

## Revised Abstract

**Background:** Intra-abdominal infections (IAIs) represent some of the most frequently encountered nosocomial infections in the healthcare setting and are mostly caused by gram-negative bacilli (GNB). *Enterobacter* spp., comprise an important part of the etiology of such infections, for which increasing drug-resistance may lead to a limitation in available therapies. In the current report we describe the incidence of *Enterobacter aerogenes* and *E. cloacae* in IAIs and their susceptibility to tigecycline and comparator agents. **Methods:** A total of 263 and 63 isolates of *E. cloacae* and *E. aerogenes*, respectively were collected from gastro-intestinal (GI) sources worldwide during 2009-2010. All isolates were collected during the Tigecycline Evaluation and Surveillance Trial (TEST). MICs were performed and interpreted according to CLSI and FDA guidelines (tigecycline) where appropriate. **Results:** The activity of tigecycline and selected comparators are shown in the Table.

<i>E. cloacae</i> (263)					<i>E. aerogenes</i> (63)				
Drug	MIC <sub>90</sub>	%S	%I	%R	Drug	MIC <sub>90</sub>	%S	%I	%R
Amikacin	8	95.8	2.3	1.9	Amikacin	8	95.2	1.6	3.2
Amox-Clav	> 32	3.0	4.2	92.8	Amox-Clav	> 32	3.2	3.2	93.7
Ampicillin	> 32	1.9	8.4	89.7	Ampicillin	> 32	1.6	15.9	82.5
Cefepime	8	90.9	2.7	6.5	Cefepime	4	96.8	0.0	3.2
Ceftriaxone	> 64	51.0	1.1	47.9	Ceftriaxone	64	57.1	3.2	39.7
Levofloxacin	> 8	80.2	4.2	15.6	Levofloxacin	> 8	84.1	1.6	14.3
Meropenem	0.5	94.3	3.0	2.7	Meropenem	0.25	93.7	1.6	4.8
Minocycline	> 16	54.4	21.7	24.0	Minocycline	16	68.3	14.3	17.5
Pip-Tazo	> 128	66.9	12.6	20.5	Pip-Tazo	128	66.7	19.1	14.3
Tigecycline	2	94.7	3.0	2.3	Tigecycline	2	96.8	3.2	0.0

%Sa, percent of isolates susceptible (S), intermediate (I) or resistant (R)

**Conclusions:** Collectively, *E. aerogenes* and *E. cloacae* comprised 7.2% of all isolates from GI sources during TEST 2009-2010. The most active agents were amikacin, cefepime, meropenem and tigecycline and all consistently exhibited susceptibility >90%. Against multi-drug resistant isolates (defined as resistant to three or more drug classes), only tigecycline exhibited percent susceptibilities of >90 against both species. Overall, resistance to tigecycline was the lowest of all agents tested.

## Introduction

*Enterobacter* is a genus of common gram-negative, facultatively-anaerobic, rod-shaped bacteria of the family *Enterobacteriaceae*. Several strains of these bacteria are pathogenic and cause opportunistic infections in immunocompromised (usually hospitalized) hosts and in those who are on mechanical ventilation. The urinary and respiratory tracts are the most common sites of infection. It is also a fecal coliform, along with *Escherichia*. Two clinically-important species from this genus are *E. aerogenes* and *E. cloacae*. The current study reports the demographics and susceptibilities of *E. aerogenes* and *E. cloacae* isolates from gastro-intestinal infections collected as part of the global Tigecycline Evaluation and Surveillance Trial (TEST) during 2009-2010.

## Materials & Methods

- Clinical isolates:** Isolates were identified to the species level and MICs determined at each participating laboratory. All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age, or gender. All sites identified each study isolate utilizing local laboratory criteria. All isolates were from the period 2009 - 2010 and originated from various countries worldwide. Multi-drug resistance (MDR) was defined as resistance to at least three antibiotic classes.
- Susceptibility testing:** Minimum inhibitory concentrations (MICs) were determined using panels manufactured by TREK Diagnostics, following manufacturer and Clinical and Laboratory Standards Institute (CLSI) instructions for broth microdilution testing [1]. Susceptibility was determined using clinical breakpoints published by the CLSI and FDA [2,3]. Tigecycline was supplied by Pfizer, Inc. (Collegeville, PA, USA). All other agents were supplied by the panel manufacturers, MicroScan (Siemens Medical Solutions Diagnostics., West Sacramento, CA, USA) and TREK (TREK Diagnostic Systems, Cleveland, OH). The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): amikacin (0.5-64); amoxicillin-clavulanic acid (0.12/0.06-32/16); ampicillin (0.06-16); cefepime (0.5-32); ceftazidime (8-32); ceftriaxone (0.06-64); meropenem (0.12-16, TREK only); levofloxacin (0.008-8); minocycline (0.5-16); tigecycline (0.008-16); piperacillin-tazobactam (0.06/4-128/4). *E. coli* ATCC 25922 and ATCC 35218 and *P. aeruginosa* ATCC 27853 were tested as quality control organisms.

## References

- Clinical and Laboratory Standards Institute. 2009. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard, 8<sup>th</sup> ed. Approved standard M7-A8. Wayne, Pa.
- Clinical and Laboratory Standards Institute. 2010. Performance Standards for Antimicrobial Susceptibility Testing; Fourteenth Informational Supplement. CLSI document M100-S20. Wayne, PA.
- Tygacil®, 2010. Tigecycline FDA product information. Pfizer, Inc. Collegeville, PA, USA.

## Acknowledgements

We gratefully acknowledge the contributions of the investigators, laboratory personnel, and all members of the Tigecycline Evaluation and Surveillance Trial program group. This study was sponsored by Pfizer Inc.

## Results

Table 1. Susceptibility of *E. cloacae* (N = 263) and *E. aerogenes* (n = 63) isolates.

<i>E. cloacae</i> (263)					<i>E. aerogenes</i> (63)				
Drug	MIC <sub>90</sub>	%S	%I	%R	Drug	MIC <sub>90</sub>	%S	%I	%R
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Tigecycline	2	94.7	3.0	2.3	Tigecycline	2	96.8	3.2	0.0

Figure 3. Number of all *E. cloacae* isolates by infection location.

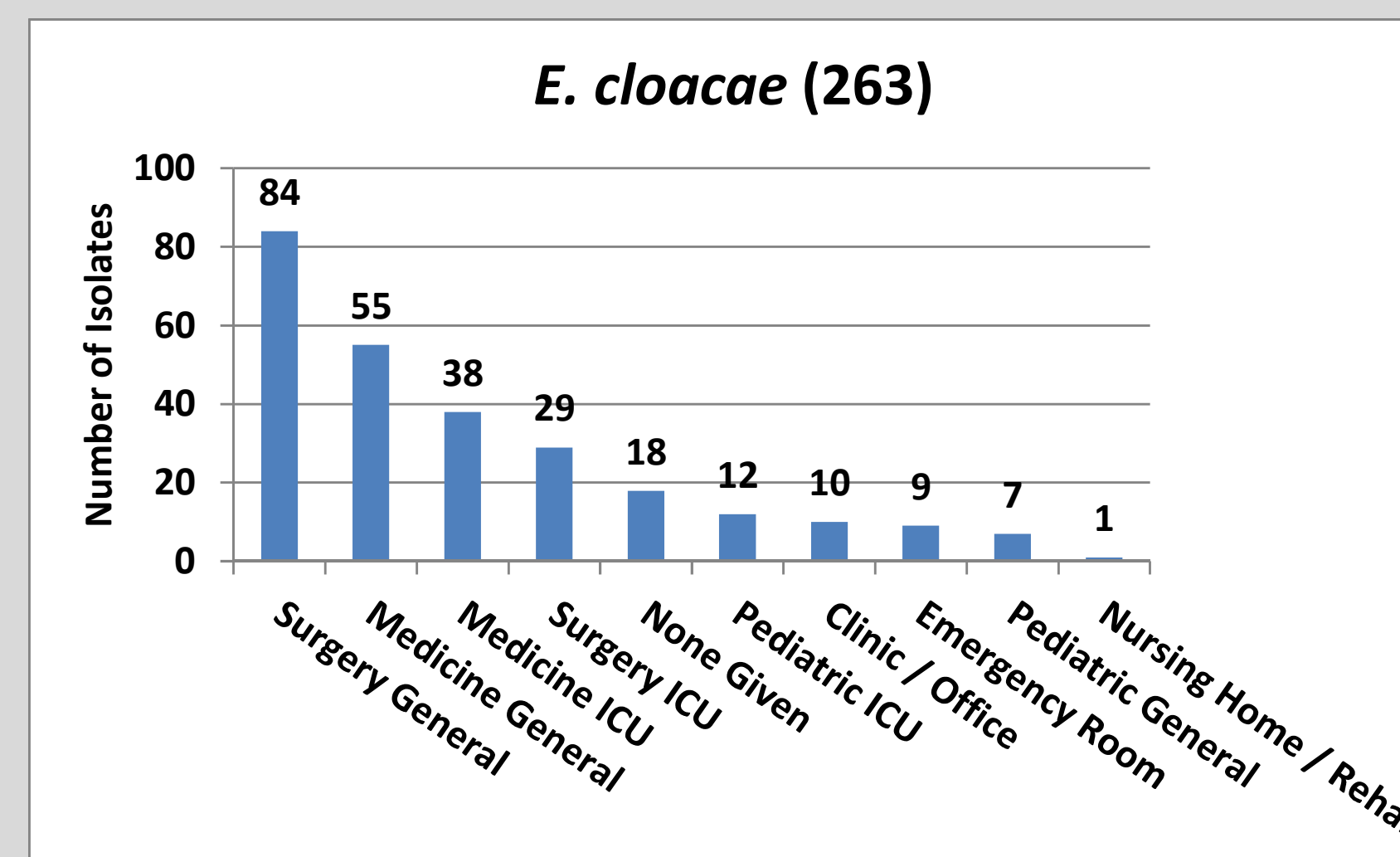


Figure 6. Susceptibility of MDR *E. aerogenes* isolates (n=26).

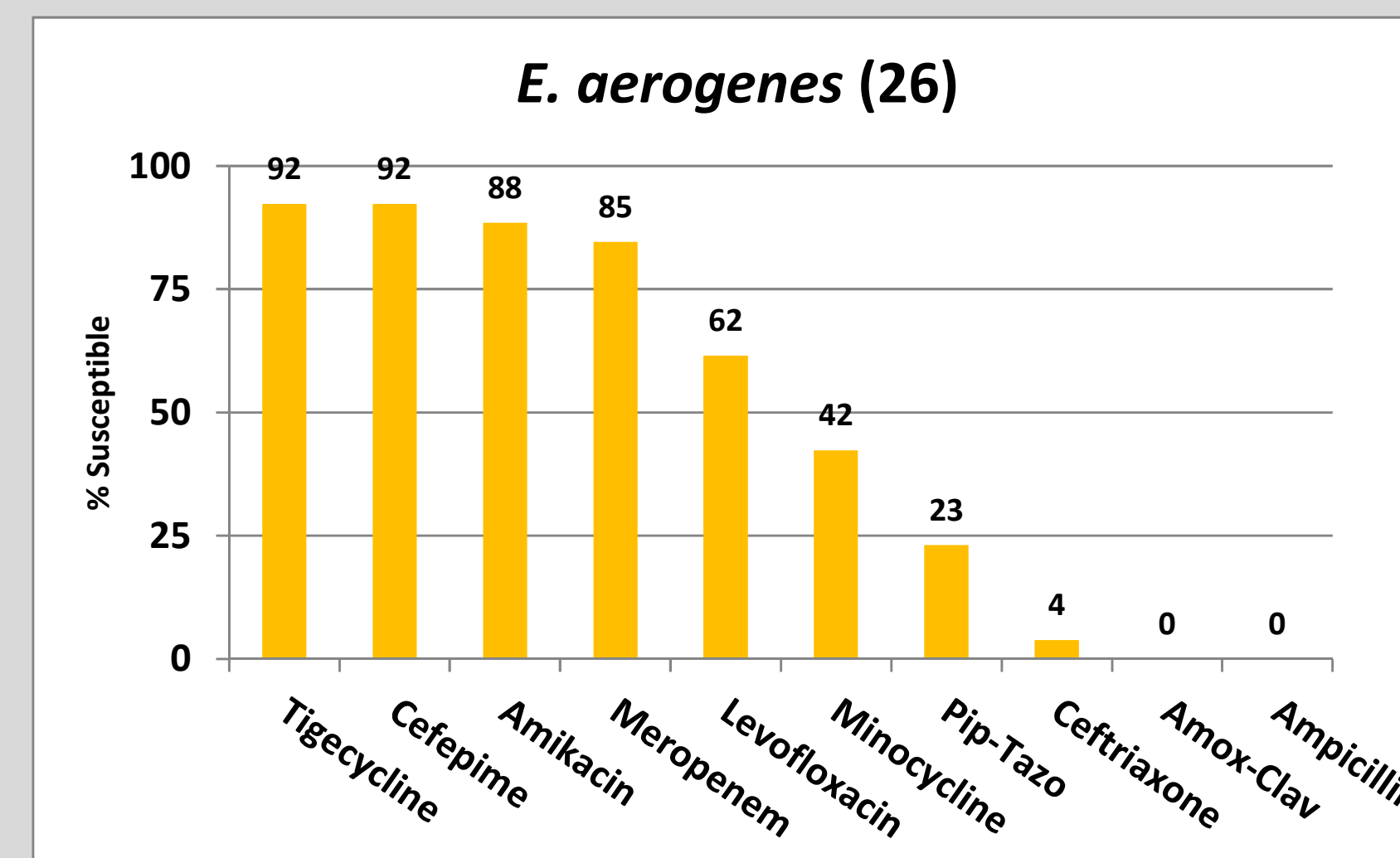


Figure 1. Number of all *E. cloacae* isolates by region.

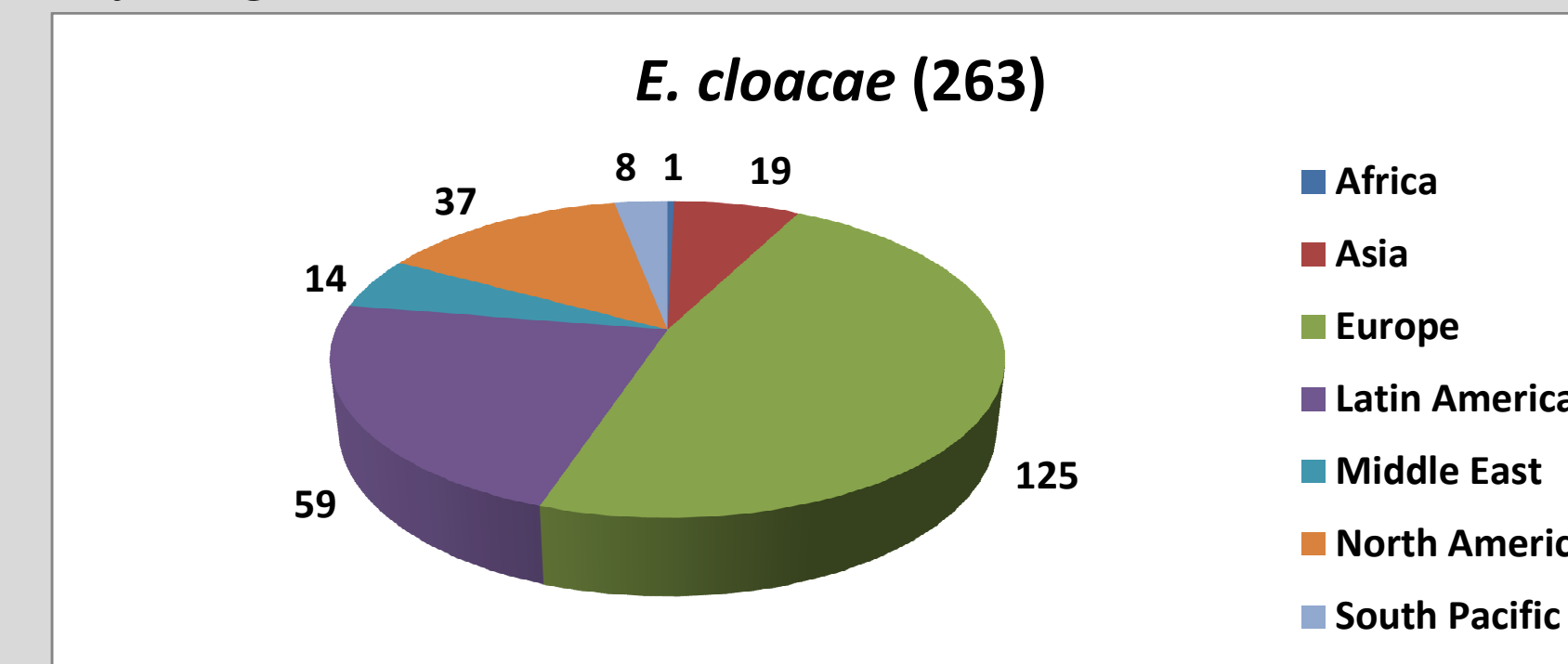


Figure 4. Number of all *E. aerogenes* isolates by infection location.

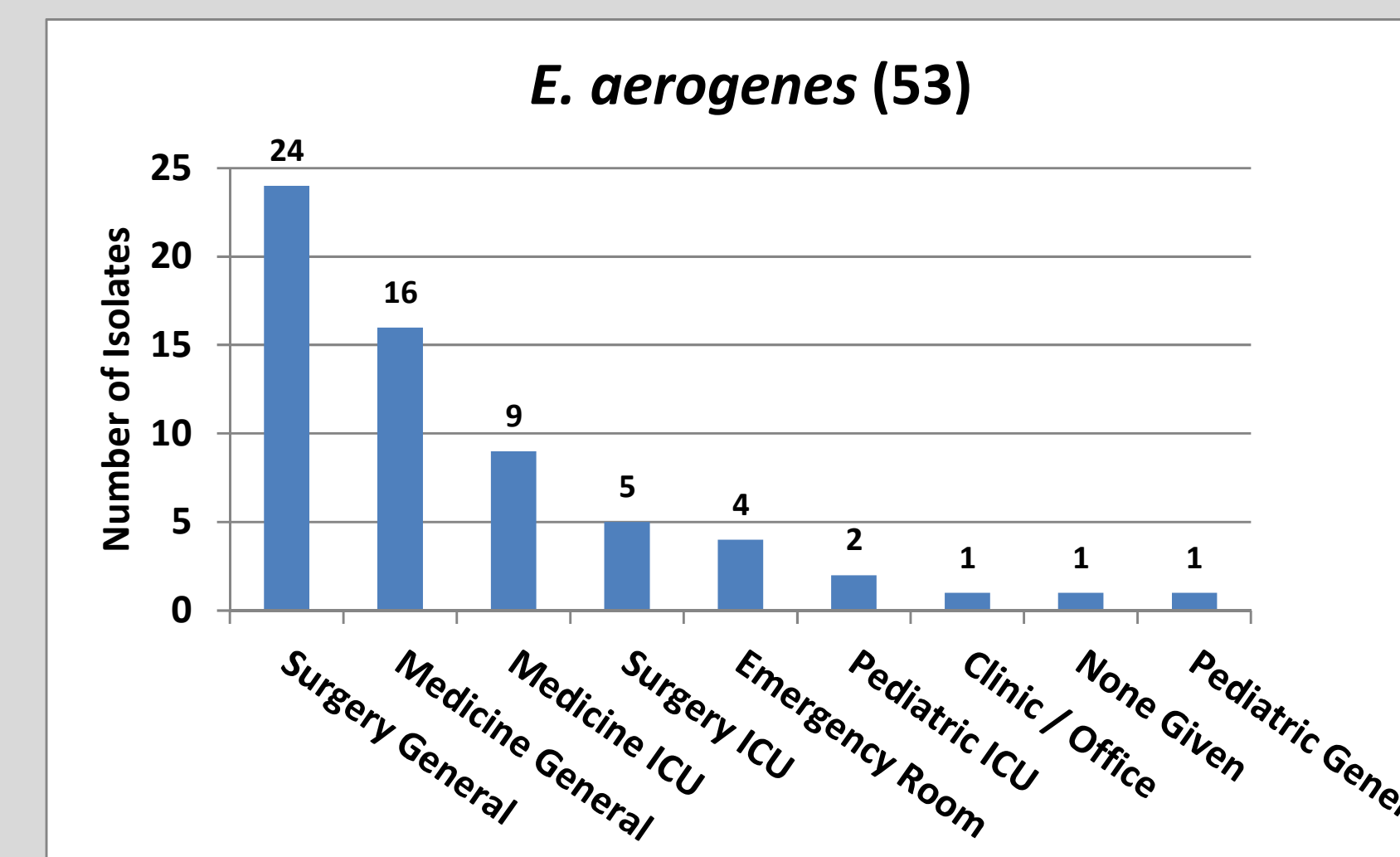


Figure 2. Number of all *E. aerogenes* isolates by region.

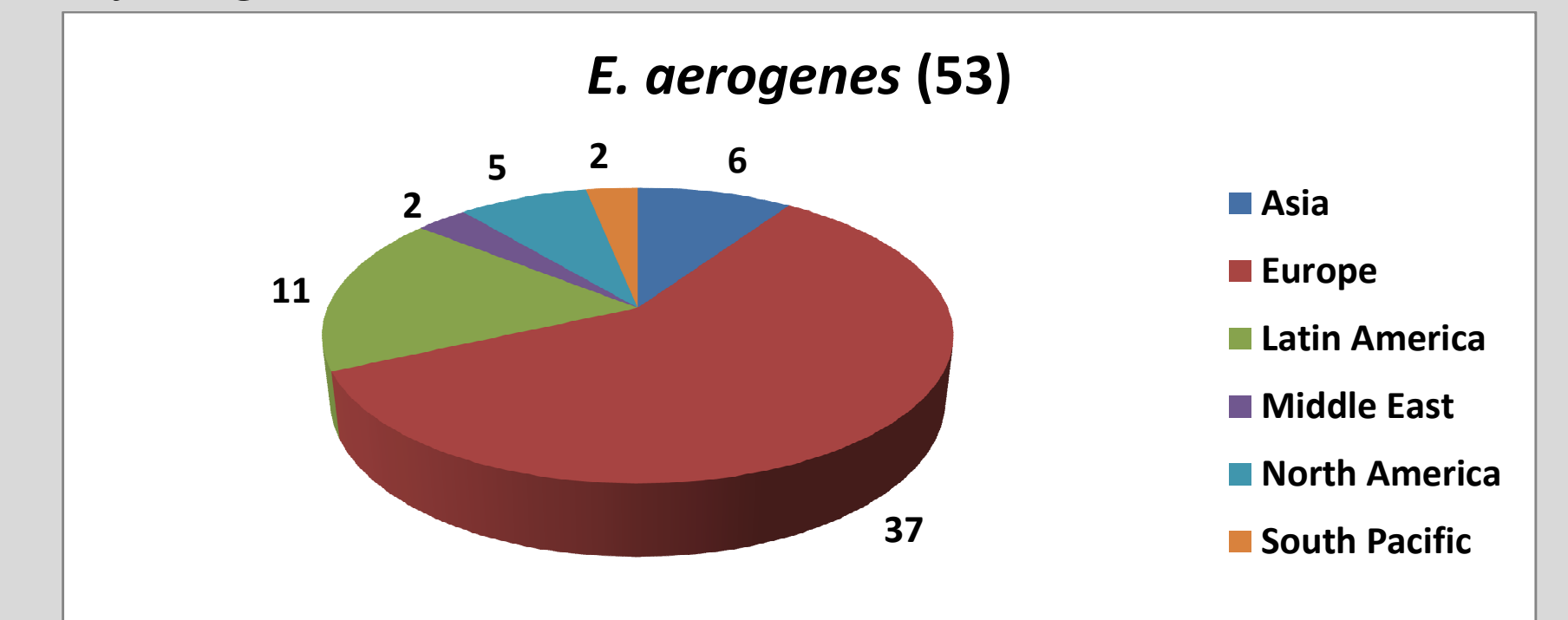
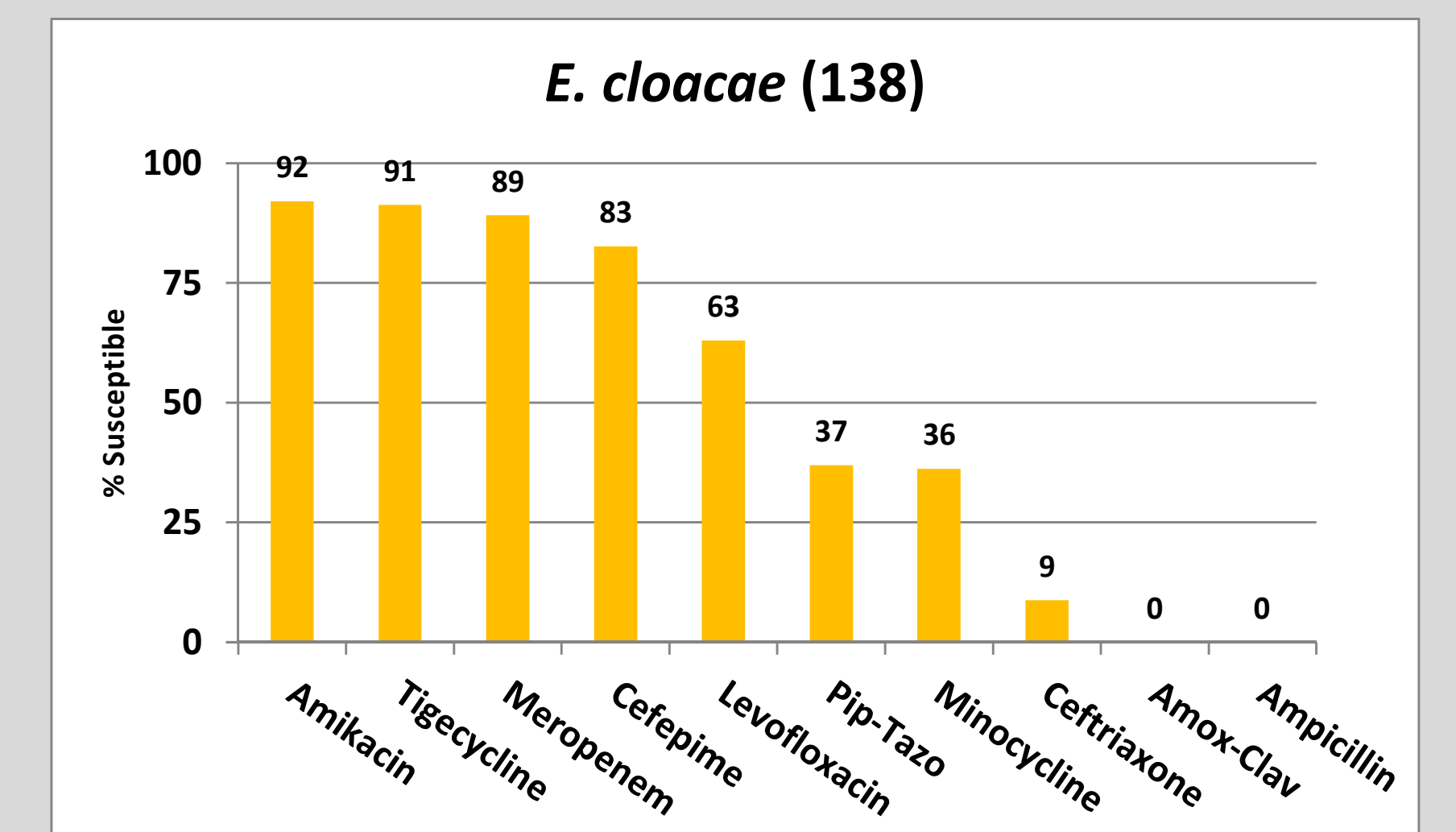


Figure 5. Susceptibility of MDR *E. cloacae* isolates (n= 138).



## Conclusions

- The most active agents were amikacin, cefepime, meropenem and tigecycline and all consistently exhibited susceptibility >90%.
- MDR isolates comprised 49% and 52% of *E. cloacae* and *E. aerogenes*, respectively.
- Against multi-drug resistant isolates, only tigecycline exhibited percent susceptibilities of >90 against both species.