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Introduction

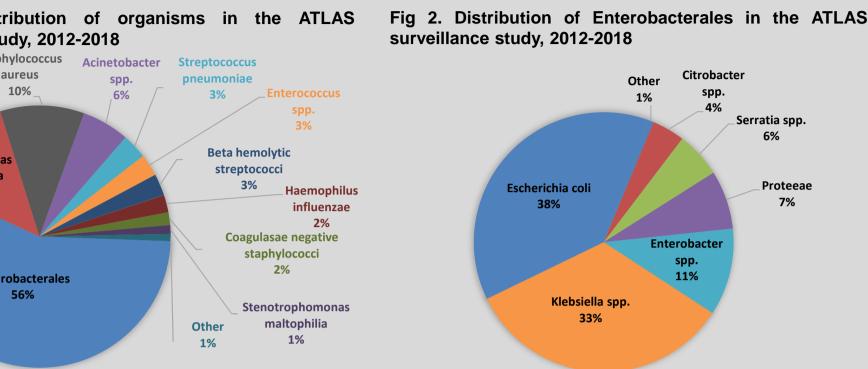
The ongoing problem of antibiotic resistance, including multidrug resistance is a global health issue. In order to determine the extent of the problem and to identify changes in the resistance patterns of global, regional and local pathogens, worldwide antibiotic surveillance programs are essential. The Antimicrobial Testing Leadership and Surveillance (ATLAS) program has provided reliable, global, regional and local in vitro susceptibility data, including mechanisms of resistance, since 2004. As it is important to monitor the emergence of new species and new resistance mechanisms over time, in this analysis we present a longitudinal analysis of resistance to commonly prescribed antimicrobials for isolates collected globally for ATLAS 2012-2018.

Methods

A total of 251,837 gram-negative and gram-positive non-duplicate, 132,363 clinical isolates were collected from multiple infection sources from 743 unique sites in 74 countries during 2012-2018 in the ATLAS program. Isolate inclusion was independent of medical history, antimicrobial use, age, or Organism identification was gender. confirmed by MALDI-TOF mass spectrometry, and susceptibility testing was performed by broth microdilution following CLSI guidelines at a central laboratory (IHMA, Schaumburg, IL, USA) [1]. Avibactam was tested at a fixed concentration of 4 µg/mL. MICs were interpreted using CLSI 2020 MIC breakpoint criteria [2]. FDA breakpoints were applied for tigecycline [3]. Quality control (QC) testing was performed on each day of testing using the appropriate ATCC control strains. Results were included in the analysis only when corresponding QC isolates tested were within the acceptable range according to CLSI guidelines [2].

Overview of ATLAS Program	Fig 1. Distribu
ATLAS	surveillance study
	Staphyloo aure
X	10%
Targeted surveillance	-
Collection of a predefined number of selected bacterial pathogens	
Global Geographic Focus	-
843 participating medical centers in 77 countries in Europe, Middle East, Africa, Asia/Pacific Rim, Latin	Pseudomonas aeruginosa
America, North America	13%
Organisms collected:	
Gram-negative and Gram-positive aerobes and facultative anaerobes, e.g. select	
Enterobacterales, P. aeruginosa, Acinetobacter spp., Haemophilus spp., Staphylococcus spp.,	
Enterococcus spp., Streptococcus spp., Moraxella spp.	Enteroba
	565
Gram-negative and Gram-positive obligate anaerobes, e.g. <i>Bacteroides</i> spp., <i>Clostridium</i> spp.	_
Antimicrobial classes tested:	
Cell wall/ cell envelope: β -lactams (penicillins, 3 rd -5 th generation cephalosporins, monobactams,	
carbapenems, β-lactam/β-lactamase inhibitor combinations); Glycopeptides; Polymyxins; Membrane	
depolarizers	Table 1
Protein synthesis: Aminoglycosides; Tetracyclines; Macrolides; Lincosamides; Oxazolidinones	from the
Totell'synthesis. Annogiyeosides, Tetracyclines, Macronides, Encosannides, Oxazonamones	
Nucleic acid synthesis: Fluoroquinolones; Antifolates	Organism Gram page
······································	Gram nega Enterobact
Total drugs/drug combinations tested: 27	CRE (5,9
Infection types:	ESBL+ (3
Intraabdominal infections	Pseudomo
Lower respiratory tract infections	Acinetobac
Urinary tract infections	Gram posi
Bloodstream infections	Enterococc
Skin and skin structure infections	S. aureus,
	S. aureus,
Community-acquired and hospital-acquired	CRE, carba
Phenotypes Isolates are collected regardless of antimicrobial susceptibility profile	susceptible
	AMK, amik vancomycii
ATLAS Surveillance program workflow	*MIC ₉₀ = 2
ATLAS Surveillance program workflow	Figure 3. Countri
Non-duplicate causative pathogens are collected at participating medical centers	green
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	A land and
The pathogens are shipped to the central laboratory (IHMA)	Verstor.
	The second s
◆	A CARLER AND
Species identification is confirmed by MALDI-TOF spectrometry	34
	1 22
◆	NORTH AMERIC
Antimicrobial susceptibility and quality control testing by broth microdilution (aerobes) or agar dilution	North /
(anaerobes) is performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines;	i and i a
MIC endpoints are determined manually (industry gold standard methodology)	and the second s
- · · · · · · · · · · · · · · · · · · ·	Start
L	SOUTH AMER
Enterobacterales, <i>Pseudomonas aeruginosa</i> , and <i>Acinetobacter baumannii</i> isolates are screened for	h Pacific Ocean
-	
presence of known resistance mechanisms (e.g. presence or alteration in genes encoding β-lactamases	
and penicillin-binding proteins, porin profiling) by PCR and Sanger sequencing or by whole genome	_ 2000 km _
sequencing (WGS)	

Results



. Activity of commonly used drugs against Gram-negative and Gram-positive isolates ne ATLAS surveillance study, 2012-2018

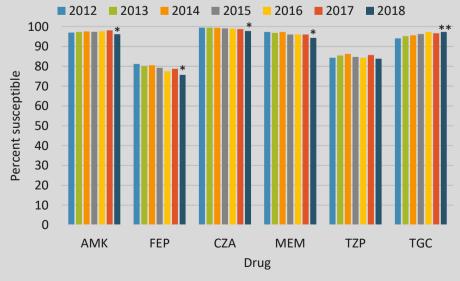
% Susceptible							
CZA	СТ	TGC	AMK	FEP	LVX	MEM	TZP
98.9	89.6	96.1	97.4	79.0	71.3	96.3	84.9
71.7	2.6	91.7	62.7	3.3	9.4	0	3.0
96.4	67.7	94.8	90.5	27.8	31.8	87.8	55.0
91.7	90.3	na	91.7	77.9	62.4	72.2	74.4
na	na	na*	61.2	47.7	48.9	51.2	47.1
СРТ	LNZ	TGC	AMP	ERY	LVX	VAN	
na	99.0	98.2	67.7	12.0	49.5	87.6	
>99.9	>99.9	99.7	na	75.6	92.0	100.0	
89.2	>99.9	98.8	na	31.0	32.6	>99.9	
	98.9 71.7 96.4 91.7 na CPT na >99.9	98.9 89.6 71.7 2.6 96.4 67.7 91.7 90.3 na na CPT LNZ na 99.0 >99.9 >99.9	98.9 89.6 96.1 71.7 2.6 91.7 96.4 67.7 94.8 91.7 90.3 na na na na* CPT LNZ TGC na 99.0 98.2 >99.9 >99.9 99.7	CZA CT TGC AMK 98.9 89.6 96.1 97.4 71.7 2.6 91.7 62.7 96.4 67.7 94.8 90.5 91.7 90.3 na 91.7 na na na* 61.2 CPT LNZ TGC AMP na 99.0 98.2 67.7 >99.9 >99.9 99.7 na	CZA CT TGC AMK FEP 98.9 89.6 96.1 97.4 79.0 71.7 2.6 91.7 62.7 3.3 96.4 67.7 94.8 90.5 27.8 91.7 90.3 na 91.7 77.9 na na na* 61.2 47.7 CPT LNZ TGC AMP ERY na 99.0 98.2 67.7 12.0 >99.9 >99.9 99.7 na 75.6	CZA CT TGC AMK FEP LVX 98.9 89.6 96.1 97.4 79.0 71.3 71.7 2.6 91.7 62.7 3.3 9.4 96.4 67.7 94.8 90.5 27.8 31.8 91.7 90.3 na 91.7 77.9 62.4 na na na* 61.2 47.7 48.9 CPT LNZ TGC AMP ERY LVX na 99.0 98.2 67.7 12.0 49.5 >99.9 >99.9 99.7 na 75.6 92.0	CZACTTGCAMKFEPLVXMEM98.989.696.197.479.071.396.371.72.691.762.73.39.4096.467.794.890.527.831.887.891.790.3na91.777.962.472.2nanana*61.247.748.951.2CPTLNZTGCAMPERYLVXVANna99.098.267.712.049.587.6>99.9>99.999.7na75.692.0100.0

penem-resistant Enterobacterales (MEM [meropenem] MIC >2 μg/mL; ESBL+, extended-spectrum β-lactamase positive; MSSA, methicillin-S. aureus; MRSA, methicillin-resistant S. aureus; na, no breakpoint; CZA, ceftazidime-avibactam; CT, ceftolozane-tazobactam; TGC, tigecycline; acin; FEP, cefepime; LVX, levofloxacin; TZP, piperacillin-tazobactam; CPT, ceftaroline; LNZ, linezolid; AMP, ampicillin; ERY, erythromycin; VAN,

es participating in the ATLAS study in



Figure 4. Percentage of susceptibility among Enterobacterales over seven years from the ATLAS surveillance study



AMK, amikacin; FEP, cefepime; CZA, ceftazidime-avibactam; MEM, meropenem; TZP, piperacillin-tazobactam; TGC, tigecycline

Percent susceptible based on CLSI 2020 breakpoints; * statistically significant decrease in susceptibility between 2012 and 2018 based on Chi-square with Yates' correction (p<0.0001): ** statistically significant increase in susceptibility between 2012 and 2018 based on Chi-square with Yates' correction (p<0.0001)

Results Summary

- The proportion of Enterobactera isolates resistant to commonly us antimicrobials has fluctuated of the seven years compared in analysis, with significant increas in resistance for amikacin (3.0% 3.8%), cefepime (18.9% to 24.4 ceftazidime-avibactam (0.5% 2.2%), and meropenem (2.7%) 5.7%), and a significant decreas resistance to tigecycline (5.9% 2.7%) between 2012-2018 (0 square with Yates' correct p<0.0001) (Figure 4).
- Piperacillin-tazobactam showed significant change in resistance over seven years of study.

Conclusions

This longitudinal analysis of seven years of global surveillance confirms rising rates of antimicrobial resistance to commonly used antibiotics. Continued monitoring is essential to understand the scope of this global public health issue, and to aid in the development of new strategies and treatments for these key pathogens.

References

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- 2. Clinical and Laboratory Standards Institute (CLSI), 2020. Performance Standards for Antimicrobial Susceptibility Testing – Thirtieth Informational Supplement, CLSI Document M100S, Pennsylvania 19087-1898 USA.
- 3. Tygacil®, 2016. Tigecycline FDA prescribing information. Pfizer, Inc., Collegeville, PA.

Disclosures

This study was sponsored by Pfizer. AstraZeneca's rights to ceftazidime-avibactam and ceftaroline fosamil, which were acquired by Pfizer in December 2016. IHMA received financial support from Pfizer in connection with the study and the development of this poster. MH, SB and DS are employees of IHMA. MD is an employee of Pfizer.

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