Review

Evidence of Antimicrobial Resistance in Bats and Its Planetary Health Impact for Surveillance of Zoonotic Spillover Events: A Scoping Review

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Abstract: As a result of the COVID-19 pandemic, as well as other outbreaks such as SARS and Ebola, bats are recognized as a critical species for mediating zoonotic infectious disease spillover events. While there is a growing concern of increased antimicrobial resistance (AMR) globally during this pandemic, knowledge of AMR circulating between bats and humans is limited. In this paper, we have reviewed the evidence of AMR in bats and discussed the planetary health aspect of AMR to elucidate how this is associated with the emergence, spread and persistence of antibiotic resistance at the human-animal interface. The presence of clinically significant resistant bacteria in bats and wild life has reflective and broad impact on zoonotic pandemic surveillance, disease transmission and treatment modalities. We searched MEDLINE through PubMed and Google Scholar to retrieve relevant studies (n=38) that provided data on resistant bacteria in bats till September 30, 2022. There is a substantial variability in the results from studies measuring the prevalence of AMR based on geographic location, bat types and time. We found all major groups of gram positive and gram negative bacteria in bats which are resistant to commonly used antibiotics. The most alarming issue is- recent studies have increasingly identified Methicillin Resistant Staphylococcus aureus (MRSA), ESBL producing and Colistin resistant Enterobacteriaceae in samples from bats. This evidence of superbugs abundance in both humans and wild mammals like bats, could facilitate a greater understanding of which specific pathways of exposure should be targeted. We believe that these data will also facilitate future pandemic prepareness as well as global AMR containment during the pandemic events and beyond.

Keywords: Antimicrobial resistance (AMR) ; Bats; Zoonotic spillover; Planetary health; One health

1. Introduction

Antimicrobial resistance (AMR) is a global One Health (OH) issue that involves various species including wild life and containment requires a holistic approach. While drug-resistant pathogens are causing a high disease burden in terms of disability-adjusted life-years and substantial economic loss to the public health sector [1, 2] , the role of the environment and spillover from wild animal reservoirs needs more attention [3]. There is increasing evidence of the spread of pathogenic drug-resistant bacteria in wild animal pop-

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ulations, including wild mammals [4-6]. Bacterial antimicrobial profiling of wildlife, including those found in both wild and urban environments, are crucial to OH prevention strategy development for AMR. Excessive and inappropriate use of antibiotics in human and animal health as well as agricultural farming practices has led to the huge rise in AMR around the world [7, 8]. Frequent AMR reports in animal, wildlife, and environmental samples demonstrate its massive proliferation and have contributed to the subsequent spread of resistance in humans [9]. Wildlife is reported to be carriers of several bacterial pathogens with high AMR and is a vector for spreading bacterial zoonoses to human [10]. Several recent studies reporting carbapenemase [11, 12] and ESBL producing bacteria in wildlife [13, 14] raise a major concern for further investigating the AMR issue in both wildlife and domestic animal origin. Due to increased interaction between wildlife and humans, it is clinically important to have a clear idea of the AMR profile of wildlife [15]. Yet, the rates, modes and drivers of acquisition are unclear, under investigated or reported inadequately[16].

Major infectious diseases causing epidemics and pandemics have emerged as zoonoses [17]. Most of the zoonotic pandemics, such as avian flu, swine flu, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), Ebola, Zika, Nipah, and Henipa viral diseases have been recognized as a global public health emergency for many years due to their rapid spread and colossal virulence [18-21]. The frequent emergence of zoonotic epidemics or pandemics and the use of antimicrobial agents to control secondary infections also triggers the rise of AMR [22, 23]. Obviously, the thousands of species of wild animals are significantly more likely to be a source of animal-to-human spillover of zoonotic pathogens [24]. Notably, most of these zoonoses (e.g. SARS, MERS, Ebola, Nipah encephalitis, and corona virus) are transmitted from bats to humans [25-27], directly or through intermediate hosts [28-30]. In addition, bats are one of the potential vectors for the transmission of both viral and bacterial zoonotic pathogens [31, 32].Considering the role of bats in most recent pandemics and disease spillover [24], the presence of drug resistant pathogens in bats and their likely impact on global AMR burden needs to be studied.

Bats are one of the free roaming wild mammals belonging to the order Chiroptera, a diverse group with a specific life cycle and different feeding habits [33]. With more than 1,300 species, bats are one of the most diverse classes of mammals, representing about 20% of the world's mammal population [33, 34].They have access from deep forests to densely populated localities. As a consequence, they acquire a wide variety of microorganisms, ranging from deadly viruses to multidrug resistant (MDR) bacterial pathogens. Despite bats being a potential reservoir of bacterial pathogens, extensive studies in the search for bat bacterial flora are lacking [33, 35]. Bacterial isolates from bats can acquire high resistance from human and domestic animals, or vice versa through contact as per previous reports [36]. In this paper, we have reviewed the published literature focusing on AMR in bacterial isolates from bats. Our study findings will help the development of OH policies and initiatives for reducing the spread of AMR from wildlife, particularly in the time of zoonotic pandemics.

2. Materials and Methods

To find relevant literature addressing AMR in bats, we searched three bibliographic databases. MEDLINE through PubMed, and Google Scholar databases were searched using the key word “bats” and different combinations of the following terms: antimicrobial resistant, antimicrobial resistance, antimicrobial susceptible, antimicrobial susceptibility, antibiotic resistant, antibiotic resistance, antibiotic susceptible, antibiotic susceptibility, antimicrobial susceptibility, multidrug resistant, and multidrug resistance. We only took into account peer-reviewed articles authored in English and released prior to September 30, 2022. The retrieved publications were screened using the Rayyan QCRI systematic review program [37] and were independently evaluated for inclusion by two review au-

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thors. When conducting the full-text screening, we explained the reasons why certain publications were excluded. Discussion with a third review author helped to settle any disagreements amongst the independent review authors. One review author (P.D.) extracted the data, while another author crosschecked it (M.A.). Disagreements were resolved through team discussion. An accurate visual summary of the screening procedure has been provided using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram [38]. Supplementary Table 1 provides a summary of all included papers (n=38) **(Table S1).** The inclusion and exclusion criteria of these articles are described below.

Inclusion criteria:

Studies published in English on the prevalence of AMR in bacterial isolates from bats focused on the following issues

- Bacterial pathogens
- Bat specimens such as feces, skin swab, oral and rectal swab/cloacal swabs, etc.
- Drug sensitivity testing done in a laboratory setting with/without Clinical and Laboratory Standards Institute (CLSI) and/or other standard organizations cutoffs for drug susceptibility testing
- Reports of resistance genes and plasmids in isolated bacterial samples

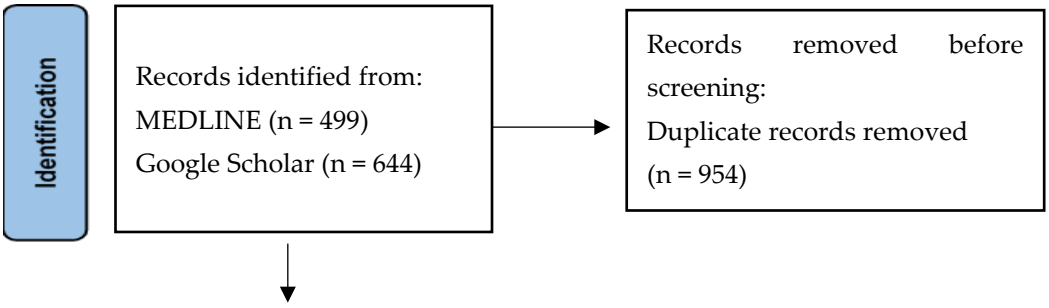
Exclusion criteria:

Duplicated population groups, editorials, perspectives, intervention studies, experimental studies, and narrative reviews studies with inadequate data including,

- Review articles
- Studies on bacteria isolated from bats without antimicrobial susceptibility, gene or plasmid detection tests results
- Studies that did not specify bacterial antimicrobial susceptibility isolated from bats

3. Results

Our initial search turned up 1143 articles in total. Following screening for duplicates and eligibility criteria, 38 papers were pertinent to the topic of AMR in bats. Finally, we considered data extraction for these 38 papers after the full-text evaluation. (Figure 1).



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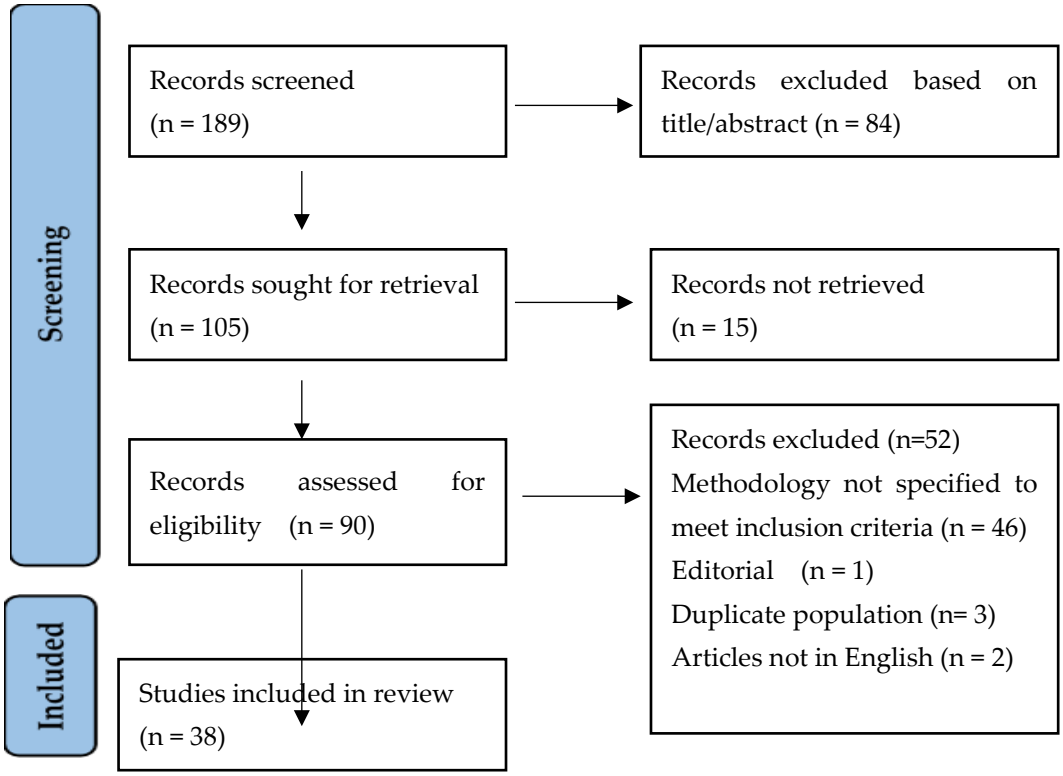

Figure 1. PRISMA flow diagram.

We have also showed the locations and publication trend of the studies conducted in bats focusing on AMR (**Figure 2).**

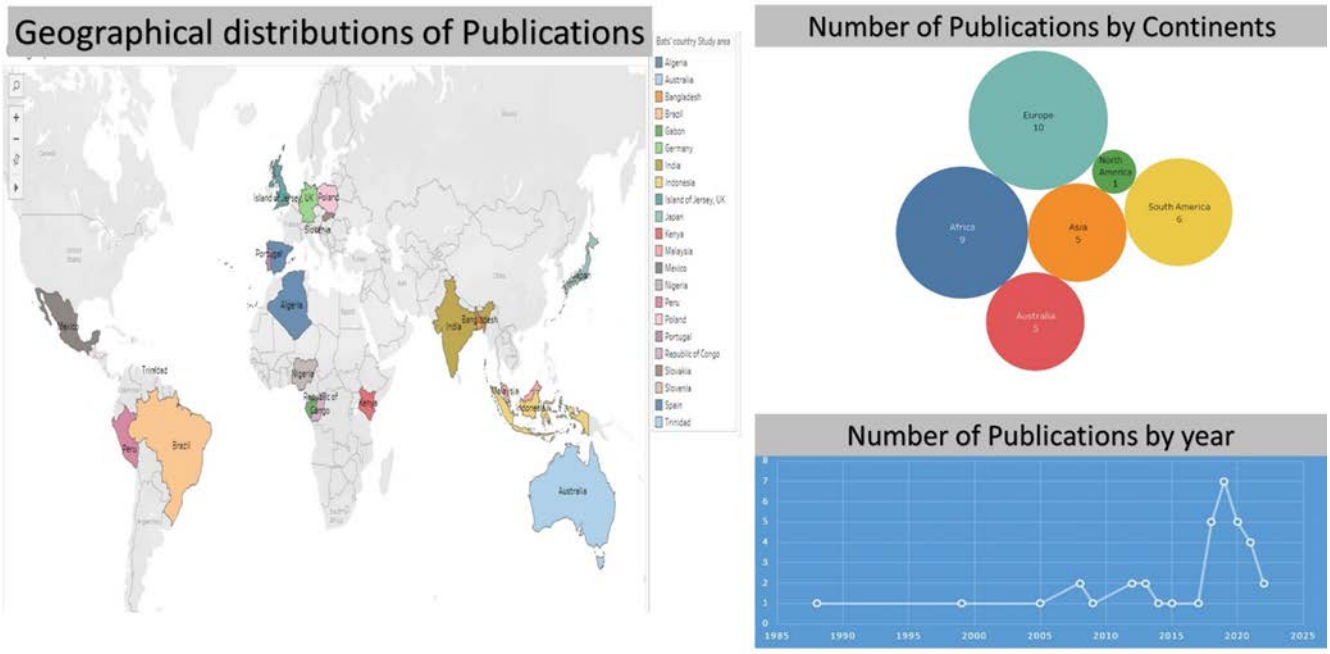

Figure 2. Geographical location and trends of the included studies

For better reporting of our reviewed articles, we categorized the studies based on the bacterial isolates - Gram-negative and Gram-positive. Within Gram-negative bacterial

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pathogens, we found *Escherichia coli (E.coli)* as the most frequently studied and reported bacteria followed by *Enterobacter, Salmonella* and *Klebsiella.* Similarly, *Staphylococcus aureus* and *Staphylococcus spp*. is the most common gram positive bacteria in bats. We described all studies by geographical region since understanding of AMR among isolates in bats might help to understand the history in specific regions and to predict the geographical spread of AMR and epidemics later.

3.1. Evidence of antibiotic resistant gram-negative bacterial pathogens in bats

Gram-negative bacteria constitute the major share of the WHO priority list of drug resistant bacteria with public health importance [39]. Undoubtedly, effective interventions to halt their spillover from wildlife to humans is crucial and need to be implemented. While acquisition of AMR in bacteria isolated from several bat species have been reported in many countries across the world [5, 40, 41], we have presented all gram negative AMR bacteria based on species and geography for better policy determination

Escherichia coli (E. coli):

In 1988, an Indonesian study was the first to reveal the AMR patterns of enteric bacteria isolated from bat feces and reported isolation of *E. coli* (n=15), resistant to sulphamethoxazole (27%), cephalothin (20%), and trimethoprim (7%) [42]. Later in 2005, a Malaysian study also reported isolation of *E. coli* from bats with low or no resistance to treated antibiotics except carbenicillin and streptomycin (7.7% each) [43]. Additionally, a study from Japan (2014) reported *E. coli* (n=26) isolated from bats and found no resistance towards treated antibiotic such as ampicillin, chloramphenicol, and nalidixic acid except streptomycin and chlorotetracylcine (3.8%) [44].

Moving from Asia to Africa, we found several studies in this region focusing on pathogenic Gram-negative bacteria from different species of bats [45-49]. Three Nigerian studies reported AMR patterns of bat *E. coli* and high levels of cephalosporin resistance [47, 50, 51]. One study reported more than 80% of isolate resistance to cefuroxime, ceftazidime and ceftotaxime [47], while the other study with *E. coli* (n=35) reported low cephalosporin resistance [52]. Most recent study by Oladiran et al., from Nigeria reported 83.33% of the isolate showing resistance towards augmentin [53]. These isolates were mostly resistant to ampicillin (48%) and tetracycline (37%) [52]. A Kenyan study found ampicillin, streptomycin and trimethoprim resistance among isolates [48]. Similar to the Nigerian and Kenyan studies, a report from Gabon also stated high levels of cephalosporin and beta lactam resistance in bat *E. coli* (n=6) [49]. All isolates were resistant against amoxicillin, ampicillin, ticarcillin, cefotaxime, ceftazidime, cefpodoxime, aztreonam, cephalexin, erythromycin, and streptomycin [49]. Notably, more than 80% of the isolates were also resistant to piperacillin, ciprofloxacin, and trimethoprim [49]. However, a study from the Democratic Republic of the Congo reported low resistance of bat isolates against treated antibiotic, except intermediate resistance against Doxycycline (89%) [46].

We found that more recent studies were conducted in Europe and molecular identification of AMR genes were also reported from some studies [32, 40, 54-57]. However, two studies from Portugal using *E. coli* (n=19 and 42) isolates reported very low resistant to amoxicillin, sulfamethoxazole-trimethoprim and tetracycline and high resistance to cefotaxime and ampicillin [54, 57]. Ampicillin resistance by *E. coli* were also commonly found in a Polish study [32]. Similar to previous studies with high streptomycin resistance [54, 57, 58], this study also reported high Kanamycin resistance (84%), another aminoglycoside.

In the Americas, two studies from Brazil observed diverse species of bats and isolated hundreds of *E. coli* species from bats' fecal and oral samples [33, 35]. Both studies reported low levels of resistance towards antibiotics such as amoxicillin-clavulanic acid, gentami-

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cin and imipenem. Against other antibiotics, the sensitivity rate was higher except ampicillin (57%) and amoxicillin (54%) [35]. A third Brazilian study also reported *E. coli* (n=17) isolates from bats resistant to ampicillin (59%) and amoxicillin (35%) [59]. Two back-to-back reports from Peru reported ESBL producing *E. coli* (n=5 and 18) from bats which showed pan-resistant to amoxicillin, amoxicillin ticarcillin, piperacillin, cefotaxime, and other antibiotics [40, 60]. A study from Trinidad reported isolation of *E. coli* (n=49) from several bat species and found most of them were resistant to erythromycin (71%) and streptomycin (26%) [61]. In a 1999 study, *E. coli* were obtained from a broad variety of mammalian species samples with Australian and Mexican origins [58]. Among the Mexican isolates, a much higher frequency of antibiotic resistance was detected among the bats' isolates than those obtained from other wild mammals. These isolates demonstrated resistance to streptomycin (100%), ampicillin (46%), and neomycin (15%). In another Australian study, high ampicillin (100%), tetracycline (69.2%), and sulfamethoxazole-trimethoprim (30.7%) resistance in beta-lactam resistant *E. coli* from bats was observed [62]. The detailed drug resistance profile of *E. coli* isolates from bats around the globe has been provided in the Supplementary Table 2 **(Table S2).**

Enterobacter:

The similar Indonesian study mentioned earlier reported isolation of *Enterobacter* (n=24) from bats that were resistant to cephalothin (96%), ampicillin (67%), and tetracycline (50%)[42]. Later in 2018, the Brazilian study reported isolating *Enterobacter* (n=20) and all isolates showed low resistance to all classes of antibiotics except ampicillin and amoxicillin (>80% isolates were resistant) [63]. However, a 2020 study from Gabon reported that all the *Enterobacter* isolates were resistant against to amoxicillin, ampicillin, amoxicillin-clavulanic acid, aztreonam, cefotaxime**,** cefepime, ceftazidime, and many other antibiotics [49].

Salmonella spp:

Reports of *Salmonella* were quite low, however, studies were found from Bangladesh [64], Australia [65], Trinidad, [61] and Brazil [33]. In 2009, *Salmonella spp*. from bats were reported from Trinidad that were highly resistant to streptomycin (100%) and erythromycin (75%) [61]. From Bangladesh and Australia, *Salmonella serotype Virchow* and *Salmonella Typhimurium* ST19 from bats fecal specimens were reported respectively and the isolates showed no resistance to any antibiotics [64, 65]. Isolation of *Salmonella spp* resistant to ampicillin (50%) and cephalexin (50%) were also reported from Brazil [33].

Klebsiella spp:

The Indonesian study also reported isolation of *Klebsiella spp* from bats' fecal samples in 1988 [42]. *Klebsiella* (n=11) isolates were found showing high resistance towards ampicillin (82%) and sulphamethoxazole (27%). A study from Japan noted isolation of *K. pneumoniae* (n=38) from bats but reported only sulfadimethoxin resistance (13%) [44]. Isolation of *K. oxytoca* (n=13) showing high ampicillin resistance (61.5%) were also reported from Brazil [33]. In 2020, *Klebsiella spp* were also isolated from Gabon but the study represented only 4 isolates antibiogram. Interestingly, all these isolates were resistant to 18 types of antibiotics including ampicillin, amoxicillin, kanamycin, nalidixic acid, ceftazidime, cefotaxime, and others [49]. Over the past three decades, the multidrug resistant (MDR) and hypervirulent *K. pneumoniae* lineages have increased and an Australian study investigated the occurrence of *K. pneumoniae* species complex (KpSC) in fruit bats [41]. None belonged to MDR clonal lineages that cause frequent nosocomial outbreaks, and no isolates were characterised as hypervirulent. All the isolates were resistant to ampicillin and amoxicillin-clavulanic acid.

ESBL producing and Colistin resistant Enterobacters:

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Drug resistance by ESBL producing Enterobacteriaceae has been drastically increasing in animals and humans [49, 66, 67]. This increase has been caused mainly due to acquiring ESBL producing genes by Enterobacters. Among the many ESBLs described in a variety of pathogens, *CTX-M, TEM*, and *SHV* types proved to be the most predominately detected across the world in animals and humans [68-70]. Other than ESBL producer, colistin resistant *Enterobacters* are also a global health threat. Despite having neurotoxic and nephrotoxic side-effects [67], colistin has been reintroduced as a final therapeutic choice for the treatment of carbapenem-resistant Gram-negative infections [71]

While ESBL genes are commonly detected in Gram-negative pathogens isolated from animal origin [72], their presence in bats with different feeding habits, such as sangivorous, insectivorous, and frugivorous, were also frequently observed [40, 54]. Benavides et al. first reported the presence of ESBL-producing *E. coli* in vampire bats (*D.rotundus*) in Peru, suggesting a wide dissemination of AMR bacteria in the community [40]. All the 5 ESBL producing *E. coli* isolates expressed plasmid *bla*$_{CTX-M-15}$ genes showing resistance towards β-lactam antibiotics. Two years later, the authors reported isolation of several genes such as bla$_{CTX-M-15}$ (39%), bla$_{CTX-M-3}$ (11.11%) bla$_{CTX-M-55}$ (44.44%), bla$_{CTX-M-65}$ (5.55%), bla$_{TEM-1B-like}$ (66.66%), and bla$_{TEM-176}$ (28%), responsible for ESBL production [60].

The study from Gabon reported multi-resistant ESBL-producing Enterobacteriaceae with 11 ESBL producing bacterial isolates (*E. coli*=6; *K. pneumoni*ae =4 *and E. cloacae*=1*)* from fruit bats that carried *bla*$_{CTX-M-15}$ and *bla*$_{SHV-11}$ as the ESBL producing genes [49]**.** The isolation of ESBL producing *E. coli* from European free-tailed bats (*T. teniotis*) was first reported in Portugal [57]. The more prevalent beta-lactamase genes detected were *bla*$_{CTX-M-1}$ (57.9%) and *bla*$_{CTX-M-3}$ (36.8%), followed by *bla*$_{SHV}$ (31.6%), *bla*$_{TEM}$ (21.1%), *bla*$_{OXA}$ (10.5%), and *bla*$_{CTX-M-9}$ (10.5%). Presence of *CTX-M* and *TEM* groups in two *E. coli* confirmed the presence of ESBL genes encoding the enzymes in a study in Poland [32]. The sequencing confirmed that these genes were *bla*$_{CTX-M-3}$, *bla*$_{CTX-M-15}$, and *bla*$_{TEM-1.}$ Later a study from Australia also reported high bla$_{TEM}$ gene (92%) acquisition by beta lactam resistant *E. coli,* with the detection of bla$_{CTX-M-27}$ (7.6%) in low levels [62]. McDougall also reported *K. pneumoniae* isolates having high bla$_{SHV-110,}$ which is also responsible for beta lactam resistance [41]. From both studies in Australia, detection of bla$_{OXA-1}$ (22.22%) in ESBL producing *E. coli* isolates [62] and bla$_{okpc-1}$ (20.5%) in *Klebsiella* isolates from bats were reported [41]. In Algeria, carbapenemase producing genes bla$_{OXA-48}$ gene and *bla*$_{KPC-3}$ in two carbapenemase producing *K. pneumoniae* isolate were also reported [5].

A study conducted in Gabon [49] found 54.5% of 11 carbapenem resistant isolates to be colistin resistant and the resistant bacteria included *E. cloacae, E. coli* and *K. pneumoniae* (4/6). Similarly, a study from Poland [32] also reported 7.9% colistin resistant *E. coli* out of 38 isolates**.** However, no studies described any molecular detection of colistin resistance genes from bats such as mcr (mobilized colistin resistance).

The average percentage of major antibiotic resistance in all gram negative bacteria obtained from bats is shown in **Figure 3**

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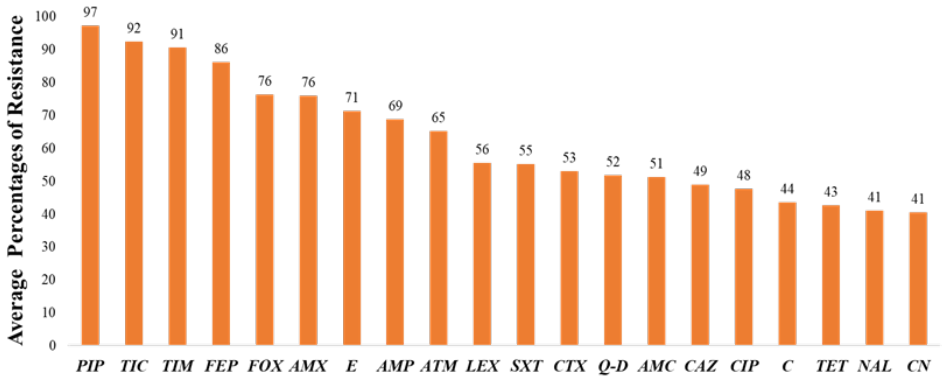

Figure 3. Major antibiotic resistance of gram negative bacteria in bats.

Piperacillin=PIP, Ticarcillin=TIC, Ticarcillin-clavulanic acid=TIM, Cefepime=FEP, Cefoxitin=FOX, Amoxicillin=AMX, Erythromycin = E, AMP=Ampicillin, Aztreonam=ATM, Cephalexin=LEX, Cefotaxime=CTX, Quinupristin-dalfopristin= Q-D, Amoxicillin-Clavulanic acid=AMC, Ceftazidime=CAZ, Ciprofloxacin=CIP, Chloramphenicol=C, Tetracycline=TET, Nalidixic acid=NAL, Gentamicin=CN

Other Gram-negative Bacteria and Genes Responsible for Drug Resistance in Bats

In addition to *E. coli, Klebsiella* and *Enterobacter,* several other Gram-negative pathogens such as *Citrobacter, Serratia* and *Acinetobacter* associated genes responsible for antimicrobial resistance were reported [33, 35, 42, 44, 73]. In 1988, Graves et al. reported isolation of *Citrobacter spp* from bats that were resistant to cephalothin (100%) [42]. Decades later in 2014, Obi et al. reported isolation of *Citrobacter freundii* that were highly sensitive to all drugs except sulfadimethoxin (28%) [44]. Claudio et al. from Brazilian study reported isolation of *Serraita marcescens, S. liquefaciens, A. baumanii,* and *Stenotrophomonas spp* [33]. Out of 36 *S. marcesences* isolates, most were resistant to ampicillin (94%), amoxicillin-clavulanic acid (97%) and cephalexin (100%). All of the isolated *Sentrophomonous spp* were resistant to ceftriaxone and imipenem [33]. Selvin et al. also reported ceftriaxone resistant *Escherichia furgusonii* [73]. Additionally, Sens-junior et al. reported that *S. liquefaciens* were resistant to amoxicillin (62.5%), amoxicillin-clavulanic acid (50%), and ampicillin (62.5%) [35].

Apart from ESBL genes, other antibiotic resistant genes were also detected in bats [32, 54]. Nowakiewicz et al. confirmed the resistance profile of 38 *E. coli* isolates and further detected associated genes [32]. The study detected *aph(3')-IIa* gene responsible for kanamycin resistance, sulphonamide resistant genes *sul1* and *su2*, and gentamicin resistance determined by the presence of aac (3)-II, aac (3)-III isolates . All streptomycin-resistant isolates were characterized by the presence of the *strA* gene. Resistance to tetracycline was found by the presence of a single *tetA* gene, *tetB,* and both *tetA* and *tetB* genes. Genetic resistance to phenicols was confirmed by the presence of the *floR* gene in two isolates, the cm1A gene present in one isolate and cat gene in six isolates [32]. Detection of streptomycin, tetracycline, sulfamethoxazole-trimethoprim, spectinomycin, and trimethoprim resistance genes were also found from *E. coli* isolated from bats [62]. Benavides et al., from Peru, reported detection of eighteen genes conferring aminoglycosides resistance at prevalence ranging from 3% (aadB) to 55% (aadA1) in multidrug-resistant *E. coli* [60].

3.2. Evidence of Antibiotic Resistant Gram-positive Bacterial Pathogens in Bats

Staphylococcus aureus and Staphylococcus spp.

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AMR in gram-positive bacteria remains a great challenge in infectious disease management [74]. Most studies focused on Gram-negative bacteria, as these are found as the predominant isolates from bat-originated specimens such as fecal, cloacal, rectal, or guano samples [40, 46, 52, 59]. Apart from Gram-negative bacteria, Gram-positive bacteria, especially *Staphylococcus spp*, were also isolated from bats [75-77].

An Australian study investigated semen, urethral and preputial swabs from *Pteropus* bats and isolated *Streptococcus* and *Staphylococcus* as predominating identified bacteria [78]. The most effective antibiotic against Gram-positive bacteria was penicillin, while the information of resistance against other broad-spectrum antibiotic was unclear. Two Nigerian studies, Akobi et al. and Olatimehin et al., reported isolation of 19.1% and 11.2% of *S. aureus* from fecal samples of the straw-colored fruit bat (*Eidolon helvum*) in 2012 [77] and 2018 [76] respectively. None of the studies observed MRSA prevalence, but both studies reported low levels of resistance against penicillin. *S. aureus* from the studies were found commonly colonized with ST1725 and ST1726 types of *S. aureus.* Akobi et al. (2012) reported no presence of Panton-Valentine leukocidin (PVL) virulent gene [77]. However, Olatimehin et al. (2018) detected PVL virulent gene in 78.6% of the isolates [76].

From Europe, reports of isolation of *Staphylococcus spp*. were found from both insectivorous and frugivorous bat species. In 2013, *Staphylococcus nepalensis* (n=5) was identified from bat guano for the first time in Slovakia [75], and vancomycin resistance was reported in the same species in 2020 from the same country [56]. In addition to this species, other *Staphylococcus* species such as *S. xylosus, S. kloosii, S. nepalensis, S. simiae, S. aureus,* and *S. sciuri* were also reported in the United Kingdom [79] and Spain [80]. All *Staphylococcus* isolates in the Spanish [80] and 2013 Slovak [75] studies were resistant to erythromycin, and high streptomycin and tetracycline resistance were also reported. High streptomycin and tetracycline resistance were also reported by these two studies. Fountain et al. reported 38.9% of *Staphylococcus* isolates to be amoxicillin resistant and 7.6% CoNS (Coagulase negative *Staphylococcus*) gave cefoxitin resistance [79]. None of the *S. aureus* isolates showed phenotypic resistance to methicillin (screening agar) and none were found to carry mecA or mecC .

Other Gram-positive organism

Other than CoNS and *S. aureus*, studies also reported other Gram-positive bacteria such as *Kocuria, Bacillus,* and *Arthrobacter* [56, 73, 78]. Selvin et al. reported isolation of *Bacillus anthracis* from bats and the isolates were resistant to ciprofloxacin (25%), tetracycline (25%), and orfloxacin (75%) [73]. Gerbakova et al. reported isolation of *Arthrobacter sp.* resistant to chloramphenicol (50%), and vancomycin (50%), as well as *Kocuria sp.* resistant to chloramphenicol (18%) and vancomycin (18%) [56]. Recently, a Polish study by Nowakiewicz et al., reported isolation of *Enterococcus faecalis* from bat guano sample and the isoaltes were highly resistant to tetracycline (69.4%), streptomycin (41.7%) and kanamycin (38.9%) [81]. Another Spanish study also reported isolation of two *Enterococcus* isolates from bats rectal swab, one out of two isolates were resisatnt to ciprofloxacin and erythromycin and both of these were resistant to quinupristin-dalfopristin [82]. The average percentage of antibiotic resistance in the gram positive bacteria obtained from bats is shown in **Figure 4.**

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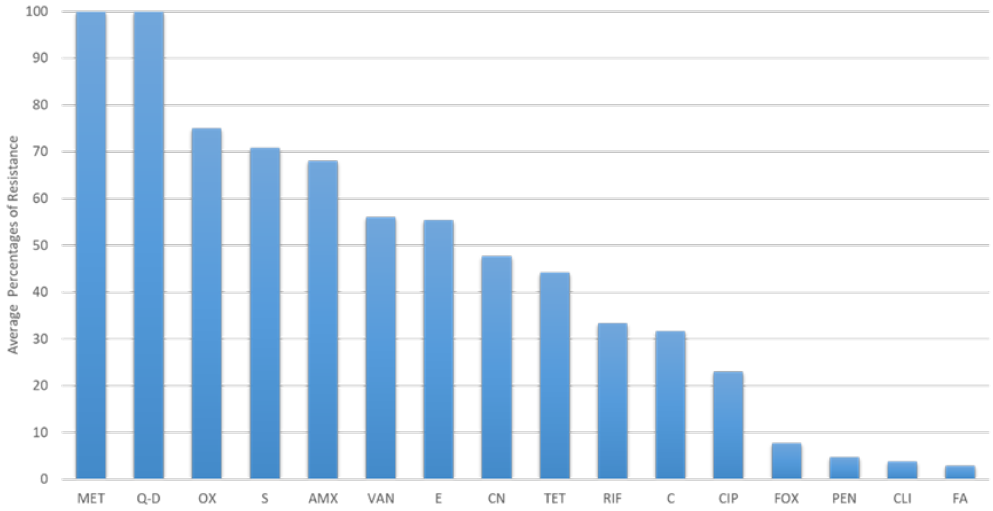

Figure 4. Major antibiotic resistance of gram positive bacteria in bats.

Methicillin=MET, Quinupristin-dalfopristin= Q-D, Oxacillin = OX, Amoxicillin=AMX, Streptomycin= S, Vancomycin=V, Erythromycin=E, Gentamicin=CN, Tetracycline=TET, Rifampicin=RIF, Chloramphenicol=C, Ciprofloxacin=CIP, Cefoxitin=FOX, Penicillin= PEN, Clindamycin= CLI, Fusidic acid = FA

Methicillin Resistant Staphylococcus aureus (MRSA)

MRSA is a widely found pathogen in hospital settings among Gram-positive *Staphylococcus*. Occurrence of MRSA has also been reported as a problem in veterinary facilities [83]. A study in 2008 found one MRSA from two bat specimens (wound and gastrointestinal tract) [84]. Further molecular analysis was performed to understand the virulence properties of the isolates. SCCmec IV cassettes were found without panton-valentine leukocidine (PVL) genes in the bat MRSA. The detailed drug resistance profile of all bacterial isolates from bats (except *E. coli)* has been provided in the Supplementary Table 3 **(Table S3).**

4. Discussion

We have presented a detailed review of the AMR profile of bats' bacterial pathogens which enlighten their probable role in disseminating AMR in the humans and the environment. Most studies in the field have focused on migratory birds as vectors for long-distance antimicrobial resistance dissemination, however, role of bat on disseminating AMR is still on the research [85]. Given the significant spatial and temporal heterogeneity in antimicrobial resistance distribution and the factors that affect its evolution, dissemination, and persistence, it is important to highlight that antimicrobial resistance must be viewed as an ecological problem. Thus, there is a significant interest worldwide in promoting a One Health perspective on AMR to enable a more accurate understanding of its ecosystem [86].

AMR from bat isolates (both Gram positive and negative) were reported in parts of Asia (Indonesia, Malaysia, Japan, and India), North and South America (Brazil, Mexico, and Peru), Africa (Algeria, Nigeria, Gabon, Trinidad, and Republic of Congo) and Europe (Germany, Slovakia, Portugal, Slovenia, United Kingdom, Poland and Spain). Three studies from Brazil [33, 35, 59] and four studies from Nigeria [47, 50, 76, 77] were very crucial in this review, these studies revealed a good pattern of AMR profile of bat isolates as all three studies reported ampicillin, amoxicillin or amoxicillin clavulanic acid, cephalosporin's resistance over the study period. Overall, all these data reported by the studies were mostly reporting bacterial isolates resistant to commonly used antimicrobials such as, amoxicillin, amoxicillin-clavulanic acid, streptomycin, tetracycline, erythromycin,

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cefoxitin and tetracycline. However, record of high resistance to various other treated drugs were lower in number.

Drug resistance patterns have been observed in both Gram-positive and -negative isolates from various bat species from around the world. In most of the studies, *E. coli* was the indicator organism that reported high resistance to clinically relevant antibiotics such as β lactams (ampicillin, amoxicillin, amoxicillin-clavulanic acid, and piperacillin), third-generation cephalosporins (ceftazidime and cefotaxime), aminoglycoside (streptomycin), tetracyclines, and quinolones (ciprofloxacin). Other than *E. coli*, all the gram negatives were also found highly resistant towards ampicillin and amoxicillin-clavulanic acid. Over the period gentamicin resistance were checked by all the studies but the fact is not alarming as all the *E. coli* isolates were mostly sensitive towards gentamicin, other reported organisms were also found sensitive toward gentamicin except there is a rise in the resistance. Cefotaxime and ceftazidime resistance were also found by many studies, however, there were no such trends in level of resistance. Antimicrobials, especially fluoroquinolones, aminoglycosides, and third- and fourth-generation cephalosporins, are listed as critically important antimicrobials for human and veterinary use according to the World Health Organization (WHO) [87, 88]. Resistance to common antibiotics by bats commensals is quite alarming and needs further evaluation. Supporting the statements of bats as a carrier of antimicrobial resistant bacteria, several published reports have shown resistance to β-lactams, cephalosporins, aminoglycosides, fluoroquinolones, and tetracycline in bacterial isolates from other wild mammals including wild boars, micro-mammals (wild rodents), and wild rabbits [4, 6, 89].

AMR exchange and transmission between wildlife, human, and domestic animals cannot be corroborated from the reports of phenotypic AMR only and as such genetic data are required to prove the existence of interfaces for resistance exchange and transmission. The collection of all antimicrobial resistance genes and their precursors in pathogenic and non-pathogenic bacteria and also in antimicrobial producing-organisms is referred as the antimicrobial resistome, a concept that has been advanced to serve as a framework for understanding the ecology of resistance on a global scale [90]. We have documented reports of genetic determinants of AMR in bats such as carbapenemase producing genes (*bla*$_{OXA}$), ESBL genes (bla$_{TEM}$, bla$_{CTX}$, bla$_{SHV}$), gentamicin (*aac (3)-II, aac (3)-III*), tetracycline (*tetA, tetB*), streptomycin (*strA*), and sulphamethoxazole (*sul1, sul2*). Previous studies also reported ESBL, AmpC β-lactamase, carbapenemase, colistin, tetracycline, chloramphenicol, and sulfonamide resistance genes in Enterobacteriaceae isolates of wildlife origin such as in wild birds and boars [15, 91-94]. ESBL and carbapenemase producing pathogens conferring resistance to cephalosporins and carbapenem, are currently major concerns for the treatment of human and veterinary illness worldwide and have been frequently reported in wildlife [6, 13, 95, 96]. Though reported in low numbers in bats and other wild mammals, development of resistance in such mechanisms is frightening.

Antibiotics released into the environment can apply selective pressure, promoting horizontal transfer of resistant genes in environmental bacterial communities and in wildlife bacterial flora [97] [98]. Due to such reason, bats can also act as a carrier of antibiotic resistant genes and plasmids [50, 54, 99] and with their long distance flying and roaming capacities, they can transmit broadly those bacteria and genes in human and domesticated animal populations [35]. Still, the bat bacterial flora and their resistant profile are poorly understood [32]. The acquisition of AMR microorganisms by bats could be due to antimicrobial resistant pollution, as the resistant developed through the exposure of wildlife to human food remains, wastewater treatment plants, and aquaculture operations having antimicrobials residues [100]. So far, it appears that the emergence of AMR occurs under selection, mostly by antibiotics, however other components, such as heavy metals or biocides, may also play a role in the development of antimicrobial resistance. As a result, the presence of clinically relevant antimicrobial resistant genes and antibiotic-resistant bacteria in wild animals that are not getting antibiotics should be seen as a sign of antimicrobial resistant pollution [100-102].

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Like other wild mammals, bats usually do not build specific shelter rather they use natural caves and artificial habitats as resting or hibernating places, [103] but deforestation and food insecurity compel them to use urban and rural habitats such as buildings and ceilings as roosting and foraging sites for breeding [104]. Habituating near human and domestic animals increases the likelihood of direct and indirect contact and sharing microflora. Anthropogenic activities such as deforestation, hunting wild animals, and caving in areas where bats usually inhabitant increases the likelihood of infection associated with bats.

5. Conclusion

The present review provides an overview of available information on antimicrobial susceptibility profile of bacteria isolated from bats. The origin of AMR in wildlife is currently a major global health concern due to identification of emerging resistant pathogens as well as the occurrence of the frequent zoonotic pandemics such as COVID-19. The current COVID-19 pandemic has also triggered the global AMR situation as many COVID positive patients were found highly resistant towards antimicrobials 98. Thus prioritizing the concept of the OH issue, to improve health care for humans and animals, there is a clear need of AMR perception from wildlife or zoonotic point of view. We observed that bats are an unpredictable source of potential pathogenic and MDR bacteria, both Gram-positive and Gram-negative. Particularly, the prevalence of AMR genes (CTX, TEM, SHV) in bats is a major concern in regard to the AMR transmission dynamics in the wildlife-human-environment nexus. The rise of AMR during and following major pandemic events irrespective of causative pathogens requires strict vigilance of surveillance of zoonotic spillover events coupled with antibiotic susceptibility data. Extensive country- or region-specific OH studies to predict the direction and pattern of AMR in bats and wild animals need to be carried out for better policy adoption and stewardship program implementation.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Table S1: Summary of the included articles Table S2: Antibiotic resistance profile of E.coli isolates in bats Table S3: : Antibiotic resistance profile of bacterial isolates (except *E.coli*) in bats

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References

1. Anderson, M., et al., *A governance framework for development and assessment of national action plans on antimicrobial resistance.* The Lancet Infectious Diseases, 2019. **19**(11): p. e371-e384.
2. Murray, C.J., et al., *Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis.* The Lancet, 2022. **399**(10325): p. 629-655.

3. Bezerra-Santos, M.A., et al., *Illegal wildlife trade: a gateway to zoonotic infectious diseases.* Trends in parasitology, 2021. **37**(3): p. 181-184.
4. Furness, L.E., et al., *Wild small mammals as sentinels for the environmental transmission of antimicrobial resistance.* Environmental Research, 2017. **154**: p. 28-34.
5. Gharout-Sait, A., et al., *Occurrence of Carbapenemase-Producing Klebsiella pneumoniae in Bat Guano.* Microb Drug Resist, 2019. **25**(7): p. 1057-1062.
6. Torres, R.T., et al., *Wild boar as a reservoir of antimicrobial resistance.* Science of The Total Environment, 2020. **717**: p. 135001.
7. Hedman, H.D., K.A. Vasco, and L. Zhang, *A Review of Antimicrobial Resistance in Poultry Farming within Low-Resource Settings.* Animals (Basel), 2020. **10**(8).
8. Landers, T.F., et al., *A review of antibiotic use in food animals: perspective, policy, and potential.* Public Health Rep, 2012. **127**(1): p. 4-22.
9. Khan, S.A., et al., *Antimicrobial resistance pattern in domestic animal - wildlife - environmental niche via the food chain to humans with a Bangladesh perspective; a systematic review.* BMC Veterinary Research, 2020. **16**(1): p. 302.
10. Asante, J., A. Noreddin, and M.E. El Zowalaty, *Systematic Review of Important Bacterial Zoonoses in Africa in the Last Decade in Light of the 'One Health' Concept.* Pathogens, 2019. **8**(2).
11. Bonardi, S. and R. Pitino, *Carbapenemase-producing bacteria in food-producing animals, wildlife and environment: A challenge for human health.* Ital J Food Saf, 2019. **8**(2): p. 7956.
12. Dolejska, M. and C.C. Papagiannitsis, *Plasmid-mediated resistance is going wild.* Plasmid, 2018. **99**: p. 99-111.
13. Darwich, L., et al., *High prevalence and diversity of extended-spectrum β-lactamase and emergence of OXA-48 producing Enterobacterales in wildlife in Catalonia.* PLoS One, 2019. **14**(8): p. e0210686.
14. Ong, K.H., et al., *Occurrence and Antimicrobial Resistance Traits of Escherichia coli from Wild Birds and Rodents in Singapore.* Int J Environ Res Public Health, 2020. **17**(15).
15. Guyomard-Rabenirina, S., et al., *Antimicrobial Resistance in Wildlife in Guadeloupe (French West Indies): Distribution of a Single blaCTX–M–1/IncI1/ST3 Plasmid Among Humans and Wild Animals.* 2020. **11**(1524).
16. Asai, T., et al., *Antimicrobial susceptibility of Escherichia coli isolates obtained from wild mammals between 2013 and 2017 in Japan.* J Vet Med Sci, 2020. **82**(3): p. 345-349.
17. Ogden, N.H., P. AbdelMalik, and J. Pulliam, *Emerging infectious diseases: prediction and detection.* Can Commun Dis Rep, 2017. **43**(10): p. 206-211.
18. Zumla, A. and D.S.C. Hui, *Emerging and Reemerging Infectious Diseases: Global Overview.* Infect Dis Clin North Am, 2019. **33**(4): p. xiii-xix.
19. Singh, R.K., et al., *Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies - a comprehensive review.* Vet Q, 2019. **39**(1): p. 26-55.
20. Simonsen, L. and C. Viboud, *A comprehensive look at the COVID-19 pandemic death toll.* eLife, 2021. **10**: p. e71974.
21. Team, W.H.O.E.R., et al., *Ebola virus disease in West Africa--the first 9 months of the epidemic and forward projections.* The New England journal of medicine, 2014. **371**(16): p. 1481-1495.
22. Langford, B.J., et al., *Antibiotic susceptibility reporting and association with antibiotic prescribing: a cohort study.* Clin Microbiol Infect, 2021. **27**(4): p. 568-575.
23. Pelfrene, E., R. Botgros, and M. Cavaleri, *Antimicrobial multidrug resistance in the era of COVID-19: a forgotten plight?* Antimicrobial Resistance & Infection Control, 2021. **10**(1): p. 21.
24. Kreuder Johnson, C., et al., *Spillover and pandemic properties of zoonotic viruses with high host plasticity.* Scientific reports, 2015. **5**: p. 14830-14830.
25. Leroy, E.M., et al., *Human Ebola outbreak resulting from direct exposure to fruit bats in Luebo, Democratic Republic of Congo, 2007.* Vector Borne Zoonotic Dis, 2009. **9**(6): p. 723-8.
26. Luby, S.P., E.S. Gurley, and M.J. Hossain, *Transmission of human infection with Nipah virus.* Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 2009. **49**(11): p. 1743-1748.
27. Singh, R.K., et al., *Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies - a comprehensive review.* The veterinary quarterly, 2019. **39**(1): p. 26-55.
28. Mohd, H.A., J.A. Al-Tawfiq, and Z.A. Memish, *Middle East Respiratory Syndrome Coronavirus (MERS-CoV) origin and animal reservoir.* Virol J, 2016. **13**: p. 87.
29. Prompetchara, E., C. Ketloy, and T. Palaga, *Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic.* Asian Pac J Allergy Immunol, 2020. **38**(1): p. 1-9.
30. Zhou, P., et al., *A pneumonia outbreak associated with a new coronavirus of probable bat origin.* Nature, 2020.
31. Allocati, N., et al., *Bat – man disease transmission : zoonotic pathogens from wildlife reservoirs to human populations.* Nature Publishing Group, 2016(May).
32. Nowakiewicz, A., et al., *Bats as a reservoir of resistant Escherichia coli: A methodical view. Can we fully estimate the scale of resistance in the reservoirs of free-living animals?* Res Vet Sci, 2020. **128**: p. 49-58.
33. Cláudio, V.C., et al., *Bacteria richness and antibiotic-resistance in bats from a protected area in the Atlantic Forest of Southeastern Brazil.* PLoS One, 2018. **13**(9): p. e0203411.
34. Mbehang Nguema, P.P., et al., *Characterization of ESBL-Producing Enterobacteria from Fruit Bats in an Unprotected Area of Makokou, Gabon.* 2020. **8**(1): p. 138.

35. Sens-Junior, H., et al., *Bacterial resistance in bats from the Phyllostomidae family and its relationship with unique health.* 2018. **38**(6): p. 1207-1216.
36. Allocati, N., et al., *Bat-man disease transmission: zoonotic pathogens from wildlife reservoirs to human populations.* Cell Death Discov, 2016. **2**: p. 16048.
37. Ouzzani, M., et al., *Rayyan—a web and mobile app for systematic reviews.* Systematic reviews, 2016. **5**(1): p. 1-10.
38. Page, M.J., et al., *PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews.* bmj, 2021. **372**.
39. WHO. *WHO priority pathogens list for R&D of new antibiotics.* [cited 2022 22.09.2022]; Available from: https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed.
40. Benavides, J.A., et al., *Extended-spectrum beta-lactamase-producing Escherichia coli in common vampire bats Desmodus rotundus and livestock in Peru.* Zoonoses Public Health, 2018. **65**(4): p. 454-458.
41. McDougall, F.K., et al., *Novel strains of Klebsiella africana and Klebsiella pneumoniae in Australian fruit bats (Pteropus poliocephalus).* Res Microbiol, 2021. **172**(7-8): p. 103879.
42. Graves, S., et al., *Antibiotic-resistance patterns of enteric bacteria of wild mammals on the Krakatau Islands and West Java, Indonesia.* Philosophical Transactions of the Royal Society of London. B, Biological Sciences, 1988. **322**(1211): p. 339-353.
43. Apun, K., et al., *Antimicrobial susceptibilities of Escherichia coli isolates from food animals and wildlife animals in Sarawak, East Malaysia.* Asian Journal of Animal and Veterinary Advances, 2008. **3**(6): p. 409-416.
44. Obi, T., et al., *Antimicrobial susceptibility in enterobacteriaceae recovered from Okinawa least horseshoe bat rhinolophus pumilus.* Wildlife Biology, 2014. **20**(1): p. 64-66.
45. Oluduro, A.O., *Antibiotic - resistant commensal Escherichia coli in faecal droplets from bats and poultry in Nigeria.* 2012. **48**(3): p. 297-308.
46. Nowak, K., et al., *Highly diverse and antimicrobial susceptible Escherichia coli display a na ï ve bacterial population in fruit bats from the Republic of Congo.* 2017. **2**: p. 1-18.
47. Afiukwa Ngozi, et al., *A three-year study on the prevalence and antibiotic susceptibility pattern of Escherichia coli isolated from cloacal swabs of wild and domestic birds in Ebonyi State, Nigeria.* EC Microbiology, 2018. **14**(5): p. 266-273.
48. Hassell, J.M., et al., *Clinically relevant antimicrobial resistance at the wildlife–livestock–human interface in Nairobi: an epidemiological study.* The Lancet Planetary Health, 2019. **3**(6): p. e259-e269.
49. Mbehang Nguema, P.P., et al., *Characterization of ESBL-Producing Enterobacteria from Fruit Bats in an Unprotected Area of Makokou, Gabon.* Microorganisms, 2020. **8**(1).
50. Oluduro, A.O., *Antibiotic-resistant commensal Escherichia coli in faecal droplets from bats and poultry in Nigeria.* Vet Ital, 2012. **48**(3): p. 297-308.
51. Oladiran, F., et al., *Molecular Characterization of Resistance and Virulence Genes in Escherichia coli Isolated from Bats (Eidolon helvum) Faeces in Osun State, Nigeria.* Journal of Advances in Microbiology, 2022. **22**(2): p. 37-48.
52. Obodoechi, L.O., et al., *Antimicrobial resistance in Escherichia coli isolates from frugivorous (Eidolon helvum) and insectivorous (Nycteris hispida) bats in Southeast Nigeria, with detection of CTX-M-15 producing isolates.* Comp Immunol Microbiol Infect Dis, 2021. **75**: p. 101613.
53. Oladiran, F., et al., *Molecular Characterization of Resistance and Virulence Genes in Escherichia coli Isolated from Bats (Eidolon helvum) Faeces in Osun State, Nigeria.* Journal of Advances in Microbiology, 2022: p. 37-48.
54. Garces, A., et al., *First report on extended-spectrum beta-lactamase (ESBL) producing Escherichia coli from European free-tailed bats (Tadarida teniotis) in Portugal: A one-health approach of a hidden contamination problem.* J Hazard Mater, 2019. **370**: p. 219-224.
55. Skok, S., et al., *Antimicrobial resistant Escherichia coli from karst waters, surfaces and bat guano in Slovenian caves.* J Acta Carsologica, 2020. **49**(2-3).
56. Gerbáčová, K., et al., *The Faecal Microbiome of Building-Dwelling Insectivorous Bats (Myotis myotis and Rhinolophus hipposideros) also Contains Antibiotic-Resistant Bacterial Representatives.* Current Microbiology, 2020. **77**(9): p. 2333-2344.
57. Garcês, A., et al., *Detection of antimicrobial resistance in faecal Escherichia coli from European free-tailed bats (Tadarida teniotis) in Portugal.* J Acta Chiropterologica, 2019(2): p. 403-409, 7.
58. Souza, V., et al., *Genetic structure of natural populations of Escherichia coli in wild hosts on different continents.* Appl Environ Microbiol, 1999. **65**(8): p. 3373-85.
59. Iovine Rde, O., et al., *Isolation of Escherichia coli and Salmonella spp. from free-ranging wild animals.* Braz J Microbiol, 2015. **46**(4): p. 1257-63.
60. Benavides, J.A., et al., *Long-term maintenance of multidrug-resistant Escherichia coli carried by vampire bats and shared with livestock in Peru.* Science of The Total Environment, 2022. **810**: p. 152045.
61. Adesiyun, A.A., A. Stewart-Johnson, and N.N. Thompson, *Isolation of enteric pathogens from bats in Trinidad.* J Wildl Dis, 2009. **45**(4): p. 952-61.
62. McDougall, F.K., W.S.J. Boardman, and M.L. Power, *Characterization of beta-lactam-resistant Escherichia coli from Australian fruit bats indicates anthropogenic origins.* Microb Genom, 2021. **7**(5).
63. Sens-Junior, H., et al., *Bacterial resistance in bats from the Phyllostomidae family and its relationship with unique health.* Pesquisa Veterinária Brasileira, 2018. **38**: p. 1207-1216.
64. Islam, A., et al., *Isolation of Salmonella Virchow from a fruit bat (Pteropus giganteus).* Ecohealth, 2013. **10**(4): p. 348-51.
65. McDougall, F. and M. Power, *Occurrence of Salmonella enterica in grey-headed flying foxes from New South Wales.* Aust Vet J, 2021. **99**(12): p. 517-521.

66. Ur Rahman, S., et al., *The Growing Genetic and Functional Diversity of Extended Spectrum Beta-Lactamases.* Biomed Res Int, 2018. **2018**: p. 9519718.
67. Luo, Q., Y. Wang, and Y. Xiao, *Prevalence and transmission of mobilized colistin resistance (mcr) gene in bacteria common to animals and humans.* Biosafety and Health, 2020. **2**(2): p. 71-78.
68. Mahmud, Z.H., et al., *Extended-Spectrum Beta-Lactamase-Producing Escherichia coli in Drinking Water Samples From a Forcibly Displaced, Densely Populated Community Setting in Bangladesh.* Front Public Health, 2020. **8**: p. 228.
69. Beigverdi, R., et al., *Prevalence of extended-spectrum β-lactamase-producing Klebsiella pneumoniae: First systematic review and meta-analysis from Iran.* J Glob Antimicrob Resist, 2019. **18**: p. 12-21.
70. Abrar, S., et al., *Distribution of bla CTX - M , bla TEM , bla SHV and bla OXA genes in Extended-spectrum-beta-lactamase-producing Clinical isolates: A three-year multi-center study from Lahore, Pakistan.* Antimicrob Resist Infect Control, 2019. **8**: p. 80.
71. Elbediwi, M., et al., *Global Burden of Colistin-Resistant Bacteria: Mobilized Colistin Resistance Genes Study (1980-2018).* Microorganisms, 2019. **7**(10).
72. Kuralayanapalya, S.P., et al., *Prevalence of extended-spectrum beta-lactamase producing bacteria from animal origin: A systematic review and meta-analysis report from India.* PLoS One, 2019. **14**(9): p. e0221771.
73. Selvin, J., et al., *Culture-dependent and metagenomic analysis of lesser horseshoe bats' gut microbiome revealing unique bacterial diversity and signatures of potential human pathogens.* Microb Pathog, 2019. **137**: p. 103675.
74. Doernberg, S.B., et al., *Gram-Positive Bacterial Infections: Research Priorities, Accomplishments, and Future Directions of the Antibacterial Resistance Leadership Group.* Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 2017. **64**(suppl_1): p. S24-S29.
75. Vandžurová, A., et al., *Staphylococcus nepalensis in the guano of bats (Mammalia).* Vet Microbiol, 2013. **164**(1-2): p. 116-21.
76. Olatimehin, A., et al., *Staphylococcus aureus Complex in the Straw-Colored Fruit Bat (Eidolon helvum) in Nigeria.* Front Microbiol, 2018. **9**: p. 162.
77. Akobi, B., et al., *Characterization of Staphylococcus aureus isolates from faecal samples of the Straw-Coloured Fruit Bat (Eidolon helvum) in Obafemi Awolowo University (OAU), Nigeria.* BMC Microbiol, 2012. **12**: p. 279.
78. de Jong, C.E., et al., *Collection, seminal characteristics and chilled storage of spermatozoa from three species of free-range flying fox (Pteropus spp.).* Theriogenology, 2005. **64**(5): p. 1072-1089.
79. Fountain, K., et al., *DIVERSITY OF STAPHYLOCOCCAL SPECIES CULTURED FROM CAPTIVE LIVINGSTONE'S FRUIT BATS (PTEROPUS LIVINGSTONII) AND THEIR ENVIRONMENT.* J Zoo Wildl Med, 2019. **50**(1): p. 266-269.
80. García, L.A., et al., *Staphylococcus Spp. from Wild Mammals in Aragón (Spain): Antibiotic Resistance Status.* J Vet Res, 2020. **64**(3): p. 373-379.
81. Nowakiewicz, A., et al., *Analysis of the occurrence and molecular characteristics of drug-resistant strains of Enterococcus faecalis isolated from the gastrointestinal tract of insectivorous bat species in Poland: A possible essential impact on the spread of drug resistance?* Environmental Pollution, 2021. **269**: p. 116099.
82. García, L.A., et al., *Antimicrobial resistance of species isolated from wild mammals in Aragón, Spain.* Journal of Veterinary Research, 2022.
83. O'Mahony, R., et al., *Methicillin-resistant Staphylococcus aureus (MRSA) isolated from animals and veterinary personnel in Ireland.* Vet Microbiol, 2005. **109**(3-4): p. 285-96.
84. Walther, B., et al., *Methicillin-resistant Staphylococcus aureus (MRSA) isolated from small and exotic animals at a university hospital during routine microbiological examinations.* Vet Microbiol, 2008. **127**(1-2): p. 171-8.
85. Elsohaby, I., et al., *Migratory Wild Birds as a Potential Disseminator of Antimicrobial-Resistant Bacteria around Al-Asfar Lake, Eastern Saudi Arabia.* Antibiotics (Basel), 2021. **10**(3).
86. Ikhimiukor, O.O., et al., *A bottom-up view of antimicrobial resistance transmission in developing countries.* Nature Microbiology, 2022. **7**(6): p. 757-765.
87. Benklaouz, M.B., H. Aggad, and Q. Benameur, *Resistance to multiple first-line antibiotics among Escherichia coli from poultry in Western Algeria.* Vet World, 2020. **13**(2): p. 290-295.
88. Organization, W.H., *Executive summary: the selection and use of essential medicines 2019: report of the 22nd WHO Expert Committee on the selection and use of essential medicines: WHO Headquarters, Geneva, 1-5 April 2019*. 2019, World Health Organization.
89. Zanardi, G., et al., *Wild Micromammals as Bioindicators of Antibiotic Resistance in Ecopathology in Northern Italy.* Animals (Basel), 2020. **10**(7).
90. Wright, G.D., *The antibiotic resistome: the nexus of chemical and genetic diversity.* Nat Rev Microbiol, 2007. **5**(3): p. 175-86.
91. Wang, J., et al., *The role of wildlife (wild birds) in the global transmission of antimicrobial resistance genes.* Zool Res, 2017. **38**(2): p. 55-80.
92. Poeta, P., et al., *Wild boars as reservoirs of extended-spectrum beta-lactamase (ESBL) producing Escherichia coli of different phylogenetic groups.* Journal of Basic Microbiology, 2009. **49**(6): p. 584-588.
93. Alcalá, L., et al., *Wild Birds, Frequent Carriers of Extended-Spectrum β-Lactamase (ESBL) Producing Escherichia coli of CTX-M and SHV-12 Types.* Microb Ecol, 2016. **72**(4): p. 861-869.
94. Bachiri, T., et al., *First Report of the Plasmid-Mediated Colistin Resistance Gene mcr-1 in Escherichia coli ST405 Isolated from Wildlife in Bejaia, Algeria.* Microb Drug Resist, 2018. **24**(7): p. 890-895.
95. Ahlstrom, C.A., et al., *Repeated Detection of Carbapenemase-Producing Escherichia coli in Gulls Inhabiting Alaska.* Antimicrob Agents Chemother, 2019. **63**(8).

 doi:10.20944/preprints202211.0183.v1

96. Guenther, S., C. Ewers, and L.H. Wieler, *Extended-Spectrum Beta-Lactamases Producing E. coli in Wildlife, yet Another Form of Environmental Pollution?* Front Microbiol, 2011. **2**: p. 246.
97. Allen, H.K., et al., *Call of the wild: antibiotic resistance genes in natural environments.* Nature Reviews Microbiology, 2010. **8**(4): p. 251-259.
98. Ashbolt, N.J., et al., *Human health risk assessment (HHRA) for environmental development and transfer of antibiotic resistance.* Environmental health perspectives, 2013. **121**(9): p. 993-1001.
99. McDougall, F., et al., *Bats as reservoirs of antibiotic resistance determinants: A survey of class 1 integrons in Grey-headed Flying Foxes (Pteropus poliocephalus).* Infect Genet Evol, 2019. **70**: p. 107-113.
100. Kraemer, S.A., A. Ramachandran, and G.G. Perron, *Antibiotic Pollution in the Environment: From Microbial Ecology to Public Policy.* Microorganisms, 2019. **7**(6).
101. Laborda, P., et al., *Wildlife and Antibiotic Resistance.* Front Cell Infect Microbiol, 2022. **12**: p. 873989.
102. Singer, A.C., et al., *Review of Antimicrobial Resistance in the Environment and Its Relevance to Environmental Regulators.* Front Microbiol, 2016. **7**: p. 1728.
103. Leivers, S.J., et al., *External temperature and distance from nearest entrance influence microclimates of cave and culvert-roosting tri-colored bats (Perimyotis subflavus).* Ecol Evol, 2019. **9**(24): p. 14042-14052.
104. Voigt, C.C., et al., *Bats and Buildings: The Conservation of Synanthropic Bats*, in *Bats in the Anthropocene: Conservation of Bats in a Changing World*, C.C. Voigt and T. Kingston, Editors. 2016, Springer International Publishing: Cham. p. 427-462.