

Supplementary Material

Table S1. Distribution of resistance pattern of *E. coli* to different antimicrobial agents according to the infection type.

Antibiotics	Wound infections	Ear infections	Burns infections	Chest infections	UTIs	Gastroenteritis	ICU	% Resistant
Cefpodoxime	22	2	4	6	5	6	5	83.3
Cefadroxil	25	3	5	7	6	6	6	96.7
Streptomycin	17	3	5	7	6	6	6	83.3
Aztreonam	12	1	3	4	6	6	5	61.7
Ceftriaxone	18	3	5	7	6	6	6	85
Cephalothin	26	3	5	7	6	6	6	98.3
Gentamycin	13	1	2	4	3	2	1	43.3
Amoxicillin/ Clavulanic	27	3	5	7	6	5	6	98.3
Ceftazidime	22	1	5	6	4	6	6	83.3
Imipenem	22	2	3	6	4	4	4	75
Meropenem	11	1	2	2	3	3	3	41.7
Cefoperazone	16	2	4	6	5	6	1	66.7
Doxycycline	23	3	4	6	5	6	6	88.3
Tetracycline	19	1	2	2	2	2	0	46.7
Ciprofloxacin	11	1	2	5	4	5	5	55
Amikacin	15	2	4	6	1	2	5	58.3
Nalidixic acid	14	2	4	7	6	5	6	73.3
Cefotaxime	25	3	4	7	6	6	6	95
Piperacillin	24	3	4	7	5	0	0	71.7
Cefepime	20	3	4	6	6	5	6	81.7
Ampicillin/sulbactam	26	2	5	6	6	6	6	95
Norfloxacin	11	3	2	5	3	5	1	50
Tobramycin	14	2	4	1	0	0	1	36.7
Sulphamethoxazole/trimethoprim	22	1	5	7	6	6	6	88.3
Nitrofurantoin	13	1	1	4	5	5	4	53.3
Chloramphenicol	12	2	4	5	3	2	1	48.3
Levofloxacin	13	2	3	1	0	1	0	33.3
Piperacillin/ Tazobactam	5	2	2	1	2	5	3	33.3
Ofloxacin	11	2	2	3	4	5	2	48.3
Azithromycin	16	2	1	5	4	0	1	50

Table S2. Distribution of *bla*_{IMP} genotype among 60 isolated *E. coli*.

<i>E.coli</i>	Source of sample	Resistance pattern of imipenem			<i>bla</i> _{IMP}
		Sensitive	Intermediate	Resistance	
1.	Wound	+	-	-	+
2.	Wound	-	-	+	+
3.	Wound	-	-	+	+
4.	Wound	-	-	+	+
5.	Wound	+	-	-	-
6.	Wound	-	-	+	+
7.	Wound	-	-	+	+
8.	Wound	-	+	-	-
9.	Wound	+	-	-	-
10.	Wound	-	-	+	+
11.	Wound	-	-	+	+
12.	Wound	-	-	+	+
13.	Wound	-	-	+	+
14.	Wound	-	-	+	+
15.	Wound	+	-	-	-
16.	Wound	-	-	+	+
17.	Wound	-	-	+	+
18.	Wound	-	-	+	+
19.	Wound	-	-	+	+
20.	Wound	-	-	+	+
21.	Wound	-	-	+	+
22.	Wound	-	-	+	+
23.	Wound	-	-	+	+
24.	Wound	-	-	+	+
25.	Wound	-	-	+	+
26.	Wound	-	-	+	+
27.	Wound	-	-	+	+
28.	Ear infection	+	-	-	-
29.	Ear infection	-	-	+	+
30.	Ear infection	-	-	+	+
31.	Burn	+	-	-	-
32.	Burn	-	-	+	+
33.	Burn	-	-	+	+
34.	Burn	+	-	-	-
35.	Burn	-	-	+	+
36.	Burn	-	-	+	+
37.	Burn	-	-	+	+
38.	Chest infection	-	-	+	+
39.	Chest infection	-	-	+	+
40.	Chest infection	+	-	-	-
41.	Urinary tract Infection	-	-	+	+
42.	Urinary tract Infection	-	-	+	+
43.	Urinary tract Infection	+	-	-	-
44.	Urinary tract Infection	-	-	+	+
45.	Urinary tract	-	-	+	+

	Infection				
46.	Urinary tract Infection	-	+	-	+
47.	Urinary tract Infection	-	-	+	+
48.	Urinary tract Infection	-	-	+	+
49.	Urinary tract Infection	-	-	+	+
50.	Urinary tract Infection	-	+	-	-
51.	Gastroenteritis	-	-	+	+
52.	Gastroenteritis	-	-	+	+
53.	Gastroenteritis	-	+	-	-
54.	Gastroenteritis	-	-	+	+
55.	Gastroenteritis	+	-	-	-
56.	Patients admitted to intensive care unit	-	-	+	+
57.	Patients admitted to intensive care unit	-	-	+	+
58.	Patients admitted to intensive care unit	-	+	-	+
59.	Patients admitted to intensive care unit	-	-	+	+
60.	Patients admitted to intensive care unit	-	-	+	+

Table S3. Distribution of *aac(6')-Ib* genotype among 60 isolated *E.coli*.

<i>E.coli</i>	Source of sample	Resistance pattern of amikacin			<i>aac(6')-Ib</i>
		Sensitive	Intermediate	Resistance	
1.	Wound	-	-	+	+
2.	Wound	+	-	-	+
3.	Wound	-	-	+	+
4.	Wound	+	-	-	-
5.	Wound	-	-	+	+
6.	Wound	+	-	-	+
7.	Wound	-	-	+	+
8.	Wound	-	-	+	+
9.	Wound	+	-	-	-
10.	Wound	-	-	+	+
11.	Wound	+	-	-	-
12.	Wound	-	-	+	+
13.	Wound	-	-	+	+
14.	Wound	+	-	-	-
15.	Wound	-	-	+	+
16.	Wound	+	-	-	+
17.	Wound	-	-	+	+
18.	Wound	+	-	-	-
19.	Wound	-	-	+	+
20.	Wound	+	-	-	-
21.	Wound	-	-	+	+
22.	Wound	+	-	-	-
23.	Wound	-	-	+	+

24.	Wound	+	-	-	+
25.	Wound	-	-	+	+
26.	Wound	+	-	-	-
27.	Wound	-	-	+	+
28.	Ear infection	-	-	+	+
29.	Ear infection	-	-	+	+
30.	Ear infection	+	-	-	-
31.	Burn	-	-	+	+
32.	Burn	-	-	+	+
33.	Burn	+	-	-	-
34.	Burn	-	-	+	+
35.	Burn	-	-	+	+
36.	Burn	-	-	+	+
37.	Burn	-	-	+	+
38.	Chest infection	+	-	-	-
39.	Chest infection	-	-	+	+
40.	Chest infection	-	-	+	+
41.	Urinary tract infection	-	-	+	+
42.	Urinary tract Infection	-	-	+	+
43.	Urinary tract Infection	-	+	-	+
44.	Urinary tract Infection	+	-	-	-
45.	Urinary tract Infection	-	+	-	-
46.	Urinary tract Infection	+	-	-	-
47.	Urinary tract Infection	-	-	+	+
48.	Urinary tract Infection	-	+	-	-
49.	Urinary tract Infection	-	+	-	-
50.	Urinary tract Infection	+	-	-	-
51.	Gastroenteritis	-	-	+	+
52.	Gastroenteritis	-	+	-	-
53.	Gastroenteritis	-	-	+	+
54.	Gastroenteritis	+	-	-	-
55.	Gastroenteritis	-	-	+	+
56.	Patients admitted to intensive care unit	-	-	+	+
57.	Patients admitted to intensive care unit	+	-	+	+
58.	Patients admitted to intensive care unit	-	+	-	-
59.	Patients admitted to intensive care unit	-	-	+	+
60.	Patients admitted to intensive care unit	-	-	+	+

Table S4. Time-killing curve for different groups infected with *E.coli* (wound no.3) resistant to both IMP & AMK .

		Control group (I)	Amikacin group (II)	Imipenem group (III)	Combination group (IV)	<i>p</i> value
0.5 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	9.35±0.01	9.36±0.02	9.31±0.01	<0.001*
	4 h	9.47±0.01	9.46±0.01	9.45±0.02	9.24±0.03	<0.001*
	8 h	10.08±0.02	10.05±0.02	10.05±0.02	9.04±0.02	<0.001*
	12 h	10.36±0.01	10.34±0.01	10.34±0	8.80±0.09	<0.001*
	24 h	10.47±0.01	10.47±0	10.47±0	7.46±0.01	<0.001*
1 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	9.22±0.02	9.25±0.01	9.19±0.04	<0.001*
	4 h	9.47±0.01	7.18±0.01	7.20±0.01	7.09±0.01	<0.001*
	8 h	10.08±0.02	7.07±0.02	7.15±0.02	6.97±0.01	<0.001*
	12 h	10.36±0.01	6.91±0.03	6.97±0.02	6.87±0.01	<0.001*
	24 h	10.47±0.01	6.75±0.04	6.81±0.03	4.7±0.02	<0.001*
2 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	8.01±0.01	8.01±0.01	7.98±0.02	<0.001*
	4 h	9.47±0.01	7.93±0.01	7.95±0.03	7.88±0.03	<0.001*
	8 h	10.08±0.02	6.72±0.05	6.82±0.02	6.65±0.04	<0.001*
	12 h	10.36±0.01	6.64±0.02	6.68±0.05	5.94±0.03	<0.001*
	24 h	10.47±0.01	5.53±0.05	5.85±0.04	4 ±0.04	<0.001*
4 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	6.87±0.06	6.89±0.02	6.72±0.05	<0.001*
	4 h	9.47±0.01	5.64±0.08	5.80±0.01	4.60±0.04	<0.001*
	8 h	10.08±0.02	4.50±0.03	4.63±0.03	0±0	<0.001*
	12 h	10.36±0.01	0±0	0±0	0±0	<0.001*
	24 h	10.47±0.01	0±0	0±0	0±0	<0.001*

* Significant p-value: <0.001.

Table S5. Time-kill studies for different groups infected with imipenem resistant *E. Coli* (W2).

		Control group (I)	Amikacin group (II)	Imipenem group (III)	Combination group (IV)	<i>p</i> value
0.5 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	6.79±0.04	9.01±0.01	8.92±0.03	<0.001*
	4 h	9.47±0.01	5.61±0.07	9.06±0.01	8.71±0.06	<0.001*
	8 h	10.08±0.02	5.58±0.06	9.10±0.01	8.02±0.01	<0.001*
	12 h	10.36±0.01	4.64±0.07	9.22±0	8.26±0.01	<0.001*
	24 h	10.47±0.01	4.50±0.01	10.2±0.01	8.09±0.01	<0.001*
1 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	6.25±1.22	8.95±0.02	6.87±0.02	<0.001*
	4 h	9.47±0.01	5.86±0.01	8.70±0.05	6.53±0.02	<0.001*
	8 h	10.08±0.02	4.52±0.02	7.90±0.03	5.78±0.03	<0.001*
	12 h	10.36±0.01	0±0	6.69±0.04	5.49±0.01	<0.001*
	24 h	10.47±0.01	0±0	6±0.02	4±0.03	<0.001*

* Significant p-value: <0.001.

Table S6. Time-kill studies for different groups infected with amikacin resistant *E. Coli* (W1).

		Control group (I)	Amikacin group (II)	Imipenem group (III)	Combination group (IV)	<i>p</i> value
0.5 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	9.28±0.01	6.69±0.04	9.25±0.02	<0.001*
	4 h	9.47±0.01	9.32±0.01	5.72±0.06	9.21±0	<0.001*
	8 h	10.08±0.02	9.45±0.01	5.48±0.01	9.01±0.01	<0.001*
	12 h	10.36±0.01	9.31±0.41	4.72±0.05	8.88±0.01	<0.001*
	24 h	10.47±0.01	10.01±0.01	4.51±0.03	8.03±0.02	<0.001*
1 mic concentration	0 h	8.20±0.02	8.20±0.02	8.20±0.02	8.20±0.02	1
	2 h	9.36±0.01	7.95±0.02	5.58±0.05	6.93±0.01	<0.001*
	4 h	9.47±0.01	7.67±0.03	4.59±0.07	6.60±0.04	<0.001*
	8 h	10.08±0.02	6.85±0.03	0±0	5.87±0.03	<0.001*
	12 h	10.36±0.01	6.52±0.03	0±0	5.50±0.03	<0.001*
	24 h	10.47±0.01	6±0.02	0±0	4±0.04	<0.001*

* Significant p-value: <0.001.

In-vivo studies

Table S7. Average blood bacterial count of *E. coli* isolated from untreated animals and animals treated with imipenem, amikacin, and combination at different time.

Organism	Time	Untreated (I)	Imipenem (II)	Amikacin (III)	Combination (IV)	<i>p</i> value
<i>E. coli</i>	3h	9.41±0.01	9.34±0.01	9.28±0.01	9.11±0.02	<0.001*
	11h	10.29±0.02	9.05±0.02	8.84±0.05	8.13±0.03	<0.001*
	27h	10.36±0.01	8.71±0.06	8.25±0.01	6.0±0.52	<0.001*

p values between different times.

	3h vs 11h	3h vs 27h	11h vs 27h
Untreated	<0.001*	<0.001*	<0.001*
Imipenem	<0.001*	<0.001*	<0.001*
Amikacin	<0.001*	<0.001*	<0.001*
Combination	<0.001*	<0.001*	<0.001*

Table S8. Gene expression of resistant *E. coli* after treatment.

<i>E. coli</i> Isolate No.	16S rRNA	<i>bla</i> -IMP	<i>aac</i> (6')-Ib		
	CT	CT	Fold change	CT	Fold change
E1 (Control)	20.57	22.38	-	23.04	-
E2	19.88	18.49	9.1896	19.73	6.1475
E3	20.31		Nd	19.31	11.0809
E4	20.16	18.19	13.7370		Nd
E5	19.54	19.53	3.5328	19.60	5.3147
E6	20.20	19.50	5.6962	21.23	2.7132

E1: Control.

E2: *E. coli* (w3) resistant for amikacin harboring *aac*(6')-Ib and imipenem harboring *bla*_{IMP}

E3: *E. coli* (W1) resistant to amikacin harboring *aac*(6')-Ib only.

E4: *E. coli* (W2) resistant to imipenem harboring *bla*_{IMP} only.

E5: *E. coli* isolate (w3) after treatment with 0.25MIC of amikacin+0.5MIC of imipenem.

E6: *E. coli* isolate (w3) after treatment with 0.25MIC of imipenem+0.5MIC of amikacin.