

1 Antimicrobial Resistance Surveillance Among Gram 2 Negative Bacterial Isolates from Patients in Khartoum State 3 Hospitals

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14

15 Abstract

16 Background

17 Antimicrobial resistance (AMR) among Gram-negative bacilli is a global health problem.
18 Surveillance of AMR is required to advise on empirical antimicrobial therapy. This study aimed
19 at evaluating the frequency and the AMR patterns of Gram-negative isolates from patients
20 treated in eight hospitals in Khartoum State, Sudan.

21 Methods

22 A cross-sectional laboratory based study was conducted over six months period at the
23 microbiology department, Soba University Hospital, Khartoum State, Sudan. All Gram-negative
24 isolates from blood, urine, wound, and sputum during the period of study were included.

25 Results

26 A total of 734 Gram-negative bacilli were isolated. *Klebsiella spp.* 249 (34%) was the most
27 frequently encountered one, followed by *Pseudomonas spp.* 153(21%), *E.coli* 123(17%),
28 *Acinetobacter spp.* 75 (10%), *Burkholderia cepacia* 42(6%), *Proteus spp.* 28(4%) *Enterobacter*

29 *spp.* 28(4%), *Stenotrophomonas maltophilia* 21(2.8%), and others gram-negative bacilli
30 15(2.2%) The analysis of the antimicrobial susceptibility patterns showed that 134 (22.3%)
31 isolates were multidrug resistant to three or more classes of antibiotics including cephalosporins,
32 β -lactam- β -lactamase inhibitor group, quinolones, aminoglycosides and carbapenems.

33 **Conclusion**

34 This high level of resistance among Gram-negative bacilli in Khartoum state hospitals is
35 alarming. The local health authorities are prompted to step up infection control program and
36 introduce the concept of antimicrobial stewardship in Khartoum State hospitals.

37 **Keywords:** Gram-negative bacilli, Multidrug resistant bacteria, laboratory base study,
38 Surveillance.

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41

42 **Introduction**

43 Antimicrobial resistance (AMR) constitutes a continuously growing threat to the effective
44 treatment of microbial infections [1]. The impact of AMR on human health, as well as the costs
45 incurred on the health-care sector and the wider societal impact, are still largely unknown [2].
46 Antibacterial drugs are widely used worldwide both in human health and food industry. Overuse
47 of these medications can favor the selection and the spread of multidrug resistant (MDR) bacteria
48 [1]. Multi drug resistance is defined as resistance to at least three different antibiotic groups, as
49 reported Masgala [3]. Antibiotic resistance among a variety of bacterial species is increasing in

50 both healthcare settings as well as community one. Extended-spectrum β -lactamase and
51 carbapenemase production are the most frequently emerging resistance mechanisms among
52 Gram-negative bacilli [4]. Gram-negative bacilli including *Enterobacteriaceae* and non-lactose
53 fermenting bacteria such as *Pseudomonas spp.* and *Acinetobacter spp.* are the main causes of
54 hospital-acquired infection in critical care units [2,5]. The rate of antibiotic resistance among
55 these pathogens has accelerated dramatically in recent years and has reached a pandemic scale
56 [2]. According to the Centre for Disease Control and Prevention Gram-negative bacilli possess
57 multiple modes of antibiotic resistance and are highly efficient in horizontally transferring
58 resistance genes between species [6]. This problem of antimicrobial resistance is particularly
59 pressing in developing countries, where the infectious disease burden is high and cost constraints
60 prevent the widespread application of newer, more expensive agents [7].

61 AMR surveillance is the most important tool for assessing the burden of AMR and for providing
62 the necessary antibiogram data, based on which the local, national, and global treatment
63 strategies can be planned. Many surveillance studies on AMR are available in developed
64 countries but unfortunately, studies on AMR surveillance are not adequate from developing ones.
65 This surveillance study was undertaken in order to find out the different types of the AMR
66 patterns of bacterial pathogens isolated from patients in Khartoum state, Sudan. This study may
67 help in formulating antibiotic policies tailored to our hospitals. These data can be used as
68 “information for action” antibiotic stewardship and interventions to optimize antibiotic
69 prescribing practice, therefore prolongs the usefulness of existing antibiotics.

70 **Material and Methods**

71 **Study design and clinical strains**

72 This is a cross-sectional laboratory based study carried out in the department of medical
73 microbiology Soba University Hospital (SUH), Sudan. A total of 734 Gram-negative isolates
74 from patients treated in eight hospitals in Khartoum state, Sudan between October 2016 to
75 February 2017. The isolates were collected from different clinical specimens including blood
76 243(33.1%), urine 230(31.3%), wounds 183(25%), sputum 22(3%), catheter tips 25(3.4%) and
77 different body fluids 31(4.2%) (including CSF, peritoneal fluid, pleural fluid, acetic fluid, and
78 synovial fluid). Microorganisms were grown on to Blood, Chocolate and MacConkey agar.
79 Then, they were identified according to standard microbiological procedures (based on colony
80 morphology, microscopy, and biochemical tests) [8]. Quality control strains were used in
81 biochemical tests and antimicrobial susceptibility testing [*Escherichia coli* (ATCC #25922) and
82 *Pseudomonas aeruginosa* (ATCC #27853)].

83 **Antimicrobial Susceptibility Testing**

84 Susceptibility testing was performed by Kirby-Bauer disc-diffusion method for all isolates
85 against the following antibiotic disc (Mast Diagnostic): Amoxicillin clavulanate (AMC) (30µg);
86 Cefuroxime (CXM)(30µg); Cephalexin (CL)(30µg); Ceftriaxone (CRO)(30µg); Ceftazidime
87 (CAZ) (30µg); Meropenem (MEM)(10µg); Imipenem (IPM) (10µg); Amikacin (AK) (30µg);
88 Gentamicin (Gen)(10 µg); Ciprofloxacin (CIP)(5 µg); Trimethoprim-sulfamethoxazole (SXT)
89 (25 µg); Temocillin (TEM) (30 µg); Azteroname (AZT)(30 µg); Nitrofrantoine (NIT) (300 µg).
90 Results were interpreted according to the Clinical Laboratory Standards Institute (CLSI)
91 guidelines [8].

92 **Classification of MDR Gram-Negative Bacilli**

93 MDR has been considered for clinically significant Gram-negative bacilli (GNB) such as
94 *Escherichia coli*, *Klebsiella spp.*, *Pseudomonas spp.* and *Acinetobacter spp.*, based on the above

95 mentioned antimicrobial resistance definition. Classes of antibiotics used for MDR-GNB
96 analysis were Aminoglycoside (AMG), Cephalosporins (CEPH), Carbapenems (CARB), and
97 Fluroquinolones (FQ) as follows: bacteria that were MDR for 4 classes of antibiotics (AMG+
98 CEPH+ CARB+ FQ) and bacteria that were MDR for 3 classes of antibiotics (either
99 AMG+CEPH +FQ, CARB+CEPH+FQ, AMG+CEPH+CARB, or AMG+FQ+CARB) [3].

100 Cephalosporins resistance was defined as resistance to ceftriaxone and ceftazidime except for
101 *Pseudomonas species*, where only ceftazidime was used. Carbapenem resistance was defined as
102 resistance to both meropenem and imipenem. Aminoglycoside resistance was defined as
103 resistance to both gentamicin and amikacin, Ciprofloxacin resistance was considered an
104 indication to fluoroquinolones resistance.

105 **Statistical analysis**

106 Data were analysed using Microsoft Excel and SPSS version 20.0. Cross tabulation was used to
107 present the different relations between data, qualitative data were performed through χ^2 test, and
108 significance was set at $p \leq 0.05$. which performed to find the differences between bacterial
109 isolates with resistance to at least one class of antibiotics by specimens (blood, urine, wound and
110 other samples) *P*- values were determined for primary and secondary outcomes.

111 **Ethical consideration**

112 Formal permission was obtained from the managers of Soba University Hospital and the
113 Institutional Research Ethics Committee of the Institute of Endemic Diseases, University of
114 Khartoum, approved this study under reference number 12/2017.

115 **Results**

116 **Bacterial identification**

117 Isolated Gram-negative bacilli showed different strains, including *E.coli* 123 (17%), *Klebsiella*
 118 *spp.* 249 (34%), *Pseudomonas spp.* 153 (21%), *Acinetobacter spp.* 75 (10%), *Burkholderia*
 119 *cepacia* 42 (6%), *Proteus spp.* 28 (4%) *Enterobacter spp.* 28 (4%), *Stenotrophomonas*
 120 *maltophilia* 21 (2.8%) and others gram-negative bacilli 15 (2.2%).

121 While isolates were distributed among the different hospital units, most of the pathogenic strains
 122 were isolated from neonatal intensive care unit (NICU) (42.7%) and pediatric units in (23.7%).
 123 *Klebsiella spp.* was the most isolated organism from all hospital units (Table 1).

124 **Table 1: Distribution of Gram-negative bacilli among different hospital wards between**
 125 **October 2016 to February 2017**

Hospital ward	ICU	NICU	Medicine	Surgery	Renal Unit	Paediatric	P-value
Bacteria	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
<i>Klebsiella spp.</i> ((249)	19 (39)	77(42.3)	45(30.6)	34(33)	24(31)	50(29)	<0.001
<i>E.coli</i> (123)	2(12.2)	9(5)	45(30.6)	22(21.3)	16(21)	25(14.2)	<0.001
<i>Pseudomonas spp.</i> (153)	9(18.4)	40(21.9)	24(16.3)	17(16.5)	19(24.3)	44(25.1)	<0.001
<i>Acintobacter spp.</i> (75)	9(18.4)	18(9.9)	9(6.1)	8(8)	7(9)	24(14)	<0.001
<i>Burkholderia cepacia</i> (42)	3(6.1)	11(6)	7(4.7)	6(6)	4(5.1)	11(6.3)	<0.001
<i>Proteus spp.</i> (28)	1(2)	3(2)	4(2.7)	9(9)	3(4)	8(5)	<0.001
<i>Enterobacer spp.</i> (28)	1(2)	10(5.5)	4(3)	3(3)	4(5.1)	6(3.4)	<0.001
<i>Stenotrophomonas</i> <i>spp.</i> (21)	1(2)	10(5.5)	3(2)	2(2)	1(1)	4(2)	<0.001
Other Gram negative bacilli (15)	0(0)	4(2.2)	6(4)	2(2)	0(0)	3(2)	<0.001
Total (734)	49(7)	182(42.7)	147(20)	103(14)	78(11)	175(23.3)	<0.001

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 127
 128 (Other Gram-negative bacilli include *Citrobacter species*, *Serratia species*, *Vebrio vurneficus*
 129 and *Morganella morganii*)
 130

131 With regard to the distribution of the isolates among different clinical specimens, *Klebsiella spp.*
 132 and *Pseudomonas spp.* were isolated mainly in blood specimens 39% and 25% respectively,
 133 while *Klebsiella spp.* and *E.coli* were 36% and 30% of urine samples. *Acinetobacter spp.* was
 134 mostly isolated from 25% of wound specimens (Table 2).

135 **Table 2: Distribution of Gram-negative bacilli among different clinical samples between**
 136 **October 2016 to February 2017**

Specimen	Blood	Urine	Wounds	Sputum	Catheter	Body	P-
Bacteria	N (%)	N (%)	N (%)	N (%)	Tips	Fluids	value
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
<i>Klebsiella spp.</i> (249)	94(39)	82(36)	50(27)	7(32)	7(28)	9(29)	<0.001
<i>E.coli</i> (123)	15(6.1)	70(30)	31(17)	2(9)	1(4)	4(12.9)	<0.001
<i>Pseudomonas spp.</i> (153)	60(25)	32(14)	42(23)	6(27.2)	7(28)	7(25)	<0.001
<i>Acintobacter spp.</i> (75)	18(7.4)	13(5.6)	25(14)	6(27.2)	7(28)	2(25)	<0.001
<i>Burkholderia</i> <i>cepacia</i> (42)	20(8)	9(4)	9(5)	1(5)	1(4)	2(6.4)	<0.001
<i>Proteus spp.</i> (28)	6(2.5)	7(3)	12(6.5)	0(0)	2(8)	1(3.2)	<0.001
<i>Enterobacer spp.</i> (28)	13(5)	8(3.5)	7(4)	0(0)	0(0)	0(0)	<0.001
<i>Stenotrophomonas</i> <i>spp.</i> (21)	12(5)	2(0.9)	5(3)	0(0)	0(0)	2(6.4)	<0.001
Other Gram negative bacilli (15)	5(2)	7(3)	2(1)	0(0)	0(0)	0(0)	<0.001
Total (734)	243(33.1)	230(31.3)	183(25)	22(3)	25(3.4)	32(4.2)	<0.001

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 138 (Other Gram-negative bacilli include *Citrobacter species*, *Serratia species*, *Vebrio vurneficus*
 139 and *Morganella morganii*)
 140 Body fluids include (CSF, peritoneal fluid, pleural fluid, acetic fluid, and synovial fluid)
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144 **Antimicrobial Resistance Pattern of Clinical Isolates**

145 Antibiotic resistance pattern are shown in Fig 1. Out of 734 isolates tested by disk diffusion test,
146 the highest percentage of resistance 97%, and 93.5% were found against ampicillin and
147 cephalexin, respectively, followed by amoxicillin/clavulanic acid 90%, cefotaxime 89.7%,
148 ceftriaxone 88.4%, and ceftazidime 79.2%. In addition, co-trimoxazole and nitrofurantoin
149 resistance were detected in 74.4 and 75.2 of isolates, respectively. Resistance rates also were
150 high in ciprofloxacin 45.2%, gentamicin 52.5% and amikacin 18.3%. Meropenem and imipenem
151 were the most effective antibiotic tested, resistant were observed with 21.6% and 16.2% of
152 isolates, respectively.

153 The antimicrobial resistance patterns of most commonly isolated organisms are shown in Fig 2.
154 The analysis of the antimicrobial susceptibility patterns of the study isolates showed high rate of
155 MDR organisms that were resistant to three or more classes of antibiotics, including carbapenem
156 and aminoglycosides. This pattern mainly among *Acinetobacter spp.*, *Pseudomonas spp.*, and
157 *Klebsiella spp.*

158 The most clinical isolates in Enterobacteriaceae family were *E.coli* and *Klebsiella spp.* in both of
159 these GNB, high rate of resistance was observed against quinolones, cephalosporins and β -
160 lactam group of drug. Resistance to carbapenem was also statistically significantly high.

161 **Multidrug Resistance in Gram Negative Bacilli (Co Resistance Patterns)**

162 The multidrug resistance pattern among clinical isolates of gram-negative bacilli have been
163 shown in Table 3. Of 600 GNB isolates recovered, 134 (22.3%) isolates were MDR i.e., resistant
164 to at least three or more classes of antimicrobial agents. About 48(8%) of all Gram negative

165 isolates were 4MDR (resistant to four classes of antimicrobial drug), while 86 (14.2%) were
 166 3MDR (resistant to three classes of antimicrobial drug). It was observed that 50% of
 167 *Acinetobacter spp.* were resistant to four major classes of antibiotics. Significant resistance to
 168 carbapenem was noted among all gram-negative bacteria.

169 **Table 3: Multi drug resistance pattern among gram-negative isolates between October**
 170 **2016 to February 2017**

Class	Resistance to	<i>Klebsiella</i> <i>spp.</i> (249)	<i>E.coli</i> (123)	<i>Pseudomonas</i> <i>spp.</i> (153)	<i>Acinetobacter</i> <i>spp.</i> (75)	Total (600)
4MDR	AMG+ CEPH+ FQ+ CARB	9 (3.6%)	1 (0.8%)	0 (0%)	38(50.6%)	48 (8%)
3MDR	AMG+ CEPH+ FQ	31(12.4%)	5(4%)	4 (2.6%)	2 (2.6%)	42 (7%)
3MDR	CARB+ CEPH+ FQ	6 (2.4%)	0 (0%)	8 (5.2%)	8 (10.6%)	22(3.6%)
3MDR	AMG+ CEPH+ CARB	2 (0.8%)	0 (0%)	5 (3.2%)	1 (1.3%)	8 (1.3%)
3MDR	AMG+ FQ+ CARB	8 (3.2%)	1(0.8%)	4 (2.6%)	1 (1.3%)	14 (2.3%)
Total		56(22.4%)	7 (5.6%)	21(13.7%)	50 (66.6%)	134 (22.3%)

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 172 AMG = Aminoglycoside. CEPH= Cephalosporins, FQ= Florquinolones, CARB= Carbapenem.

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177 Discussion

178 Infection with MDR Gram-negative bacilli is a major problem worldwide, associated with
179 increased patients morbidity and mortality [9]. In Sudan, the increasing number of MDR bacteria
180 is a real clinical challenge [10,11]. This study was undertaken; to determine the occurrence of
181 different types of AMR pattern of the bacterial pathogens isolated from patients treated in
182 various wards of hospitals.

183 In this study, *Klebsiella* and *Pseudomonas* strains were more prevalent in blood specimens while
184 *Klebsiella* and *E.coli* strains were more frequently isolated in urine specimens.

185 *Klebsiella pneumoniae* is an important causative agent of nosocomial and community-acquired
186 Gram-negative bacteremia. It can cause various infections, including blood stream infections,
187 wound infections, pneumonia, urinary tract infections and intra-abdominal infections [12,13]. In
188 this study, *Klebsiella spp.* was the most pathogenic strain isolated from the blood specimens
189 mainly in neonatal sepsis in a high rate (39.8%). Most of these strains resistant to cephalosporins
190 and other class of antibiotics including carbapenem as reported worldwide [7,13,14].

191 *E.coli* is the commonest urinary tract pathogen causing complicated and uncomplicated UTI [16]
192 but in this study most observed pathogens in urine specimens were *E.coli* 30% and *Klebsiella*
193 *spp.* 36%. This finding in Sudan is concordant with that of de Francesco et al, 2007 where *E.coli*
194 was found in 42.4% of Gram-negative isolates [17]. This also goes with results that were
195 obtained in Tanzania where *E.coli* was detected in 38% of the Gram-negative isolates and 25%
196 of all Isolates [18]. Likewise, many authors have the same finding in Pakistan and India [18,19].

197 Non-lactose Fermenting Gram negative bacilli such as *Pseudomonas spp.* and *Acinetobacter spp.*
198 were the mostly isolated from ICU patients from blood, wound and sputum specimens, the

199 isolation rates were 18.4% for both. In this study we found that *Pseudomonas spp.* were
200 associated with 25% of blood stream infections and 23% of wound infection while
201 *Acinetobacter spp.* mainly with wound infection in 25% concordant with Gales et al 2010 [20].

202 *Pseudomonas spp.* was reported as highly associated in health care setting by Jean-Louis Vincent
203 et al.,[21]. While Javeri Jitendra R et al., also reported that *Acinetobacter spp.* as the second
204 most common in an ICU of tertiary care center [22].

205 Resistance of gram negative bacilli has emerged widely and multidrug resistance has been
206 reported by many studies causing challenge to treatment of nosocomial infections. The resistance
207 pattern was commonly reported in classes such as cephalosporins, carbapenem, aminoglycosides
208 and quinolones [2,23–25]. In this study, we observed high rate of ESBL, resistant to
209 ceftazidime and ceftriaxone in addition to resistance to ampicillin and amoxicillin/clavulanic
210 acid.

211 The most resistant strain was *Acinetobacter spp.*, being resistant to all four classes of antibiotics
212 used in 50.6% of isolates. About 73.7% of *Acinetobacter* were found to be resistant to
213 meropenem, and 66.7% to imipenem, while in cephalosporins classes more than 91% of the
214 isolates were resistant. *Acinetobacter spp.* also have high resistance rate to Aminoglycosides and
215 quinolones 63.2% for amikacin and 79% for both gentamicin and ciprofloxacin. This increasing
216 resistance among *Acinetobacter spp.* has become a public-health issue because they play an
217 important roles in nosocomial infections [24].

218 *Klebsiella spp.* and *E.coli* were the most isolated pathogens in this study with relatively high
219 resistance rate, about 9 to 22% of them were resistant to carbapenem. And they have highly
220 resistant rate to ceftazidime and cephalexin, 80.6% and 92% respectively. This is much higher

221 than the observation in 2013 by Ali in Soba University hospital that Ceftriaxone and ceftazidime
222 resistance ranged from 56% to 79% [14,26]. Aminoglycoside resistance among *Klebsiella spp.*
223 and *E.coli* was 16.7% and 12.1% respectively to amikacin, which is lower than Normratha 2015
224 observation who found the resistance rate to amikacin 37% of *Klebsiella spp.* and 23% of *E.coli*
225 [23]. Gentamicin resistance among both *Klebsiella spp.* and *E.coli* was up to 53%, which is
226 slightly higher than Normratha study [23]. *E.coli* was highly resistant to Quinolones group like
227 ciprofloxacin in 66.4% than *Klebsiella spp.* 42% this finding is much lower than observation by
228 Moolchandani 2017 [25].

229 *Pseudomonas spp.* was significantly resistant to carbapenem in 22% of isolates and was highly
230 resistant to ceftazidime in 81% followed by gentamicin 57.5%, ciprofloxacin in 22.5% and
231 amikacin 9.5%. That was reported in many studies [4,27].

232 The high level of resistance in the current study can be attributed to the unrestricted use of
233 antibiotics in Sudanese hospitals, which plays an important role in increasing carbapenem
234 resistance [25]. During this study, 134 gram negative bacilli resistance to three or four classes of
235 antibiotics in a period of six months were isolated, which is relatively higher rate than study in
236 the period performed in SUH from January 2011 to June 2013 and reported 80 bacterial strains
237 resistant to all available antibiotics including meropenem [26].

238 In Sudan most laboratories do not test for ESBL and Carbapenemase producer and report; based
239 on disc diffusion test; an ESBL producer as sensitive to cephalosporins. ESBL producer in
240 addition to cephalosporin resistant it may be associated with other resistance gene like *qnr* of
241 quinolones [28]. This may in turn give false impression to the clinicians and mask the true
242 picture of the high prevalence of antibiotic resistance. Moreover, there is limited choice of

243 available antibiotics other than cephalosporins in Sudan that increased the prescription of
244 cephalosporin for treatment of infectious diseases and meropenem for ESBL producer.

245 **Conclusion**

246 In conclusion, there was high prevalence of Gram-negative bacterial pathogen associated
247 hospital and community acquired infections with increasing resistance to available antibiotics.
248 We need to implement of strict infection control measures and activate the antimicrobial
249 stewardship, policed to decrease the spread of MDR pathogens in Sudanese hospitals.

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255 **Conflict of interests**

256 All the authors declare on conflicts of interests.

257 **Transparency Declaration**

258 No conflict of interests to declare.

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265 **References**

- 266 1. Harris P, Paterson, D and Rogers B. Facing the challenge of multidrug- resistant gram-
267 negative bacilli in Australia. Clin Focus. 2015;202:243–7.
- 268 2. Mehrad B, Clark NM, Zhanel GG, Iii JPL. Antimicrobial Resistance in Hospital-Acquired
269 Gram-Negative Bacterial Infections. Chest. 2015;1413–21.
- 270 3. Masgala A, Kostaki K II. Multi Drug Resistant Gram Negative Pathogens in Long Term
271 Care Facilities: A Steadily Arising Problem. J Infect Dis Diagn. 2015;(1):101.
- 272 4. Karaiskos I, Giamarellou H. Multidrug-resistant and extensively drug-resistant Gram-
273 negative pathogens: current and emerging therapeutic approaches. Expert Opin
274 Pharmacother. 2014;15(10):1351–70.
- 275 5. Rosenthal VD, George D, Mehta Y, Leblebicioglu H, Ahmed Z, Al-mousa HH, et al.
276 International Nosocomial Infection Control Consortiu (INICC) report, data summary of 43
277 countries for 2007-2012. Device-associated module. Am J Infect Control. 2014;42:942–
278 56.
- 279 6. Huang TD, Bogaerts P, Berhin C, Hoebeke M, Bauraing C, Glupczynski Y. Increasing
280 proportion of carbapenemase-producing Enterobacteriaceae and emergence of a MCR-1
281 producer through a multicentric study among hospital-based and private laboratories in
282 Belgium from September to November 2015. Eurosurveillance. 2017.
- 283 7. Report G. Antimicrobial resistance. 2014.
- 284 8. Testing S. M100 Performance Standards for Antimicrobial. 27th ed. 2017. 106-143 p.

- 285 9. Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF. Multidrug resistance ,
286 inappropriate empiric therapy , and hospital mortality in *Acinetobacter baumannii*
287 pneumonia and sepsis. *Crit Care*. 2016;20:1–10.
- 288 10. Yousif M. The prevalence of Extended Spectrum β -lactamase and AmpC- Producing
289 Bacteria in a Sudanese Tertiary Hospital. *Sudan Med J*. 2015;5(3):10-17.
- 290 11. Ibrahim M, Bilal N, Hamid M. Comparison of phenotypic characteristics and
291 antimicrobial resistance patterns of clinical *Escherichia coli* collected from two unrelated
292 geographical areas. *Glob J Heal Sci*. 2014;(6):126–35.
- 293 12. Meatherall BL, Gregson D, Ross T, Pitout JD, & Laupland KB. Incidence, risk factors,
294 and outcomes of *Klebsiella pneumoniae* bacteremia. *Am J Med*. 2009;122:866–873.
- 295 13. Cao X, Xu X, Zhang Z, Shen H, Chen J, Zhang K. Molecular characterization of clinical
296 multidrug-resistant *Klebsiella pneumoniae* isolates. *Ann Clin Microbiol Antimicrob*.
297 2014;1:13–6.
- 298 14. Ali MA. the prevalence and characterization of antibiotic resistance among Gram-negative
299 bacilli. University of Khartoum; 2013.
- 300 15. Tzouveleki LS, Markogiannakis A, Psychogiou M, Tassios PT, & Daikos GL.
301 Carbapenemases in *Klebsiella pneumoniae* and other Enterobacteriaceae: an evolving
302 crisis of global dimensions. *Clin Microbiol Rev*. 2012;25:682–707.
- 303 16. Karlowsky J, Jones M, Thornsberry C, Critchley I, Kelly L, Sahm D. Prevalence of anti-
304 microbial resistance among urinary tract pathogens isolated from female outpatients
305 across the US in 1999. *Int J Antimicrob Agents*. 2001;18:121–7.

- 306 17. de Francesco MA, Giuseppe R, Laura P, Riccardo N NM. Urinary tract infections in
307 Brescia, Italy: Etiology of uropathogens and antimicrobial resistance of common
308 uropathogens. *Med SciMonit.* 2007;13:136–44.
- 309 18. Blomberg B, Olsen BE, Hinderaker SG, Langeland N, Gasheka P, Jureen R, Kvale G, and
310 Midtvedt T. Antimicrobial resistance in urinary bacterial isolates from pregnant women in
311 rural Tanzania: implications for republichealth. *Scandinavian. J Infect Dis.*
312 2005;37(4):262–8.
- 313 19. Haider G, Zehra N, Munir AA and HA. Risk factors of urinary tract infection in
314 pregnancy. *J Pak Med Assoc.* 2010;60(3):21–36.
- 315 20. Zavascki AP, Carvalhaes CG, Picao RC GA. Multidrug-resistant *Pseudomonas aeruginosa*
316 and *Acinetobacter baumannii*: resistance mechanisms and implications for therapy. *Expert*
317 *Rev Anti infet ther.* 2010;(8):71–93.
- 318 21. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD et al. International study
319 of the prevalence and outcomes of infection in intensive care units. *JAMA.*
320 2009;302(21):2323–9.
- 321 22. Javeri JR, Patel SM, Nayak SN, Desai K PPA. study on bacteriological profile and drug
322 sensitivity & resistance pattern of isolates of the patients admitted in intensive care units
323 of a tertiary care hospital in Ahmadabad. . *Natl J Med Res.* 2016;2(3):330–4.
- 324 23. Nandihal NW. Profile of Urinary Tract Infection and Quinolone Resistance among
325 *Escherichia coli* and *Klebsiella* species isolates. *IntJCurrMicrobiolAppSci.*
326 2015;4(7):749–56.

- 327 24. Diene SM RJ. Carbapenemase genes and genetic platforms in Gram-negative bacilli:
328 Enterobacteriaceae, Pseudomonas and Acinetobacter species. Clin Microbiol Infect Off
329 Publ Eur Soc Clin Microbiol Infect Dis. 2014;30(9):831– 8.
- 330 25. Moolchandani K, Sastry AS, Deepashree R, Sistla S, Harish BN, Mandal J. Antimicrobial
331 Resistance Surveillance among Intensive Care Units of a Tertiary Care Hospital in
332 Southern India. J Clin Diagn Res. 2017;11(2):1–7.
- 333 26. Elhag KM. Review Article Diversification of antibiotics as a means to control
334 antimicrobial resistance and improve treatment options in Sudan. Sudan Med J.
335 2013;49(3):128–35.
- 336 27. Magiorakos A-P, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al.
337 Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an
338 international expert proposal for interim standard definitions for acquired resistance. Clin
339 Microbiol Infect. 2012;18(3):268–81.
- 340 28. Paterson DL, Mulazimoglu L, Casellas JM, Ko W-C, Goossens H, Von Gottberg A, et al.
341 Epidemiology of Ciprofloxacin Resistance and Its Relationship to Extended-Spectrum -
342 Lactamase Production in Klebsiella pneumoniae Isolates Causing Bacteremia. Clin Infect
343 Dis. 2000;30(3):473–8.

344

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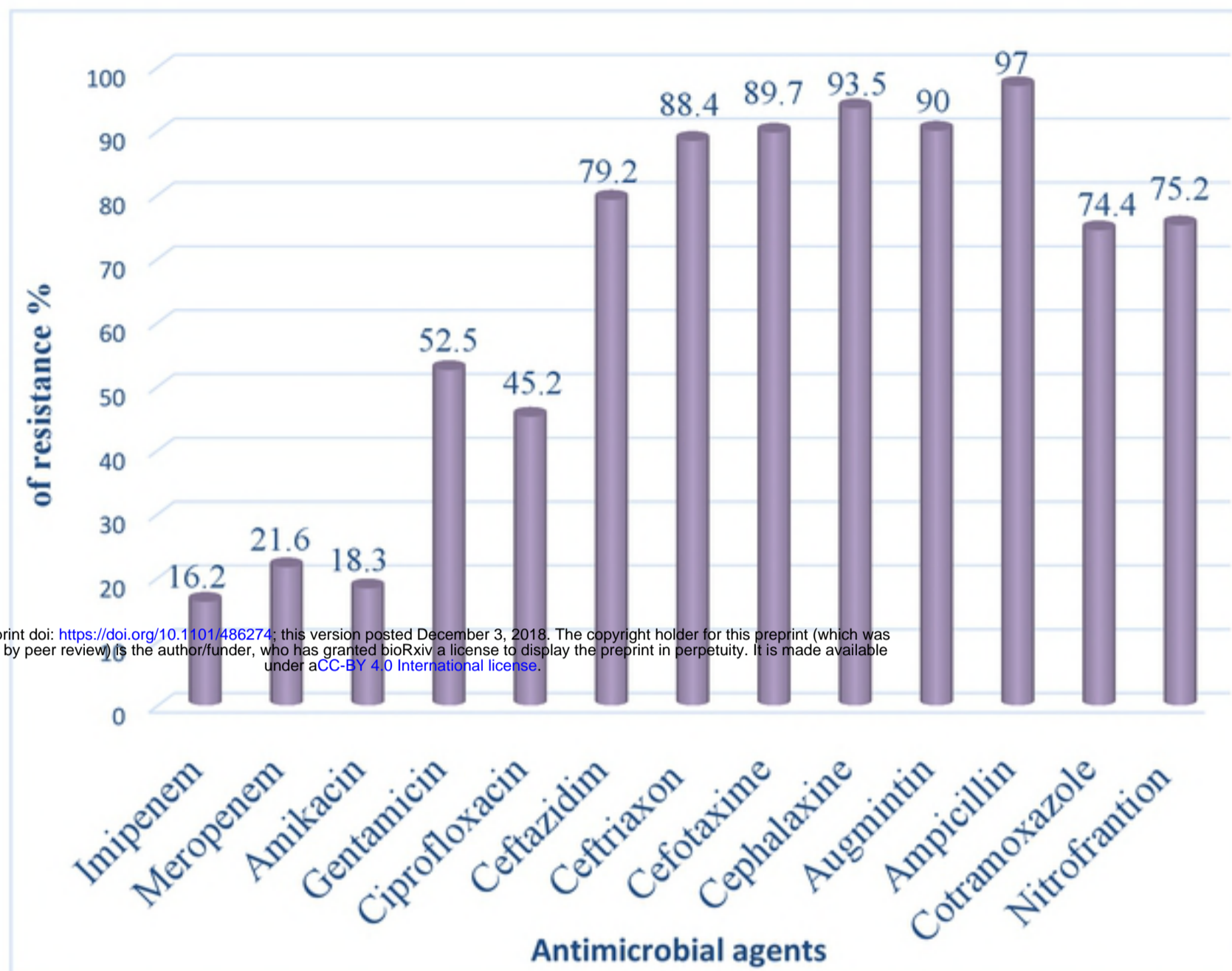
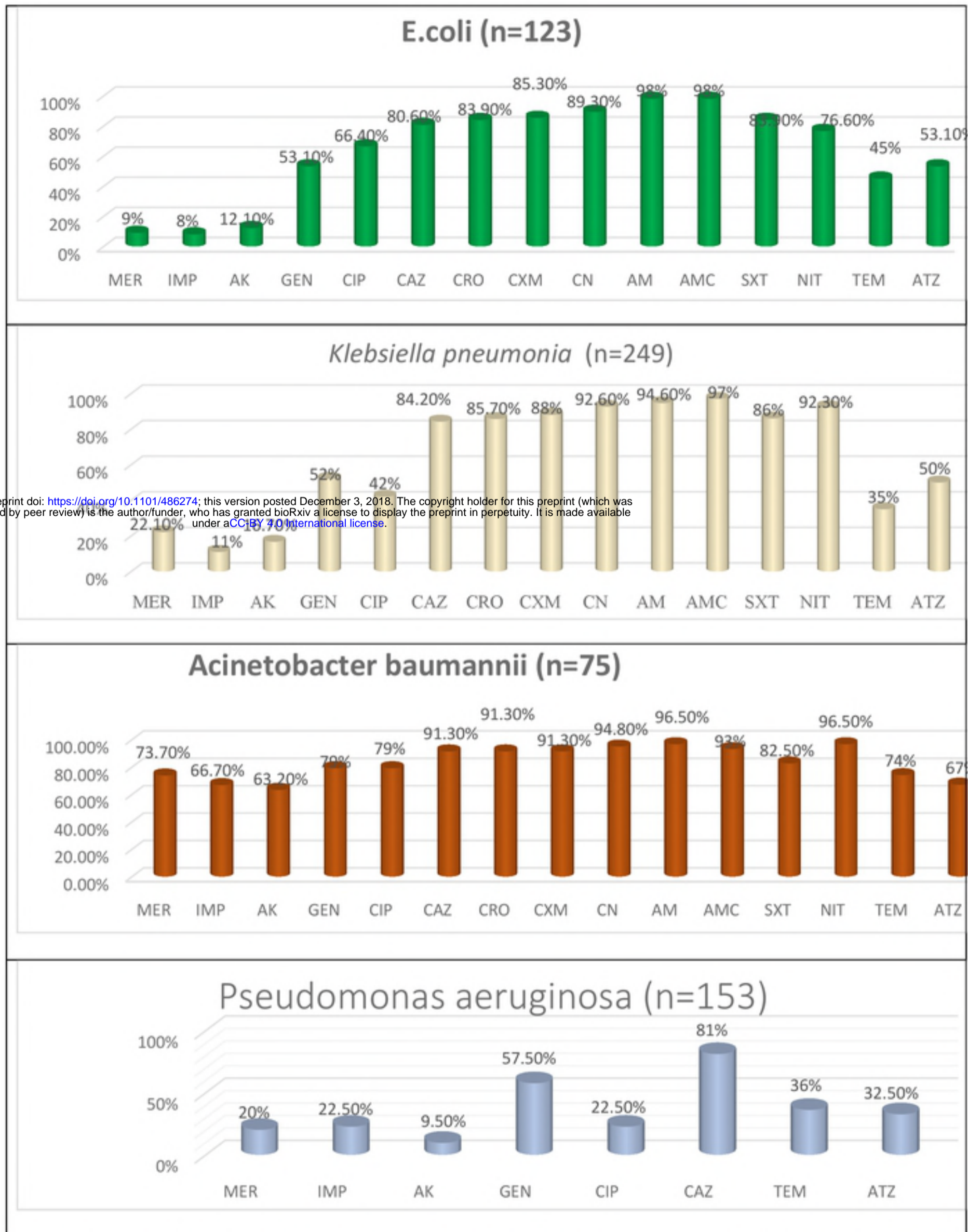


Fig 1: Antimicrobial Resistance pattern among different Gram-negative bacilli isolated from patients treated at Khartoum state hospitals between October 2016 to February 2017.



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Figure2: Sensitivity pattern among commonly isolated organisms' different antibiotics between October 2016 to February 2017. (MER-Meropenem, IMP-Imipenem, AK- Amikacin, GEN-Gentamicin,CIP-Ciprofloxacin,CAZ-Ceftazidime, CRO-CeftriaxoneCXM-Cefuroxime, CN-cephalexin,