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ABSTRACT

**Background:** A nationwide survey was conducted in Japan from 2018–2019 to investigate the antimicrobial susceptibility of pathogens isolated from surgical site infections (SSI).  
**Methods:** The resulting data were compared with that obtained in earlier surveys, conducted in 2010, 2014–2015, and 2018-2019.  
**Results:** Seven main organisms were collected, and in total 2078 isolates were studied. Although a significant increase of extended-spectrum β-lactamase (ESBL) producing organisms among Enterobacteriaceae was demonstrated in 2014–15 (13.5%) compared with 2010 (4.4%), the incidence remained 6.6% in 2018–19. Only one carbapenemase-producing Enterobacteriaceae isolates were identified in the 2018–2019 study. The geometric mean (GM) MICs for ESBL producing isolates in 2018–2019 were 0.08 µg/mL for meropenem, 2.67 µg/mL for tazobactam/piperacillin, 0.40 µg/mL for tazobactam/ceftolozane, 6.35 µg/mL for cefoxitin, and 1.12 µg/mL for gentamycin. Antibiotic susceptible rate in *Pseudomonas aeruginosa* was 95.5% in meropenem, 93.9% in piperacillin/tazobactam, 100% in tazobactam/ceftolozane, 97.0% in cefepime, 90.9% in ciprofloxacin, and 86.4% in gentamycin. There was no significant difference in methicillin resistance rate of *Staphylococcus aureus* isolates among 3 study periods (72.5% in 2010, 53.4% in 2014–2015, and 53.3% in 2018-19). MRSA isolates with a vancomycin minimum inhibitory concentration (MIC) of 2µg/mL accounted for 9.7% in 2010, 1.2% in 2014–2015, and 3.1% in 2018-19. GM MICs for MRSA isolates were 2.09 µg/mL for linezolid, 0.32 µg/mL for tedizolid, and 0.61 µg/mL for daptomycin. GM MICs in linezolid and daptomycin for the isolates in 2018–19 tended to be increased compared with isolates in 2010 (1.74 to 2.09 and 0.35 to 0.61 µg/mL, respectively). More than 90% of isolates belonging to the *Bacteroides fragilis* group remained susceptible to tazobactam/piperacillin, meropenem, and metronidazole. In contrast, lower levels of susceptibility were observed for moxifloxacin (65.3%), cefmetazole (47.2%) and clindamycin (38.9%).  
**Conclusion:** Overall, the surveillance data clarified trends in antimicrobial susceptibility for organisms commonly associated with SSI.

Background

Internationally, surgical site infections (SSI) make up a large percentage of hospital-acquired infections. The nationwide survey of the antimicrobial susceptibility of bacteria isolated from surgical site infections (SSI) in Japan were investigated in 2010<sup>1</sup> and 2014-2015<sup>2</sup>. And the nationwide survey was conducted in Japan from 2018–2019 to investigate the antimicrobial susceptibility of pathogens isolated from SSI.

1. Takesue Y, et al: J Infect Chemother. 2012; 18: 816-826.  
2. Takesue Y, et al: J Infect Chemother. 2017; 23: 339-348.

Methods

- 7 main organisms were analyzed (*Echerichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *B. fragilis* group species, *S. aureus*, and *Enterococcus faecalis*).
- 27 medical centers around Japan participated in 2018-2019 study
- Tested antimicrobial agents: cefoxitin (CFX), ceftazidim (CAZ), cefepime (CFPM), aztreonam (AZT), meropenem (MEPM), sulbactam/ampicillin (SBT/ABPC), piperacillin/ tazobactam (PIPC/TAZ), ceftolozan/tazobactam (CTLZ/TAZ), ciprofloxacin (CPFX), moxifloxacin (MFLX),, gentamycin (GM), tigecycline (TGC), colistin (CL), metronidazole (MNZ), clindamycin (CLDM), vancomycin (VCM), teicoplanin (TEIC), linezolid (LZD), tedizolid (TZD), daptomycin (DAP)
- PIPC/TAZ, TCLZ/TAZ: fixed concentration of 4 µg/mL TAZ was used.

RESULTS

Table 1. Change of the incidence of antibiotic resistant Enterobacteriaceae

	ESBL producing organisms			CPE		
	2010	2014-15	2018-2019	2010	2014-15	2018-2019
<i>E. coli</i>	9/95 (9.5%)	35/152 (23.0%)	9/104 (8.7%)	0	0	0
<i>K. pneumoniae</i>	0/53	6/56 (10.7%)	3/28 (10.7%)	1 (1.9%)	1 (1.8%)	0
<i>E. cloacae</i>	0/58	0/96 (0%)	0/49 (0.0%)	1 (1.7%)	1 (1.0%)	1 (2.0%)
Total	9/206 (4.4%)	41/304 (13.5%)	12/181 (6.6%)	2 (1.0%)	2 (0.7%)	1 (0.6%)

ESBL: extended-spectrum β-lactamase; CPE: Carbapenemase producing Enterobacteriaceae

Table 3. Antibiotic susceptibility in *E. cloacae* and *P. aeruginosa*

	Susceptible rate (%)					
	<i>E. cloacae</i>			<i>P. aeruginosa</i>		
	2010 (n=58)	2014-15 (n=95)	2018-19 (n=49)	2010 (n=108)	2014-15 (n=136)	2018-19 (n=66)
PIPC/TAZ	81.0	83.3	83.7	92.6	93.4	93.9
CTLZ/TAZ	–	–	81.6	–	–	100.0
CAZ	74.1	68.8	75.5	89.8	94.1	95.5
CFPM	100.0	92.7	95.9	91.7	95.6	97.0
MEPM	100.0	97.9	98.0	93.5	91.9	95.5
AZT	77.6	71.9	81.6	86.1	89.7	92.4
GM	100.0	97.9	98.0	100.0	99.3	86.4
CPFX	79.3	89.5	95.9*	90.7	89.0	90.9

\*: vs. 2010 survey CPFX, P = 0.019

Table 5. Change of antibiotic susceptibility in MRSA

	2010 (n=103)		2014-15 (n=86)		2018-19 (n=32)	
	Susceptible rate (%)	GM MIC (µg/mL)	Susceptible rate (%)	GM MIC (µg/mL)	Susceptible rate (%)	GM MIC (µg/mL)
VCM*	100.0	1.055	100.0	0.851	100.0	0.841
TEIC	100.0	0.823	100.0	0.824	100.0	0.723
LZD	100.0	1.736	100.0	1.845	100.0	2.089
TZD	–	–	–	–	100.0	0.317 <sup>†</sup>
DAP	100.0	0.352	100.0	0.374	100.0	0.608
TGC	–	–	–	0.365	–	0.339

\*: MRSA isolates with a MIC of 2µg/mL accounted for 9.7% in 2010, 1.2% in 2014–2015, and 3.1% in 2018-19.

<sup>†</sup>: vs. LZD, P < 0.001

GM MICs in LZD and DAP in 2018–19 tended to be increased compared with 2010 (1.74 to 2.09 and 0.35 to 0.61 µg/mL, respectively).

Table 2. Antibiotic susceptibility in ESBL-producing Enterobacteriaceae

	2010 (n=9)		2014-15 (n=40)		2018-19 (n=12)	
	Susceptible rate (%)	GM MIC (µg/mL)	Susceptible rate (%)	GM MIC (µg/mL)	Susceptible rate (%)	GM MIC (µg/mL)
MEPM	100.0	0.063	100.0	0.065	91.7	0.084
PIPC/TAZ	100.0	2.000	92.5	2.979	91.7	2.670
CTLZ/TAZ	–	–	–	–	91.7	0.397*
CFX	–	–	80.0	6.169	83.3	6.350
GM	88.9	0.680	75.0	1.552	83.3	1.122
CPFX	66.7	0.431	27.5	8.877 <sup>†</sup>	16.7	7.556
TGC	–	–	–	0.297	–	0.354
CL	–	–	–	–	91.7	0.891

\*: vs. PIPC/TAZ, P = 0.180, <sup>†</sup>: vs. 2010 survey, P = 0.081

GM: Geometric mean

Table 4. Antibiotic susceptibility rates for *Bacteroides fragilis* group species

	Susceptible rate (%)		
	2010 (n=108)	2014-2015 (n=113)	2018-19 (n=72)
ABPC/SBT	91.7%	79.6%	80.6% <sup>*</sup>
PIPC/TAZ	97.2%	92.9%	90.3%
CFX	86.1%	66.4%	65.3% <sup>*</sup>
MEPM	98.1%	94.7%	90.3%
MFLX	–	61.9%	65.3%
CLDM	59.3%	46.9%	38.9% <sup>*</sup>
MNZ	100.0%	100.0%	100.0%

<sup>\*</sup>: vs. 2010 survey, SBT/ABPC, P = 0.029; CFX, P = 0.001, CLDM, P = 0.007

SUMMARY

1. Although a significant increase of ESBL-producing organisms was demonstrated in 2014–15 (13.5%) compared with 2010 (4.4%), the incidence remained 6.6% in 2018–19.
2. Only one CPE isolates were identified in the 2018–2019.
3. Low geometric mean (GM) MICs (< 1 µg/mL) for ESBL producing isolates in 2018–2019 were demonstrated in MEPM (0.08 µg/mL), TAZ/CTLZ (0.40 µg/mL).
4. High susceptibility rate against all antibiotics measured was observed in *P. aeruginosa*
5. Low levels of susceptibility were observed for MFLX, CFX and CLDM among isolates belonging to the *Bacteroides fragilis* group.
6. There was no significant difference in MRSA rate among *S. aureus* during 3 study periods (72.5% in 2010, 53.4% in 2014–2015, and 53.3% in 2018-19).
7. GM MICs for MRSA isolates were 2.09 µg/mL for LZD, 0.32 µg/mL for TZD, and 0.61 µg/mL for DAP.

CONCLUSIONS

Japanese surveillance data clarified no significant trends for lowering antibiotic susceptibility over a decade in organisms commonly associated from SSI.