 58% of all published African data on colistin resistance, reflects the historical emphasis of surveillance programmes on the clinical rather than the environmental or veterinary sectors [17,20].

The epidemiology of mobile colistin resistance in African hospitals is dominated by *E. coli* and *K. pneumoniae*, which together account for most *mcr*-positive clinical isolates [17,20]. In contrast, plasmid-mediated colistin resistance remains uncommon in *P. aeruginosa* and *A. baumannii*, where chromosomal mechanisms more often mediate resistance [69]. These non-Enterobacterales, together with *K. pneumoniae*, are also common isolates from other clinical specimens, such as diabetic foot ulcers [3] and respiratory specimens from patients with chronic obstructive pulmonary disease [84], and *A. baumannii* strains carrying pili-based biofilm genes such as *csu* have been described among multidrug-resistant isolates [4]; colistin remains a last-resort option for such infections, which makes mcr surveillance in these species relevant. Clinical detection also varies by specimen type, with gastrointestinal specimens and stool isolates consistently exhibiting the highest prevalence of *mcr* genes (approximately 42%), reflecting intestinal colonisation as an important reservoir for subsequent transmission [19]. Conversely, bloodstream isolates generally demonstrate substantially lower detection rates (approximately 3.6%), suggesting that invasive infections caused by *mcr*-positive organisms remain comparatively uncommon despite increasing intestinal carriage [19].

Despite several reports on mobile colistin resistance across Africa, regional differences further illustrate the heterogeneous distribution across the continent. North African countries, particularly Egypt, Algeria, and Tunisia, are major hotspots for clinical *mcr-1* dissemination, with reports of isolates frequently co-harbouring clinically important carbapenemase genes such as $bla_{\text{NDM-1}}$ and $bla_{\text{OXA-48}}$ [18,21]. In Southern Africa, South African tertiary hospitals have documented localised outbreaks and high levels of phenotypic colistin resistance, reaching 50.95% in selected healthcare facilities, largely driven by *mcr-1*-positive *K. pneumoniae* carried on highly transmissible IncHI2, IncI2, and IncX4 plasmids [19]. Although reports from West and East Africa remain comparatively limited, increasing surveillance from countries such as Nigeria and Kenya indicates the gradual emergence of *mcr*-mediated resistance within an already expanding multidrug-resistant bacterial landscape [24].

Across African clinical settings, *mcr-1*, particularly the *mcr-1.1* subvariant, remains the predominant *mcr* determinant, accounting for over 80-90% of reported *mcr* genes [9,85]. Its widespread dissemination has been largely attributed to highly transferable IncHI2, IncI2, and IncX4 plasmids, which facilitate HGT among clinically important *Enterobacterales* [17,25,86,87]. Nevertheless, genomic surveillance is revealing increasing genetic diversity. Emerging variants such as *mcr-9* and *mcr-10* have recently been identified in clinical *Enterobacterales*, especially in South Africa and Egypt [13]. Of particular concern is *mcr-9*, which often remains phenotypically silent until activated by specific regulatory mechanisms, allowing it to circulate undetected within healthcare environments [13,71]. Meanwhile, *mcr-10.1* has become one of the most frequently deposited African *mcr* subvariants in global genomic databases, highlighting its increasing epidemiological significance [13]. Other variants, including *mcr-2, mcr-3, mcr-5,* and *mcr-8*, are detected only sporadically in clinical settings and are more commonly associated with environmental or animal reservoirs [64,69].

3.3. Food-Producing Animals

Food-producing animals are increasingly recognised as important reservoirs and potential transmission routes for *mcr* genes [22,43]. Across Africa, rising demand for animal protein and the intensification of livestock production have been associated with increased AMU for treatment, prophylaxis, and productivity enhancement [88]. Evidence from livestock systems, particularly poultry, pigs, and cattle, implicates these sectors in the selection, maintenance, and dissemination of *mcr*-harbouring bacteria, especially where veterinary oversight, antimicrobial regulation, and stewardship remain limited [64,88]. Aquaculture has also been recognised globally as a potential reservoir for colistin-resistance determinants, although Africa-specific data remain comparatively limited [89,90]. Widespread colistin use for therapeutic, prophylactic, and metaphylactic purposes has created favourable conditions for the emergence of resistant bacterial populations in animal gastrointestinal microbiota.

Among livestock-associated bacteria, *E. coli* is the most commonly reported carrier of *mcr* genes, although these determinants have also been detected in *Salmonella*, *Klebsiella*, and other Enterobacterales [91]. Intensive farming environments, characterised by high stocking densities, frequent antimicrobial exposure, and close animal-to-animal contact, can promote the selection and transmission of resistant bacteria [88]. Across Africa, studies have documented *mcr*-positive bacteria in food-animal sectors, particularly poultry, with additional reports from swine and cattle production systems. These reservoirs are particularly important because they provide a continuous source of resistant bacteria that can then spread into food systems, environmental compartments, and human populations.

3.4. Food Chain and Food Products

The food chain represents a critical interface through which colistin-resistant bacteria and *mcr* genes may be transmitted from food-animal reservoirs to human populations. Resistant microorganisms originating from livestock can contaminate animal-derived food products at multiple stages of production, including on-farm production, transport, slaughter, processing, retail distribution, and domestic food preparation [92]. The cumulative effect of these sequential contamination events increases the likelihood that resistant bacteria persist throughout the farm-to-fork continuum, creating opportunities for human exposure through food consumption and handling.

Evidence from Africa supports the persistence of antimicrobial-resistant bacteria throughout food production systems. Farm-to-fork investigations conducted in KwaZulu-Natal, South Africa, demonstrated the persistence of antibiotic-resistant *E. coli* across intensive poultry and pig production chains, including farm, transport, abattoir, and final food-product stages [92,93]. Similarly, metagenomic analyses from poultry production systems in Maputo, Mozambique, revealed that poultry-associated bacterial communities and clinically important antimicrobial resistance genes persisted from farms to live-bird markets and processing environments, identifying open-air markets as important interfaces for the dissemination of antimicrobial resistance [94]. Although these studies did not specifically investigate *mcr* genes, they provide compelling evidence that resistant bacteria and mobile resistance determinants can survive and spread throughout food production systems. Direct evidence of foodborne transmission of mobile colistin resistance has been reported from Egypt, where *mcr-1*-positive *Enterobacterales* have been isolated from retail chicken meat, raw beef, ready-to-eat beef products, and raw-milk cheese [95,96]. These findings indicate that meat, poultry, dairy products, and other animal-derived foods may serve as important vehicles for transmitting *mcr*-harbouring bacteria to consumers. These findings further support evidence from several regions suggesting that *mcr* genes may occur at higher frequencies in food-animal and retail food reservoirs than in human clinical samples, supporting foodborne exposure as an important potential pathway in the epidemiology of colistin resistance [29,97].

The African food system presents several unique factors that may further facilitate the dissemination of mobile colistin resistance. In many low- and middle-income settings, informal slaughter facilities [98], live-animal markets [99], and open-air retail environments [100] operate with limited biosecurity and hygiene controls, thereby increasing the risk of bacterial contamination during slaughter, carcass dressing, and meat handling. Inadequate cold-chain infrastructure and prolonged storage at ambient temperatures may further promote bacterial survival and proliferation before products reach consumers [101]. These risks are amplified in informal food markets, which supply a substantial proportion of animal-source foods in many African countries and often function outside routine microbiological surveillance and regulatory oversight. Consequently, resistant bacteria originating from livestock may enter the food chain long before reaching formal retail systems, allowing resistance determinants to disseminate widely through local food distribution networks.

Consumer practices also significantly shape the extent of foodborne exposure. Consuming contaminated or inadequately cooked meat, cross-contamination of kitchen surfaces and utensils, and poor hand hygiene during food preparation [102] may facilitate colonisation of the human gastrointestinal tract by *mcr*-carrying bacteria. Even without clinical disease, these organisms may establish themselves within the intestinal microbiota, where HGT enables the dissemination of *mcr* genes to commensal and pathogenic bacteria. The widespread consumption of ready-to-eat foods and street-vended meat products in many African urban centres represents an additional, yet poorly studied, exposure pathway. Because these foods are often prepared under variable hygienic conditions and may be

repeatedly handled after cooking, they offer further opportunities for contamination and subsequent transmission of antimicrobial-resistant bacteria.

Overall, the evidence suggests that the food chain is a plausible transmission route (interface) linking livestock production, food processing, retail markets, and human populations, rather than only a passive conduit. While direct evidence of foodborne *mcr* transmission in Africa remains relatively limited, documented *mcr*-positive bacteria in retail food products, combined with evidence of AMR persistence throughout production chains, supports the food system as a plausible component of the African One Health transmission network.

3.5. Environmental Reservoirs

Environmental compartments are important reservoirs of mobile colistin resistance and plausible routes for its movement across One Health systems. Although clinical and agricultural settings often represent identifiable points of antimicrobial selection pressure, environmental reservoirs provide extensive ecological niches in which resistance determinants may persist, accumulate, and move between human, animal, and natural systems. Surface waters, wastewater systems, agricultural soils, irrigation water, and manure-impacted farmlands have all been implicated as reservoirs of colistin-resistant bacteria and/or *mcr* genes in Africa. In South Africa, Snyman et al. reported colistin-resistant Gram-negative bacteria and detected *mcr-3* and *mcr-5* variants in river and stormwater samples from the Western Cape [103], while Igwaran et al. detected *mcr-1* in *E. coli* from final effluents of wastewater treatment plants in the Eastern Cape [76]. In North Africa, Drali et al. detected *mcr-1*-positive multidrug-resistant *E. coli* from seawater along the Algiers coast, and Touati et al. reported colistin-resistant bacteria from Algerian farmlands, including *mcr-1*- and *mcr-3*-positive *E. coli* recovered from agricultural soil, irrigation water, and manure [54,61]. Similarly, Hassen et al. identified ESBL-producing and colistin-resistant Enterobacteriaceae, including isolates carrying *mcr-1*, from a biological industrial wastewater treatment plant in Tunisia [63]. These findings show that African environmental matrices contain mcr-positive bacteria and therefore serve as reservoirs of mobile colistin resistance, particularly where untreated wastewater, animal waste, agricultural runoff, and community contamination intersect.

Anthropogenic activities largely drive the environmental dissemination of antimicrobial resistance. Farmers often apply livestock manure containing resistant bacteria and antimicrobial residues to agricultural land, while inadequately treated municipal and hospital wastewater can release resistant bacteria and resistance determinants into rivers, streams, and other receiving water systems [104–106]. Several African studies support these pathways: in Ghana, antibiotic-resistant *E. coli*, including $bla_{\text{CTX-M}}$-positive isolates, were recovered from lettuce-production environments comprising poultry manure, irrigation water, and soil, while in Malawi, multidrug-resistant *E. coli* and *K. pneumoniae* were detected across poultry/pig manure, agricultural soils, and vegetables in urban farm systems [107]. Wastewater studies provide parallel evidence for aquatic dissemination, with multidrug-resistant *E. coli* and *Enterococcus* spp. reported in raw and treated wastewater and receiving river water in KwaZulu-Natal, South Africa, and multidrug-resistant Gram-negative bacteria, including ESBL producers, detected in hospital wastewater from Korle Bu Teaching Hospital in Accra, Ghana [104,106]. Once introduced into these environments, resistance genes, including plasmid-borne determinants such as *mcr*, may persist within complex microbial communities and continue to circulate through HGT, particularly where MGEs, residual antimicrobials, manure inputs, and wastewater contamination sustain selective pressure. Contaminated water sources used for irrigation, livestock watering, aquaculture, and domestic purposes create additional opportunities for reintroduction into human and

animal populations. In many African countries, limited wastewater treatment infrastructure and sanitation systems further increase environmental exposure, plausibly increasing human and animal exposure to mcr-positive bacteria from environmental reservoirs.

Unlike clinical reservoirs, where AMR is largely driven by antimicrobial exposure and patient-to-patient transmission within relatively confined healthcare settings, environmental reservoirs function as open, highly interconnected ecosystems that simultaneously receive resistant bacteria and resistance genes from multiple human and animal sources. Wastewater, surface waters, agricultural soils, sediments, and manure-amended fields serve as convergence points where bacteria from hospitals, livestock operations, domestic sewage, and agricultural activities coexist, interact, and exchange mobile genetic elements. These environments therefore provide favourable conditions for HGT, which may allow mcr genes to persist and spread even without direct colistin exposure. Moreover, environmental reservoirs continuously reconnect with human and animal populations through irrigation water, food production, recreational water use, livestock watering, and wastewater reuse, creating recurring opportunities for exposure to resistance determinants across One Health interfaces. Consequently, the available detections show that the environment is a reservoir of mcr-positive bacteria that receives inputs from several sectors. Direct evidence that environmental compartments sustain or amplify mcr over the long term in Africa (for example, repeated sampling showing persistence or growth of *mcr*-positive bacteria after contamination sources are removed) is currently lacking, and this is a research priority.

3.6. Wildlife and Interfaces with Human Activity

Wildlife may contribute to the ecology of mobile colistin resistance by carrying resistant bacteria across geographic and ecological boundaries, but to our knowledge, direct detection of mcr genes in African wildlife is currently confined to wild birds (see below). African studies have shown that wildlife can harbour antimicrobial-resistant bacteria at human–animal–environment interfaces. In Zambia, ref. [108] reported antimicrobial-resistant *E. coli* and Shigella spp. from wildlife and livestock at a wildlife–livestock interface, with multidrug-resistant isolates detected in wild animals, including impala and ostrich [108]. Similarly, ref. [109] detected antibiotic-resistant Enterobacterales from wildlife-origin samples in Senegal, including non-human primates, and identified multidrug-resistant *E. coli* carrying $bla_{CTX\text{-}M\text{-}15}$ on MGEs [109]. Wild birds, rodents, non-human primates, and other free-ranging animals could plausibly acquire mcr-harbouring bacteria through contact with contaminated water, agricultural waste, landfill sites, and human settlements. Once colonised, these animals may act as mobile carriers, transporting resistance determinants across large distances and introducing them into previously unaffected ecosystems.

Africa's wildlife diversity and extensive wildlife–livestock–human interfaces create opportunities for the exchange of antimicrobial-resistant bacteria between animals, humans, and the environment, although the rate and direction of such exchange remain unquantified. In the African context, migratory bird populations are particularly important because they traverse multiple countries and continents while interacting with diverse environmental habitats. In Egypt, ref. [110] sampled migratory birds and broiler-farm environments over five winter seasons and reported multidrug-resistant Salmonella enterica and *E. coli*, with resistance genes such as *sul1*, *tetA*, bla_{TEM}, and *qnrA* detected in isolates from migratory birds and poultry farms [54]. In Algeria, ref. [111] recovered β-lactam- and colistin-resistant Enterobacterales from faecal samples of migratory white storks (*Ciconia ciconia*), including *E. coli*, *K. pneumoniae*, *P. mirabilis*, and *C. freundii*; the study detected ESBL genes, $bla_{OXA\text{-}48}$, $bla_{NDM\text{-}5}$, and *mcr-1* [111], supporting the role of migratory birds as sentinels or carriers of clinically important resistance determinants. These species are increasingly recognised as sentinels and potential disseminators of antimicrobial resistance, including mobile colistin

resistance [112]. Urban expansion, agricultural encroachment, ecotourism, and the growing overlap between human activities and natural ecosystems further intensify wildlife–human interfaces. Through these interactions, resistant bacteria may move bidirectionally between wildlife, domestic animals, environmental reservoirs, and human populations. Wildlife involvement therefore extends the transmission network beyond traditional human and livestock systems, highlighting the need for surveillance approaches that capture the full ecological complexity of colistin resistance dissemination.

To clarify the evidence for wildlife, direct detections of *mcr* in African wildlife are, to our knowledge, restricted to wild birds: *mcr-1* was detected in Enterobacterales from long-distance migratory white storks (*Ciconia ciconia*) in Algeria [111], and *mcr-1* and *mcr-2* were reported in wild birds in Egypt [77]. Other African wildlife studies discussed above reported antimicrobial-resistant Enterobacterales at wildlife–livestock interfaces, in non-human primates and in migratory birds [108–110], but did not report *mcr* genes. To our knowledge, no studies have detected mcr in wild mammals, reptiles, or aquatic wildlife in Africa, so statements about wildlife in this review refer to wild birds unless otherwise stated.

Table 1 summarises the temporal evolution of mobile colistin resistance in Africa, highlighting the progressive diversification of mcr variants and the expansion of reservoirs from food-animal systems to integrated human, animal, and environmental interfaces.

4. Drivers of Colistin Resistance in Africa

4.1. Co-Selection and Persistence of mcr-Bearing Plasmids

Although colistin use directly selects for *mcr* genes, restricting colistin alone is unlikely to eliminate mobile colistin resistance. Plasmid-mediated *mcr* determinants are frequently co-located with resistance genes encoding ESBLs, carbapenemases, aminoglycoside-modifying enzymes, tetracycline resistance, fluoroquinolone resistance, and sulfonamide resistance, resulting in multidrug-resistant plasmids [113]. Consequently, exposure to unrelated antimicrobial classes can simultaneously maintain selective pressure for *mcr*-bearing plasmids, even without colistin use. Co-selection is particularly important in African livestock production, where tetracyclines, sulfonamides, and β-lactams remain among the most widely used antimicrobial classes [114–117]. Reports of *mcr*-positive *E. coli* and *K. pneumoniae* co-harbouring ESBL genes show how co-selection contributes to the persistence of multidrug-resistant plasmids within livestock reservoirs [30,118]. Similarly, in clinical settings, the extensive use of β-lactams and fluoroquinolones may indirectly maintain *mcr*-positive plasmids, thereby reducing the effectiveness of interventions that focus exclusively on restricting colistin [14]. These findings suggest that stewardship should target multiple antimicrobial classes rather than colistin alone (Section 6).

4.2. Environmental Amplification

Environmental systems are reservoirs that receive and may amplify mobile colistin resistance. Here, "amplify" means an increase in the abundance of mcr-bearing bacteria or plasmids within a compartment (for example, through growth, selection by residues, or gene transfer); this has been described for resistance genes in general [119], but for mcr in Africa the direct evidence is still limited to detections in wastewater, surface water, soil and manure (Section 3.5). Untreated or inadequately treated wastewater originating from hospitals, households, pharmaceutical industries, and livestock production systems frequently introduces resistant bacteria, antimicrobial residues, and mobile genetic elements into rivers, agricultural soils, sediments, and wastewater treatment systems [119]. These environmental compartments provide favourable ecological conditions for bacterial persistence, biofilm formation, and horizontal gene transfer, facilitating the maintenance and dissemination of *mcr* genes [5,111].

Environmental contamination also establishes multiple exposure pathways linking environmental reservoirs to human and animal populations. In many African settings, surface waters contaminated by wastewater are commonly used for irrigation, livestock watering, aquaculture, and domestic activities, creating opportunities for resistant bacteria to re-enter food production systems and human communities [118]. The persistence of antimicrobial residues within these environments further enhances the co-selection of multidrug-resistant plasmids. Environmental reservoirs may therefore do more than passively accumulate resistance, but evidence that they sustain mcr after the initial sources of contamination have been removed is lacking and should be tested in longitudinal studies.

4.3. Climate Change

Climate change is increasingly recognised as an indirect driver of antimicrobial resistance, including mobile colistin resistance. Rising temperatures, altered precipitation patterns, flooding, and prolonged drought influence bacterial survival, environmental persistence, and rates of HGT [120]. Elevated temperatures may accelerate bacterial replication and plasmid exchange, while flooding can promote sewage overflows and disperse resistant bacteria from hospitals, farms, and communities into shared aquatic ecosystems [119]. Climate-mediated environmental disturbances further modify resistance reservoirs by altering microbial community structure and nutrient availability. Increased temperatures, flooding, and sediment disturbance may enhance bacterial survival and release previously sequestered resistance genes into surrounding aquatic environments [121]. Climate change also affects livestock production by increasing disease burden, altering vector distributions, and promoting greater AMU for disease prevention and treatment [122]. Consequently, climate change is more likely to act as an indirect modifier that intensifies existing biological and environmental pressures than as an independent cause of *mcr* emergence.

4.4. Infrastructure, Governance, and Sanitation

The persistence and dissemination of *mcr* genes are further reinforced by deficiencies in infrastructure and governance. Weak environmental regulation, poor pharmaceutical waste disposal, and inadequate sanitation contribute to the continuous release of antimicrobial residues and resistant bacteria into natural ecosystems [5,111,119]. Informal sewage systems, open defecation, and inadequate management of hospital and livestock waste further exacerbate environmental contamination, particularly in rapidly urbanising areas. Regulatory challenges extend beyond environmental management. Inconsistent enforcement of AMS policies, insufficient laboratory capacity, and limited surveillance infrastructure reduce many African countries' ability to detect, monitor, and respond to emerging resistance threats. These systemic limitations create conditions that allow *mcr* genes to persist and circulate across interconnected One Health interfaces.

4.5. Human and Animal Mobility

The world is now a global village, where rapid transboundary movement has enabled human pathogens to cross international borders and initiate global epidemics within hours [123]. Thus, the movement of humans, animals, and food products can spread *mcr*-harbouring bacteria across local, national, and international scales. Livestock trade through porous borders mixes animals from diverse epidemiological backgrounds, while informal livestock markets and unregulated slaughter systems increase opportunities for bacterial transmission through close animal contact and inadequate hygiene [124]. Seasonal transhumance and pastoral livestock movement further facilitate interactions among domestic animals, wildlife, and environmental reservoirs, enhancing regional circulation of resistance determinants [75]. Human mobility also contributes to the spread of mobile

colistin resistance. International travel, labour migration, and population displacement enable colonised individuals to transport *mcr*-positive Enterobacterales across national boundaries [125,126]. Likewise, international trade in food products, aquaculture commodities, and animal feed may introduce resistant bacteria into new production systems. Together, these interconnected movement pathways highlight the importance of coordinated cross-border surveillance, livestock traceability, veterinary inspections, and genomic epidemiology for limiting the continental spread of mobile colistin resistance [73,89,104].

5. Transmission Pathways Across One Health Interfaces

The transmission of *mcr* genes across Africa can be conceptualised as an interconnected One Health network in which humans, animals, food systems, wild birds, and the environment are linked through the pathways described below; the strength of evidence differs among these pathways [22,25]. Unlike chromosomal colistin resistance, which is largely restricted to vertical inheritance within bacterial lineages, plasmid-mediated *mcr* genes can undergo rapid HGT, enabling dissemination across bacterial species, host populations, and environmental compartments [9]. Consequently, resistance may not be confined to a single reservoir but may circulate among interconnected One Health interfaces, driven by antimicrobial selection pressure, ecological connectivity, and the MGEs.

Livestock production systems are likely a major source of selection for mcr-bearing bacteria within this transmission network. The widespread use of colistin in poultry, pig, and cattle production, as well as in aquaculture, continuously generates sustained selective pressure favouring the emergence and persistence of *mcr*-harbouring bacteria [65]. Intensive production systems characterised by high stocking densities and frequent antimicrobial exposure facilitate bacterial colonisation, clonal expansion, and plasmid exchange among enteric bacteria, particularly *Escherichia coli*, which remains the predominant carrier of *mcr* genes across Africa [29]. These production systems may therefore act as continuous sources from which resistant bacteria disseminate into food systems, surrounding environments, and human populations.

The food chain provides one of the most direct transmission pathways linking animal reservoirs to humans [91]. Resistant bacteria may contaminate animal-derived food products during slaughter, processing, transportation, retail handling, and household preparation [23]. Consuming contaminated or undercooked meat, poultry, seafood, and dairy products may facilitate intestinal colonisation by *mcr*-positive bacteria. At the same time, poor food-handling practices increase the risk of cross-contamination in households and food-service environments. Because the gastrointestinal tract provides favourable conditions for bacterial persistence and HGT, foodborne exposure may be an important mechanism for establishing *mcr* genes within the human microbiome. Reports of higher *mcr* prevalence in animal-derived food products than in human clinical isolates further support the significance of this transmission pathway [127].

Environmental pathways are probably the most extensive and interconnected component of the transmission network, although this has not been quantified. Livestock manure, hospital effluents, municipal wastewater, pharmaceutical waste, and agricultural runoff continuously introduce resistant bacteria, antimicrobial residues, and mobile genetic elements into soils, rivers, lakes, sediments, and wastewater treatment systems [121,127]. Unlike clinical environments, environmental reservoirs receive inputs from multiple sources simultaneously, creating ecological hotspots where diverse bacterial communities coexist and exchange resistance determinants. These contaminated environments then reconnect with human and animal populations through irrigation, aquaculture, livestock watering, recreational water use, and domestic water supplies, potentially creating feedback loops that sustain the persistence and redistribution of *mcr* genes across One Health interfaces.

Direct occupational exposure constitutes another important transmission route. Farmers, veterinarians, abattoir workers, and others who work near livestock repeatedly encounter colonised animals, contaminated manure, and farm environments, increasing their likelihood of acquiring *mcr*-harbouring bacteria [118]. Companion animals may further contribute to transmission by acting as intermediary hosts, linking environmental contamination with household environments and thereby facilitating the movement of resistant bacteria between humans and animals [97].

Wildlife, particularly migratory wild birds, may extend the geographical reach of mobile colistin resistance beyond agricultural and clinical settings: mcr-1 has been detected in migratory white storks in Algeria [111] and, together with mcr-2, in wild birds in Egypt [77]. Wild birds, migratory waterfowl, rodents, and other free-ranging animals may acquire *mcr*-positive bacteria through contact with contaminated water bodies, agricultural landscapes, or waste disposal sites, and then disseminate them across local, regional, and international scales [93]. Surface waters contaminated by wildlife faeces may subsequently become secondary reservoirs that could introduce resistant bacteria into irrigation systems, aquaculture, fisheries, and drinking water supplies, thereby extending transmission across ecological boundaries [119].

Underlying each of these transmission pathways is the remarkable mobility of *mcr* genes. Conjugative plasmids belonging to the IncI2, IncHI2, and IncX4 incompatibility groups facilitate efficient horizontal transfer among diverse Gram-negative bacteria [128]. Furthermore, the association of *mcr-1* with the insertion sequence ISApl1 within the composite transposon Tn6330 enhances the gene's ability to mobilise between plasmids and chromosomal DNA, increasing its persistence and dissemination [122]. The frequent co-localisation of *mcr* genes with determinants encoding resistance to extended-spectrum β-lactams, carbapenems, aminoglycosides, tetracyclines, and fluoroquinolones further promotes co-selection, allowing unrelated AMU to maintain *mcr*-bearing plasmids even where colistin use has been reduced.

Thus, these interconnected transmission pathways suggest that a connected One Health network, rather than isolated reservoirs, better explains mobile colistin resistance in Africa; this inference comes from co-detection and shared mobile elements rather than from longitudinal or genomic transmission studies, and the relative contribution of each reservoir remains unknown. Livestock production is a probable source of selection, food systems a plausible route of human exposure, environmental reservoirs a probable site of persistence and genetic exchange, wild birds a possible means of geographical dispersal, and mobile genetic elements the common vehicle across sectors. This integrated transmission framework highlights why interventions focused on a single reservoir are unlikely to succeed and underscores the need for coordinated One Health strategies that simultaneously strengthen AMS, food safety, environmental management, wastewater treatment, genomic surveillance, and cross-sectoral collaboration.

6. Gaps and Research Priorities

Despite growing recognition of mobile colistin resistance as a major One Health threat, substantial knowledge gaps continue to limit understanding of its epidemiology, transmission dynamics, and public health significance across Africa.

Current evidence remains geographically fragmented, with a disproportionate concentration of studies originating from a small number of countries, particularly South Africa, Egypt, Tunisia, Algeria, and Nigeria. Consequently, large regions of Central, East, and parts of West Africa remain underrepresented, creating important blind spots in the continental understanding of *mcr* distribution and dissemination patterns. Future surveillance efforts

should prioritise geographic expansion to generate representative data to inform regional and continental risk assessments [95].

Another critical limitation is the predominance of cross-sectional investigations. Most studies provide snapshots of *mcr* occurrence within specific hosts or environments but offer limited insight into temporal trends, persistence, seasonal variability, or transmission pathways. Longitudinal studies that simultaneously monitor human, animal, food, and environmental reservoirs are urgently needed to determine how resistance evolves and circulates within interconnected African ecosystems. Such studies would provide stronger causal evidence and help identify critical intervention points within transmission networks.

Although more studies report the presence of mcr genes, relatively few have used whole-genome sequencing (WGS), metagenomics, or comparative genomics to elucidate transmission pathways. As a result, important questions remain regarding the mobility of resistance determinants, plasmid ecology, clonal dissemination, and the relative contributions of HGT versus clonal expansion. Greater investment in genomic surveillance infrastructure would enable the identification of high-risk clones, MGEs, and transmission events across One Health interfaces. Integrating genomic data with epidemiological and environmental information should therefore be considered a research priority for the continent.

The environmental dimension of mobile colistin resistance remains particularly underexplored. While environmental reservoirs are increasingly recognised as important sources and amplifiers of resistance, studies investigating wastewater treatment systems, agricultural soils, surface waters, sediments, and irrigation networks remain limited. Furthermore, most environmental investigations focus on detection rather than understanding the ecological processes that facilitate persistence and dissemination. Future research should examine the fate of *mcr* genes within environmental matrices, the influence of wastewater treatment processes on resistance dynamics, and the role of environmental hotspots in facilitating HGT.

Evidence on how wildlife contributes to colistin resistance transmission remains sparse across the continent. Although wildlife species have been implicated as potential reservoirs and dispersal agents of AMR, systematic investigations remain scarce in Africa despite the continent's exceptional biodiversity and extensive wildlife–livestock–human interfaces. Long-distance migratory birds, peri-urban wildlife, and species inhabiting protected areas adjacent to agricultural systems warrant particular attention. Understanding the ecological role of wildlife in maintaining and disseminating mcr genes will be essential to developing comprehensive One Health surveillance strategies.

Climate change's role in shaping the future epidemiology of mobile colistin resistance is another emerging research frontier. Increasing temperatures, extreme weather events, flooding, droughts, and changing agricultural practices may alter bacterial ecology, antimicrobial usage patterns, and environmental dissemination pathways. However, empirical data linking climate variables to *mcr* emergence and spread in African contexts remain scarce. Interdisciplinary studies integrating microbiology, environmental sciences, climate modelling, and public health are therefore needed to understand how climate-related changes may influence resistance dynamics in the coming decades.

From a policy perspective, evidence on the effectiveness of interventions designed to reduce colistin resistance remains limited. Few African studies have evaluated the impact of AMS programmes, restrictions on veterinary colistin use, wastewater treatment improvements, or integrated One Health surveillance initiatives. Future implementation research should identify context-specific interventions that are both effective and feasible within resource-constrained settings. Such evidence will be critical for translating scientific knowledge into sustainable policy action.

Finally, research needs to move beyond siloed, sector-specific investigations toward integrated One Health frameworks. Future studies should simultaneously incorporate human, animal, food, wildlife, and environmental components using harmonised methodologies and shared surveillance platforms. The development of continental genomic databases, standardised laboratory protocols, and collaborative surveillance networks would significantly strengthen Africa's capacity to detect, monitor, and respond to emerging mobile threats of colistin resistance.

Because evidence on the effectiveness of interventions in Africa is limited, the priorities in Table 2 are based on transmission evidence and the gaps reviewed above. They should be implemented alongside evaluation, rather than treated as proven solutions. The few intervention data available include an assessment of a regulatory intervention on colistin resistance in commensal *E. coli* from chickens in South Africa [60] and evidence from outside Africa that composting reduces *mcr-1* in livestock manure [65]. Priorities 1–5 address the pathways described in Sections 3–5; priority 6 addresses the evidence gap itself.

Table 2. Intervention priorities derived from the reservoirs, drivers and evidence gaps identified in this review.

Priority	Pathway or Gap Addressed	Evidence	Suggested Actions
1. Multi-class antimicrobial stewardship in human and veterinary sectors	Co-selection; antimicrobial use in livestock and hospitals (Sections 2.3 and 4.1)	*mcr* co-located with ESBL, carbapenemase and other resistance genes [12,22]; tetracyclines, sulfonamides and β-lactams widely used in African livestock [114–117]; restricting colistin alone is unlikely to remove *mcr* [30]	Restrict non-therapeutic and over-the-counter colistin; monitor use of several antimicrobial classes on farms and in hospitals; build stewardship programmes with built-in evaluation [49,60]
2. Geographically broader, harmonised One Health surveillance	Geographic bias and sector-specific studies (Section 6)	Evidence concentrated in South Africa, Egypt, Tunisia, Algeria and Nigeria; Central, East and parts of West Africa under-represented (Section 6)	Extend sampling to under-represented regions; use shared protocols and platforms; sample human, animal, food, wastewater and wild-bird compartments together
3. Genomic surveillance linked to epidemiological data	Transmission inferred rather than demonstrated (Section 6)	Few studies have used whole-genome sequencing or metagenomics; IncI2, IncX4 and IncHI2 plasmids and ISApl1 are recurrent vehicles [25,128]	Isolate-level sequencing across sectors; plasmid and insertion-sequence typing; a shared continental genomic database
4. Wastewater, effluent and manure management	Environmental reservoirs (Sections 3.5 and 4.2)	*mcr* detected in wastewater-plant effluent, rivers, seawater, farm soil and manure in South Africa, Algeria and Tunisia [54,61,63,76,103]; composting reduced *mcr-1* in manure outside Africa [65]	Treat hospital, abattoir and livestock effluent; compost manure before land application; monitor *mcr* in effluents and receiving waters

Table 2. *Cont.*

Priority	Pathway or Gap Addressed	Evidence	Suggested Actions
5. Food-chain controls in informal slaughter and retail settings	Food chain (Sections 3.4 and 5)	*mcr-1*-positive Enterobacterales in retail meat, beef products and cheese in Egypt [70,95,96]; informal slaughter and markets with limited hygiene [98–100]	Improve hygiene, cold chain and inspection; include retail foods in surveillance; consumer food-safety education
6. Implementation research on intervention effectiveness	Evidence gap on what works (Section 6)	Few African evaluations of stewardship, veterinary colistin restrictions, wastewater upgrades or integrated surveillance [60]	Before-and-after or controlled evaluations that measure *mcr* prevalence in humans, animals, food and the environment

7. Materials and Methods

This study was conducted as a narrative review of mobile colistin resistance in Africa, using a One Health framework to integrate evidence from human, animal, food, wildlife, and environmental reservoirs. The review covered literature from the earliest reports of colistin resistance to publications available through 2026, with particular emphasis on recent evidence on the emergence and dissemination of mobile *mcr* genes.

We identified relevant literature using commonly used biomedical and multidisciplinary databases, including PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, as appropriate to the topic. Search concepts included combinations of "colistin resistance", "mobile colistin resistance", "*mcr*", individual *mcr* gene variants (e.g., *mcr-1* to *mcr-10*), "antimicrobial resistance", "One Health", and the names of African countries and regions. We identified additional relevant studies through reference-list screening of key publications and reviews. The evidence considered included human clinical isolates, animals, food products, wildlife, wastewater, surface water, agricultural environments, and other environmental reservoirs.

The retrieved literature was qualitatively synthesised around the review's major themes: molecular mechanisms of mobile colistin resistance, epidemiology across African One Health reservoirs, drivers of resistance, transmission pathways, and surveillance and research gaps. We paid particular attention to *mcr* variants, bacterial hosts, mobile genetic elements, co-occurring resistance determinants, and evidence of connectivity between human, animal, food, wildlife, and environmental compartments. We graded statements as direct detection (an *mcr* gene or protein was identified in the sector concerned) or inference (a link proposed from co-occurrence, shared mobile elements, or ecological reasoning); we worded inferences as such throughout. As a narrative review, the study did not involve formal systematic review screening, meta-analysis, or quantitative pooling of effect estimates.

8. Conclusions

This review highlights the widespread distribution of *mcr* genes across Africa and underscores their significance as an emerging One Health threat. Evidence shows that *these* genes, particularly *mcr-1*, are present in human clinical isolates, food-producing animals, food products, environmental reservoirs, and wild birds, demonstrating circulation across multiple sectors. Livestock production systems appear to be important selection sources, while food chains, contaminated water sources, wastewater systems, and environmental pathways plausibly transmit the gene between sectors. Multiple interacting factors,

including AMU in animal production, inadequate wastewater treatment, environmental contamination, weak regulatory frameworks, and increasing human and animal mobility, drive the dissemination of mobile colistin resistance. The frequent association of *mcr* genes with highly mobile plasmids and other antimicrobial resistance determinants further promotes their persistence and spread through HGT and co-selection. A key finding of this review is that mcr-positive bacteria are detected in every sector examined, including environmental reservoirs, which receive inputs from human, animal and agricultural sources and are plausible routes of exposure; the evidence therefore supports a connected network of reservoirs rather than isolated ones, but whether environmental reservoirs independently maintain mcr over time remains unproven and the relative contribution of each reservoir is still to be quantified. However, important knowledge gaps remain, particularly in underrepresented regions of Africa, as well as in environmental and wildlife surveillance, and genomic investigations that link transmission pathways. Addressing these gaps will require strengthened surveillance systems, expanded genomic monitoring, improved AMS, and coordinated One Health interventions (Table 2). Sustained collaboration across human, animal, agricultural, and environmental sectors will be essential to limit the spread of mobile colistin resistance and preserve colistin's effectiveness as a last-resort therapeutic option.

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Abbreviations

The following abbreviations are used in this manuscript:

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
arnBCADTEF	Operon encoding the enzymes that synthesise L-Ara4N and transfer it to lipid A
DAG	Diacylglycerol
ESBL	Extended-spectrum β-lactamase
GlcN	Glucosamine
HGT	Horizontal gene transfer
Inc	Plasmid incompatibility group (e.g., IncI2, IncX4, IncHI2)
IS	Insertion sequence (e.g., ISApl1)
L-Ara4N	4-amino-4-deoxy-L-arabinose
LPS	Lipopolysaccharide
mcr/MCR-1	*mcr* denotes mobile colistin resistance genes (mcr-1 to mcr-12); MCR-1, etc., denote the encoded phosphoethanolamine transferases (not methyl-coenzyme M reductase)
MGE	Mobile genetic element
MgrB/mgrB	Negative regulator of PhoP/PhoQ and its gene
pEtN	Phosphoethanolamine

PE	Phosphatidylethanolamine
PhoP/PhoQ, PmrA/PmrB	Two-component regulatory systems controlling lipid A modification
PmrD	Connector protein linking the PhoP/PhoQ and PmrA/PmrB systems
pmrCAB	Operon encoding the pEtN transferase PmrC and the regulators PmrA and PmrB
ST	Sequence type
WGS	Whole-genome sequencing

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