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### ► To cite this version:

David Lupande-Mwenebitu, Sophie Alexandra Baron, Larbi Zakaria Nabti, Octavie Lunguya-Metila, Jean-Philippe Lavigne, et al.. Current status of resistance to antibiotics in the Democratic Republic of the Congo: A review. *Journal of Global Antimicrobial Resistance*, 2020, 22, pp.818-825. 10.1016/j.jgar.2020.07.008 . hal-03149719

**HAL Id: hal-03149719**

**<https://amu.hal.science/hal-03149719>**

Submitted on 22 Aug 2022

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1 **Current status of resistance to antibiotics in Democratic Republic of Congo: a Review**

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21 **Keywords:** Antimicrobial resistance genes, Democratic Republic of Congo,

22 *Enterobacteriaceae*, Extended-spectrum  $\beta$ -lactamases, methicillin-resistant *Staphylococcus*

23 *aureus*.

24

25 **Abstract**

26 An overview of the literature was conducted to assess prevalence and mechanisms of  
27 antibiotic resistance to date, mainly to  $\beta$ -lactam antibiotics, cephalosporins, carbapenems,  
28 colistin and tigecycline in DR Congo. English and French publications were listed and  
29 analysed using PubMed/Medline, Google Scholar and African Journals database between  
30 January 1<sup>st</sup>, 1990 and December 31, 2019. For the 30 published articles found: i) Bacterial  
31 resistance to antibiotics concerned both Gram-negative and Gram-positive bacteria; ii)  
32 Multidrug resistance prevalence was the same in half of *Streptococcus pneumoniae* isolates;  
33 iii) A worrying prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) was noted,  
34 associated with co-resistance to several other antibiotics; iv) Resistance to 3rd generation  
35 cephalosporins was very high in *Enterobacteriaceae*, mainly due to *bla*<sub>CTX-M-1</sub> group and  
36 *bla*<sub>SHV</sub> genes. Data on carbapenem and colistin resistance were not available until now.  
37 Further work is required to set up a surveillance system for antibiotic resistance in this  
38 country.

39

## 40 **Introduction**

41           There is a growing concern on antimicrobial resistance (AMR) worldwide [1].  
42 Resistance against antimicrobial agents in clinically relevant bacteria is one of the most  
43 imminent threats to public health and especially to our most vulnerable patient populations  
44 [2,3]. The treatment of bacterial infections in Africa is largely empirical and, in most  
45 instances, there are no laboratory results to guide therapy [4,5]. The spread of AMR bacteria is  
46 problematic for the medical community as a whole as it compromises empirical treatment  
47 regimens by delaying the administration of appropriate antibiotic therapy and reducing  
48 appropriate treatment options [6,7]. AMR remains a real challenge in resource-limited  
49 countries due to a lack of available antibiotics with multidrug-resistant isolates being labelled  
50 on the basis of a small number of antibiotics tested, with economic consequences and yet the  
51 use of the old molecules is very effective. The consequences of AMR are not limited to  
52 patients with infections, but to a whole system including the environmental and agro-pastoral  
53 sector that hemming enough resistance genes. Hence, there is a need for action to significantly  
54 reduce the expansion of the phenomenon, whose distribution varies considerably from one  
55 country to another [8,9]. To combat the global threat of AMR, improved surveillance to detect  
56 emerging and long-term resistance trends is vital, several global initiatives, such as the  
57 Fleming Fund, have been recently established to improve laboratory capacity in low- and  
58 middle-income countries [10].

59           As recently reported, there is a link between antibiotic resistance genes found in  
60 human pathogens and those found in non-pathogenic, commensal and environmental  
61 organisms, prompting further studies of natural and human-associated reservoirs of resistance  
62 genes [11]. Many hypotheses can be evoked, even though the relationship between antibiotic  
63 use and antibiotic resistance remains complex [12]. Resistance selection pressure continues as

64 antimicrobials are released into the environment, largely while remaining in their active  
65 forms. These drugs frequently found in wastewater for example contributed greatly to the  
66 environmental selection of antibiotic-resistant bacteria [13-17]. As reported by many health  
67 care settings, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*  
68 have been identified as emerging organisms of concern for multidrug resistance, and have  
69 encouraged researches in this area [18,19]. Resistance to antibiotics is the result of either by  
70 reducing its affinity, lowering its concentration, or destroying it in order to effectively reduce  
71 or cancel the interaction with its target [20]. Therefore, depending on the involved  
72 mechanism, the resistance level can vary considerably [21].

73 Over the past decade, the increase in multidrug resistance of Gram-negative rods and  
74 in particular the spread of resistance to carbapenems in *Enterobacteriaceae*, *Pseudomonas*  
75 *spp.* and *Acinetobacter spp.*, has prompted the return of colistin (or polymyxin E) as a  
76 treatment of last resort. Extended-spectrum  $\beta$ -lactamase (ESBL)-producing pathogens and  
77 methicillin resistant *Staphylococcus aureus* (MRSA) are endemic in many hospitals  
78 worldwide and are also increasingly detected in the community [22-25]. Carbapenem-resistant  
79 enterobacterial infections (CRE) are being increasingly observed, mainly in health care  
80 facilities, but also in the community; they are associated with management difficulties due to  
81 the lack of alternative active molecules and cause outbreaks difficult to control in health care  
82 facilities in low-income countries where hygiene is poor and the population is overcrowded,  
83 in addition to an epidemic context of ESBL that was still not effectively controlled [26].

84

## 85 **Challenge of humanitarian disaster, infectious diseases and AMR spread in war context**

86 In Democratic Republic of Congo (DRC), data on AMR are scarce; some bacteria are  
87 being included in surveillance cross sectional study, such as *Salmonella* spp. and *S. aureus*,  
88 but there are unknown prospects focused on other bacteria and in many parts of the country  
89 [27,28]. The DRC is a vast country (2.3 million km of area) divided into 26 provinces. Each  
90 province is divided into health districts, which in turn are divided into health zones (called  
91 “zones de santé”). A health zone in the DRC corresponds to what is internationally referred to  
92 as a health district [29]. The conflict in DRC has resulted in a health-system collapse and  
93 created a humanitarian disaster. An estimated 5.4 million excess deaths occurred from 1997 to  
94 2004, with fewer than 10% attributable to violence and the rest to preventable and treatable  
95 medical conditions, such as malaria, diarrhea, pneumonia, and malnutrition [30]. Armed  
96 conflicts and other disastrous natural phenomena can lead to major population displacements.  
97 An emergency unsustainable infrastructure is temporarily built, and often with overcrowding,  
98 insufficient if not insufficient drinking water and sanitation, which gives its populations a risk  
99 of exposure to communicable diseases, especially those with epidemic potential [31]. The  
100 country had been the site of two wars involving multiple African nations and armed conflict  
101 between rebels and soldiers for the past 16 years, characterized by extreme violence, massive  
102 population displacements from east to west, and the collapse of all existing infrastructure  
103 [32,33]. Massive population movements are at the root of most risk factors, people are  
104 displaced to regions and areas where resources and services are insufficient and where contact  
105 with other naïve populations with new vectors of infectious diseases is potentially more  
106 frequent. This leads to large numbers of people going to camps, often associated with  
107 overcrowding, inadequate housing and poor water conditions, resulting in the spread of  
108 pathogenic microorganisms, as reported by UNHCR in January 2018 in Eastern Congo (**Fig.**  
109 **1**) [34,35].

110 The deterioration of health services is probably one of the main risk factors for communicable  
111 diseases in this type of humanitarian disaster, both for individuals and populations. Access to  
112 health care in such conditions is impossible, which is a key risk factor for the serious  
113 progression of most communicable diseases in the individual. As the spread and detection of  
114 cases becomes a major challenge, emergency measures to be implemented remain  
115 unavailable, including public health services, vaccination, communicable disease prevention  
116 and control measures and surveillance, making epidemics more likely, more difficult to detect  
117 and more difficult to control [35,36].

118

## 119 **Review methods**

120 For this review, we searched PubMed/Medline, Google Scholar and African Journals for  
121 articles written in French and in English on bacterial resistance to antibiotics in DR Congo.  
122 We used the search terms “bacterial resistance”, “antibiotic and resistance”, “antimicrobial  
123 resistance”, “microbial resistance”, “susceptibility”, “resistance” combined with the name of  
124 Democratic Republic of Congo. We screened the search results for relevant, methodologically  
125 rigorous studies and conducted a forward search of the references of many of the relevant  
126 results to identify additional studies. Articles were reviewed and publications using original  
127 data on antibiotics resistance in humans and environment samples were included. The studies  
128 site, study period, organism isolated, the resistance phenotype observed, the molecular  
129 methodology used as well as the antimicrobial resistance genes found were appraised and  
130 analysed. This review on antibacterial resistance in DRC focuses on available published  
131 literature on the subject dating from 1990 to December 31<sup>st</sup>, 2019.

132

## 133 **Resistance pattern among Gram-negative and Gram-positive bacteria**

### 134 *Enterobacteriaceae:*

135 For *Enterobacteriaceae*, the emergence and spread of CTX-M type ESBLs are global, with  
136 the highest prevalence observed in low-income countries, particularly in the community with  
137 an estimated carrying prevalence of 70%, 35% and 15% respectively in Asia, the Eastern  
138 Mediterranean Basin and Africa [24].

### 139 *Salmonella*

140 *Salmonella* spp. is the most studied bacterial genus in DRC as a result of the research  
141 set up and is still ongoing since 2008 on bacteremia. Indeed, since the first publications on  
142 bacteremia, the prevalence of resistance to ampicillin, chloramphenicol and cotrimoxazole are  
143 particularly high (90 – 100%) [37,38]. The most frequently isolated species are *Salmonella*  
144 *enteritidis*, *Salmonella typhimurium* and *Salmonella* Typhi. The level of resistance is as high  
145 for *S. Typhi* as it is for non-Typhi *Salmonella* (NTS). Ampicillin, chloramphenicol and  
146 cotrimoxazole are no longer susceptible in more than 70% of isolates [38,39,40]. For  
147 Muyembe et al. in 2009, all isolates (11 isolates) of *S. Typhi* were resistant to ampicillin and  
148 cotrimoxazole [41]. Finally, a decreased susceptibility to ciprofloxacin was also observed  
149 between 59 to 65% [42,43,44]. Several resistance genes were detected in *Salmonella* spp.  
150 strains isolated from DRC including, *bla*<sub>TEM-1b</sub> and *bla*<sub>SHV-2a</sub> genes [27,37,43]. Moreover, *S.*  
151 *Typhi* harboring *bla*<sub>CTX-M</sub> genes has been described in blood cultures in a bacteremic patient in  
152 2018 [45]. Resistance to chloramphenicol, aminoglycosides, quinolones and sulfonamides is  
153 correlated to the presence of *catA1*, *strA/B*, *sul1*, *dfrA1* genes and the *aac(6')-Iaa* gene  
154 [37,40]. Some mutations on *gyrA* gene, as well as the presence of *qnrB1* and *aac(6')-Ib-cr*  
155 genes were found in strains resistant to fluoroquinolones (Table 1 and Table 2). Puyvelde et

156 al., in 2019, analysed the entire genome of 81 strains of *S. typhimurium* by high-throughput  
157 sequencing. They reported that 67% of the isolates (54/81) were ESBL-producers and 63%  
158 were multidrug resistant (MDR), according to the definition used for *Salmonella* spp., i.e.  
159 resistant to both ampicillin, chloramphenicol and cotrimoxazole. Several resistances genes  
160 were found, including *catA*, *bla*<sub>TEM-1</sub>, *bla*<sub>SHV-2A</sub>, *dfrA*, *dfrA1*, *dfrA14*, *mphA* and a mutation in  
161 the *gyrA* gene (S83Y) [46]. Bieke et al., in 2019, analysed 295 *S. Typhi*, 93 of which were  
162 sequenced (WGS): 38.4% (114/295) were resistant to ampicillin, chloramphenicol and  
163 cotrimoxazole; 24.5% (73/295) had decreased sensitivity to ciprofloxacin, mainly due to  
164 mutations detected in the *gyrA* (S83E, S83Y, D87Y, D87G, A119E) and *gyrB* (E466D,  
165 S464Y) genes [47].

## 166 *Escherichia coli*

167 *E. coli* is one of the most isolated microorganisms in bacteriology laboratories. A  
168 single emerging clonal group of *E. coli*, designated sequence type 131 (ST131) by multilocus  
169 sequence typing, has been identified as a factor in the AMR epidemic in *E. coli*, especially for  
170 first-line agents such as fluoroquinolones and extended-spectrum cephalosporins. *E. coli*  
171 contains a wide array of genetic diversity, most notably among genes that confer virulence  
172 and resistance [48,49]. In DRC, five studies carried out in 2001, 2014 and 2015 showed that  
173 the resistance rates of *E. coli* varied from 65 to 90% to penicillin [42,50,51], from 6 to 15% to  
174 ceftriaxone and 15.4% to 31.5% to ciprofloxacin [52,53]. For studies in which resistance  
175 genes were sought, the *bla*<sub>CTX-M-15</sub> and *bla*<sub>SHV-18</sub> genes were reported (Table 1) [53,54]. In  
176 Bukavu, a recent study conducted in 2019 by Irengue et al. using whole genome sequencing of  
177 21 *E. coli* strains showed that 33% of the strains (7 out of the 21 *E. coli*) belonged to ST131  
178 and exhibited more virulence genes as compared to compared to the same clone in the NCBI  
179 database. The majority of ESBL genes included *bla*<sub>CTX-M-15</sub> and *bla*<sub>SHV-12</sub> in all the isolates.

180 Several other AMR genes have been found including *bla*<sub>OXA-1</sub>, *bla*<sub>TEM-1</sub>, as well as genes  
181 encoding resistance to aminoglycosides, quinolones, chloramphenicol, rifampicin,  
182 tetracyclines and sulfonamides. As a matter of fact, *bla*<sub>CTX-M-15</sub> gene is the most frequently  
183 found ESBL gene among African hospital strains [55,56].

#### 184 ***Klebsiella pneumoniae***

185 *K. pneumoniae* is a frequent cause of nosocomial infections and has also emerged as an  
186 agent of severe community-acquired infections, including pyogenic liver abscess, pneumonia,  
187 and meningitis. *K. pneumoniae* clinical isolates are evolving toward increasing levels of  
188 antimicrobial drug resistance, placing this species among the infectious bacterial pathogens  
189 that are most challenging to control [57]. In a study on urinary tract infection aetiologies in  
190 Bukavu, Leonid et al. found that *K. pneumoniae* was the second most frequently identified  
191 microorganism after *E. coli* [53]. Its resistance profile in studies published in the DRC in 2012  
192 and 2015 showed a resistance rate of less than 35% for both amoxicillin/clavulanate acid  
193 (14%-19%), ceftriaxone (14% -19%) and ciprofloxacin (12%-33%). One out of the 21 strains  
194 of *K. pneumoniae* was phenotypically resistant to imipenem. No further studies were  
195 performed to screen for the carbapenemase genes. Studies have shown that the use of  
196 carbapenems promotes the emergence of carbapenemase-producing isolates. In Bukavu, the  
197 use of these molecules is increasingly becoming part of the therapeutic arsenal of clinicians  
198 [58]. The resistance genes described for *K. pneumoniae* in DRC are the *bla*<sub>CTX-M-15</sub> and  
199 *bla*<sub>SHV-18</sub> genes, as previously reported for *E. coli* [52,54,59].

#### 200 **Others Gram-negative bacteria (including non-fermenting rods)**

201 The available data do not allow the resistance profile of these other bacteria to be  
202 established, given the small number of isolates tested (Table 2). Those microorganisms are  
203 *Citrobacter freundii*, *Enterobacter* spp., and *Proteus* spp. *Enterobacter cloacae* is an

204 opportunistic pathogen that can cause several types of infections in the lower respiratory tract,  
205 surgical sites, urinary tract and central nervous system. Moreover, this species is frequently  
206 associated with nosocomial infections during outbreaks, emphasizing the need for rapid  
207 detection and typing of such pathogens. *C. freundii* is considered a commensal of the  
208 intestinal tract of humans and other animals. However, this species can also cause diarrhea  
209 and other infections in humans [60,61]. De Boeck et al. in Kinshasa reported the presence of  
210 *bla*<sub>CTX-M-15</sub>, *bla*<sub>SHV-18</sub> and *bla*<sub>SHV-2-like</sub> genes in *C. freundii* and *E. cloacae* strains,  
211 demonstrating that the two ESBL genes are widely disseminated in *Enterobacteriaceae*  
212 [54,59]. In a recent study conducted by Leonid et al., out of the 78 analysed strains of *Vibrio*  
213 *cholerae*, all were resistant to cotrimoxazole and nalidixic acid, 12% (9/78) had reduced  
214 susceptibility to ciprofloxacin and 14% (11/78) were resistant to ampicillin. They were still  
215 sensitive to chloramphenicol and tetracyclines. Many AMR genes were detected (Tab. 1) [62].  
216 Finally, there are no data available on the occurrence and resistance profile of non-fermenting  
217 Gram-negative bacilli in RDC.

## 218 **Resistance pattern among Gram-positive bacteria**

### 219 *Staphylococcus aureus*

220 *S. aureus* is one of major human pathogens, associated with wide spectrum of  
221 localized or systemic infections including wound infections, osteomyelitis, food poisoning,  
222 endocarditis, as well as more serious illnesses, such as pneumonia and bacteremia [63,64]. In  
223 RDC, the prevalence of bacterial infections caused by methicillin-resistant *S. aureus* (MRSA)  
224 varied from 16 to 64% [28,44,65,66,67], which is similar to the prevalence reported in other  
225 African countries [68]. The reported prevalences of antibiotics resistance are as follows: 33 to  
226 72 % against to tetracyclines, 5 to 54 % against cotrimoxazole, 31 % against gentamicin, 26 to  
227 69% against erythromycin and 20 to 59% against ciprofloxacin [28,44,66].

## 228 ***Streptococcus pneumoniae***

229 *S. pneumoniae* is the leading cause of pneumonia and bacterial meningitis. It is  
230 commonly encountered in children and in immunocompromised and elderly populations and  
231 it has considerable implications for healthcare systems worldwide [69]. To date, multidrug-  
232 resistant *S. pneumoniae* (MDR-SP) have been isolated from both adults and children around  
233 the world. These isolates are resistant to penicillin, clindamycin, cotrimoxazole and  
234 erythromycin [70]. In DRC, a study performed on 23 *S. pneumoniae* isolates, showed that the  
235 prevalence of penicillin resistance was 34%, 21% to cotrimoxazole and 13% to cefuroxime  
236 (Table 2) [71]. Serotyping had not been completed, yet it would give us valuable information  
237 on circulating strains depending on the vaccine used. A recent study of 163 nasal carriage  
238 isolates of *S. pneumoniae* in children under 60 months of age reported 62% (n=101) of  
239 resistance to penicillin G, 42% (n=68) to ampicillin, and 37% (n=61) to ceftriaxone. Almost  
240 all strains were resistant to cotrimoxazole (94%) and 43% (n=70) were resistant to more than  
241 three classes of antibiotics [72].

## 242 **Perspectives**

243 Surrounded by nine neighboring countries, the DRC faces many security and health  
244 challenges, including population movement, high mortality rates and recurrent endemic  
245 diseases, which make it impossible for the health system to make antibiotic resistance a  
246 priority. With an annual budget of about US\$6 billion, 1.2% of which is allocated to the  
247 health sector, for a population estimated at 85 million [73]. Despite the existence of 39  
248 officially recognized medical schools, most of which are located in urban areas, the training  
249 of clinical microbiologists remains a real problem because entirely self-financed, so that the  
250 number of microbiologists is very low in relation to actual needs [29]. The DRC is almost last  
251 with its human development index (168/169), public spending on health is among the lowest

252 with two dollars per capita. In this context of advanced poverty, investment in laboratory  
253 materials and other diagnostic equipments for infectious diseases is therefore impossible. The  
254 WHO recommends a minimum of \$35 per capita to safeguard a country's population [74]. Out  
255 of the 424 hospitals in the country, very few have organized a microbiology service due to  
256 lack of electricity, infrastructure and especially qualified personnel, as the only university in  
257 the country that trains them markets 2 to 4 clinical microbiologists per year [75]. The serious  
258 threat of antibiotic resistance in the DRC is the ineffectiveness of the antibacterial molecules  
259 available on the market, which means that the use of old molecules which prove to be more  
260 active with multidrug resistant isolates elsewhere should quickly orient the regulatory  
261 authorities to change procurement policies.

262 In light of these challenges, there is an urgent need to create collaborative networks  
263 with all microbiology laboratories across the country, which will then be linked to external  
264 laboratories to effectively address the AMR problem.

265

## 266 **Conclusion**

267 This review summarizes the current state of our knowledge regarding antimicrobial  
268 susceptibility of the common organisms causing serious community and hospital-acquired  
269 infections in DRC. Many studies focused on *Salmonella* spp., *S. aureus* and *V. cholerae*.  
270 Bacterial resistance to antibiotics concerns both Gram negative and Gram-positive bacteria.  
271 Multidrug resistance prevalence is almost common in half of *S. pneumoniae* isolates. More  
272 disturbing, we can note a worrying prevalence of MRSA with co-resistance to several other  
273 antibiotics, and of ESBL-producers in *Enterobacteriaceae* with the diffusion of *bla*<sub>CTX-M-15</sub> and  
274 *bla*<sub>SHV-18</sub> genes. Data on non-fermenting Gram negative bacilli, as well as carbapenem and  
275 colistin resistance, are not available.

276 **Ethical issues**

277           There are no ethical concerns with this paper and ethical review board approval was  
278 not required as no human subjects were involved.

279 **Financial support**

280           This work was supported by the French Government under the « Investissements  
281 d’avenir » (Investments for the Future) program managed by the Agence Nationale de la  
282 Recherche (ANR, fr: National Agency for Research), (reference: Méditerranée Infection 10-  
283 IAHU-03). This work was supported by Région Provence-Alpes-Côte d’Azur and European  
284 funding FEDER PRIM1.

285

286 **Transparency declaration:**

287           The authors declare no conflict of interest.

288

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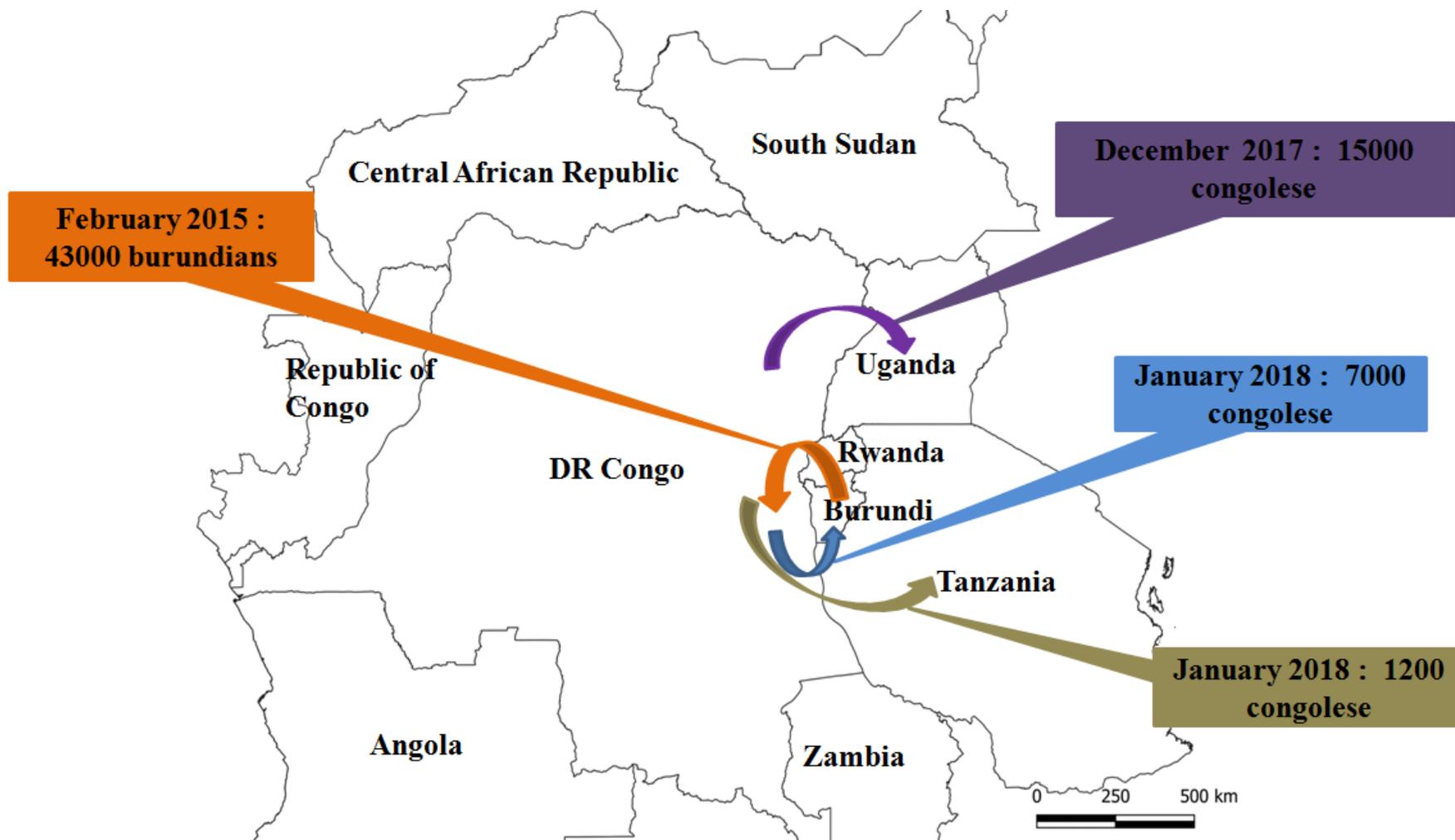
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534 **Figure 1:** Movement of population in the context of armed conflict in Eastern part of Democratic Republic of Congo.

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537 **Figure 2:** Localization of published data on antimicrobial resistance in Democratic Republic of the Congo.

538

539 **Table 1:** Main antimicrobial resistance genes found in Democratic Republic of Congo

540

Species	Methods	N° of strains	Antibiotic resistance genes	References
<i>Salmonella</i> spp.	PCR, gene sequencing, whole genome sequencing	453	<i>bla</i> <sub>CTX-M-15</sub> , <i>bla</i> <sub>SHV-2a</sub> , <i>mph(A)</i> , <i>gyrA</i> mutation, <i>qnrB1</i> , <i>aac(6')-Ib-cr</i> , <i>bla</i> <sub>TEM-1</sub> , <i>bla</i> <sub>TEM-1b</sub> , <i>catA1</i> , <i>strA/B</i> , <i>sull</i> , <i>dfrA1</i> , <i>aac(6')-Iaa</i>	[27,37, 38, 40, 43,45,47,77]
<i>E. coli</i>	PCR, Whole genome sequencing	21	<i>bla</i> <sub>CTX-M-1</sub> , <i>bla</i> <sub>TEM</sub> , <i>bla</i> <sub>CMY</sub> , <i>bla</i> <sub>OXA</sub> , <i>aac3</i> , <i>ant2''</i> , <i>ant3''</i> , <i>aph3''</i> , <i>aph6</i> , <i>pbp2</i> , <i>aac6'</i> , <i>qnrB</i> , <i>mphA</i> , <i>cat</i> , <i>catA</i> , <i>catB</i> , <i>arr</i> , <i>folp</i> , <i>sull</i> , <i>sullI</i> , <i>tetA</i> , <i>tetB</i> , <i>tetD</i> , <i>dhfr</i>	[53,56]
<i>Klebsiella</i> spp.	PCR	3	<i>bla</i> <sub>CTX-M-15</sub> , <i>bla</i> <sub>SHV</sub> variants	[59]
<i>S. aureus</i>	PCR, Whole genome sequencing	148	<i>aac(6')-aph(2'')</i> , <i>tetK</i> , <i>emrC</i> , <i>mecA</i> gene found, mutation in <i>femA</i> gene found, <i>dfrG</i> , <i>rpoB</i> , <i>emrC</i>	[28,44]
<i>Vibrio cholerae</i>	Whole genome sequencing	78	<i>cardB</i> , <i>intSXT</i> , <i>sxt/R391</i> , <i>sullI</i> , <i>sull</i> , <i>qnrVC</i> , <i>aph3-dprime</i> , <i>aph6</i> , <i>drfA</i> , <i>dhfr</i> , <i>flor</i> , <i>gyrA</i> (S83I), <i>parC</i> (S85L)	[46]

**Table 2.** Prevalence of resistance among bacteria isolated in Democratic Republic of Congo

Study period	Microorganism isolated (year of isolation)	Prevalence of resistance % (N)	Gene identified	References
1993	<i>Salmonella</i> spp.(1986)	90% (n=90) of resistance to ampicillin, chloramphenicol, streptomycin and tetracycline	ND <sup>a</sup>	[76]
2001	<i>Salmonella</i> spp. and <i>E. coli</i> (1990)	100% of resistance to ampicillin and chloramphenicol for <i>S. enteritidis</i> , 65% (n=46) of resistance to ampicillin and chloramphenicol for <i>E. coli</i> (n=19)	ND	[42]
2009	<i>Salmonella</i> Typhi (2005)	All the strains (n=11) exhibited resistance to ampicillin (>256 mg/L) and cotrimoxazole (>32 mg/L)	ND	[41]
2010	<i>Salmonella</i> spp.(2006)	For <i>S. typhimurium</i> , high proportion of isolates were resistant to ampicillin (85.7%), chloramphenicol (92.5%), and cotrimoxazole (94.7%), 6.1% of <i>S. enteritidis</i> tested were resistant to nalidixic acid and ciprofloxacin, 10.2% of <i>S. enteritidis</i> isolates were resistant to gentamicin. 89.7% of <i>S. Typhi</i> isolates presented a similar antimicrobial resistant profile as the one observed among NTS <sup>b</sup>	Two isolates displayed resistance to cefoxitin (32mg/L); the presence of the genes <i>bla</i> <sub>CMY-1</sub> , <i>bla</i> <sub>CMY-2</sub> , <i>bla</i> <sub>ACC</sub> , <i>bla</i> <sub>CTX-M</sub> , and <i>bla</i> <sub>TEM</sub> was negative	[39]
2013	<i>Salmonella typhimurium</i> (2006)	100% (n=11) of resistance to ampicillin, cotrimoxazole, and chloramphenicol	<i>bla</i> <sub>TEM-1b</sub> , <i>catA1</i> , <i>strA/B</i> , <i>sul1</i> , <i>dfrA1</i> , <i>aac(6')-Iaa</i>	[37]
2014	<i>Salmonella</i> spp. (2011)	96% (n=180) of resistance to ampicillin; chloramphenicol and cotrimoxazole,	<i>bla</i> <sub>SHV-2a</sub> , <i>mph(A)</i>	[38]
2014	<i>Salmonella</i> spp. (2012)	72.2% (n=18) of <i>S. Typhi</i> isolates showed co-resistance to ampicillin and cotrimoxazole, 33.3% showed additional resistance to chloramphenicol and hence were MDR <sup>c</sup> . 97.6% (n=85) of NTS isolates were MDR; 1.0 % <i>S. typhimurium</i> isolate had additional DCS <sup>d</sup>	<i>gyrA</i> gene mutation found	[40]
2015	<i>Salmonella</i> spp. (2014)	<i>S. Typhi</i> isolates (n=164), MDR and DCS rates were 37.8%	<i>gyrA</i> mutation found, <i>qnrB1</i> , <i>aac(6')</i> -	[27]

		and 37.2%, respectively. MDR were 90.2% and 79.7%, respectively for <i>S. typhimurium</i> (386) and <i>S. enteritidis</i> (390). ESBL production was observed in 12.7% of <i>S. typhimurium</i> isolates	<i>Ib-cr</i> , <i>bla</i> <sub>TEM-1</sub>	
2017	<i>Salmonella</i> Typhi (2015)	Production of ESBL <sup>e</sup> was confirmed by PCR, the first time in DR Congo on <i>S. Typhi</i> . The isolate further showed decreased ciprofloxacin to pefloxacin and nalidixic acid with resistance	<i>bla</i> <sub>CTX-M-15</sub>	[43]
2018	<i>Salmonella</i> Typhi (2017)	ESBL-producing <i>S. Typhi</i> isolate with a decreased ciprofloxacin susceptibility	<i>bla</i> <sub>CTX-M-15</sub>	[45]
2018	<i>Salmonella</i> spp. (2014)	27% (n=60) of resistance to cefuroxime, 20% to ceftriaxone and norfloxacin	ND	[80]
2019	<i>Salmonella typhimurium</i> (2016)	67% (54/81) were ESBL producers and 63% were MDR (resistance both to ampicillin, chloramphenicol and cotrimoxazole).	<i>catA</i> , <i>bla</i> <sub>TEM-1</sub> , <i>dfrA</i> , <i>dfrA1</i> , <i>dfrA14</i> , <i>bla</i> <sub>SHV-2A</sub> , <i>mphA</i> , <i>gyrA</i> mutation (S83Y)	[46]
2019	<i>Salmonella</i> Typhi (2017)	38.4% (114/295) were resistant to ampicillin, chloramphenicol and cotrimoxazole; 24.5% (73/295) had decreased sensitivity to ciprofloxacin	<i>gyrA</i> (S83E, S83Y, D87Y, D87G, A119E), <i>gyrB</i> (E466D, S464Y)	[47]
2012	<i>Enterobacteriaceae</i> (2011)	7.4% (n=190) ESBL-producing <i>Enterobacteriaceae</i>	<i>bla</i> <sub>CTX-M-1</sub> group	[59]
2014	<i>Enterobacteriaceae</i> and Non fermenting Gram-negative rods (2013)	16.3% (n=643) of isolates displayed a MDR phenotype; 80% (n=25) of isolates were ESBL-producers	<i>bla</i> <sub>CTX-M-1</sub> group	[53]
2014	<i>Enterobacteriaceae</i> (2013)	100% (n=79) of resistance to tetracycline, over 90% of resistance to ampicillin, cotrimoxazole and chloramphenicol and over 65% of resistance to norfloxacin	ND	[51]

2015	<i>Enterobacteriaceae</i> (2014)	100% (n=112) of resistance to cotrimoxazole, 67-100% of resistance to ampicillin and > 50% of them were ESBL producers	ND	[52]
2015	<i>Enterobacteriaceae</i> and Gram-positive cocci (2015)	98% (n=38) of <i>E. coli</i> and 65% (n=22) of <i>S. aureus</i> resisted to penicillin, and 92% of <i>E. coli</i> and 73% of <i>S. aureus</i> resisted to cefotaxime	ND	[50]
2012	<i>Klebsiella</i> spp. and <i>E. aerogenes</i> (2010)	5.3% (150) of ESBL producers (8 isolates).	5 <i>bla</i> <sub>CTX-M</sub> genes and 3 <i>bla</i> <sub>SHV</sub> variants	[54]
2019	<i>Escherichia coli</i> (2014)	All isolates were MDR corresponding to ESBL producers (n=21). Twenty-one (21/21) and 19/21 strains were susceptible to imipenem and amikacin, respectively	<i>bla</i> <sub>CTX-M-1</sub> , <i>bla</i> <sub>TEM</sub> , <i>bla</i> <sub>CMY</sub> , <i>bla</i> <sub>OXA</sub> , <i>aac3</i> , <i>ant2''</i> , <i>ant3''</i> , <i>aph3''</i> , <i>aph6</i> , <i>pbp2</i> , <i>aac6'</i> , <i>qnrB</i> , <i>mphA</i> , <i>cat</i> , <i>catA</i> , <i>catB</i> , <i>arr</i> , <i>folP</i> , <i>sulI</i> , <i>sulIII</i> , <i>tetA</i> , <i>tetB</i> , <i>tetD</i> , <i>dhfr</i>	[56]
2014	<i>Staphylococcus</i> spp.(2013)	63.5% (n=74) of <i>S. aureus</i> and 90% (n=15) of CNS <sup>f</sup> were MRSA <sup>g</sup> and MR-CNS, respectively	ND	[66]
2015	<i>Staphylococcus aureus</i> (2011)	16% (n=63) of MRSA	ND	[65]
2016	<i>Staphylococcus aureus</i> (2014)	33% (n=100) were MRSA, 72% of resistance to cyclins and 54% of resistance to cotrimoxazole	<i>mecA</i> , mutation in <i>femA</i> gene found, <i>dfrG</i> , <i>rpoB</i> , <i>emrC</i>	[28]
2017	<i>Staphylococcus aureus</i> (2016)	36% (n=45) of isolates were MRSA	ND	[67]
2017	<i>Staphylococcus aureus</i> (2013)	25% (n=108) were MRSA, 31% were resistant to aminoglycosides, 26 % to macrolides and 20 % to ciprofloxacin	<i>aac(6')-aph(2'')</i> , <i>tetK</i> , <i>emrC</i>	[44]
2015	<i>Vibrio cholerae</i> (2013)	98% (n=36) of resistance to cotrimoxazole, 71% to nitrofurantoin and 18% to nalidixic acid.	ND	[77]
2015	<i>Vibrio cholerae</i> (2012)	Although sensitivity to fluoroquinolones seemed to be preserved, strain resistance patterns continued to evolve with	MLVA genotyping, no resistance genes searched	[78]

		the circulation of isolates resistant to tetracyclines and ampicillin from 2007 to 2010, and displayed a single antimicrobial drug susceptibility profile: resistance to most antimicrobial drugs (chloramphenicol, erythromycin, cotrimoxazole) except cyclines and fluoroquinolones.		
2019	<i>Vibrio cholerae</i> (2017)	100% (n=78) of resistance and nalidixic acid, 12% and 14% of resistance to ciprofloxacin and ampicillin, respectively	<i>cardB</i> , <i>IntSXT</i> , <i>sxt/R391</i> , <i>sullI</i> , <i>sullI</i> , <i>qnrVC</i> , <i>aph3-dprime</i> , <i>aph6</i> , <i>drfA</i> , <i>dhfr</i> , <i>flor</i> , <i>gyrA</i> (S83I), <i>parC</i> (S85L),	[62]
2016	<i>Streptococcus pneumoniae</i> and <i>Haemophilus influenzae</i> (2014)	83% (n=23) of <i>S. pneumoniae</i> isolates were resistant to penicillin, 28% (n=23) of <i>H. influenzae</i> were resistant to amoxicillin/clavulanate acid	ND	[71]
2018	<i>Streptococcus pneumoniae</i> (2015)	70 out of the 163 isolates (43%) of the pneumococci were MDR (non-susceptible to $\geq 3$ classes of antimicrobial agents, including the $\beta$ -lactams).	ND (PCR done for serotyping only)	[72]

<sup>a</sup> ND, not determined; <sup>b</sup> NTS: Non Typhi *Salmonella*; <sup>c</sup> MDR: multidrug resistant; <sup>d</sup> DCS: Decreased Ciprofloxacin Susceptibility; <sup>e</sup> ESBL: extended spectrum  $\beta$ -lactamase; <sup>f</sup> CNS: coagulase negative *Staphylococcus*; <sup>g</sup> MRSA: methicillin resistant *S. aureus*.