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A comparison between conventional and stratified antibiograms for antibiotic empirical therapy among the most bacterial pathogens

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ABSTRACT

Antibiograms provide important data regarding antimicrobial selection during empirical therapy and for monitoring yearly trends in antimicrobial resistance in healthcare settings. Antibiograms tailored to hospital location or specimen type are called stratified antibiograms. This retrospective study compared conventional and stratified antibiograms for *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii,* and *Pseudomonas aeruginosa* at the Hua-Hin hospital between January 2015 and December 2015. Stratified antibiograms were specific to the specimen type or ward were constructed after eliminating duplicate samples. Susceptibilities of 2,323 bacterial isolates of *E. coli, S. aureus, K. pneumoniae, A. baumannii,* and *P. aeruginosa* (32.6%, 15.6%, 15.4%, 16.0%, and 20.4%, respectively) were analyzed and percentage antimicrobial susceptibility did not differ between the stratified antibiogram for the first specimen alone and the conventional antibiogram. Similarly, percentage susceptibility between intensive care unit (ICU) and non-ICU wards or specimen type was comparable between the antibiograms. However, percentage susceptibilities of urinary *P. aeruginosa* isolates to amikacin, gentamicin, and ciprofloxacin were 60.6, 59.2, and 57.7, respectively, which was lower than that seen in the conventional antibiogram, namely, 84.1% (amikacin), 83.5% (gentamicin), and 80.1% (ciprofloxacin). Thus, stratified antibiograms, categorized by specimen type or ward, may be more useful in selecting appropriate empirical therapy.

Keywords: antibiogram; bacteria; specimen; intensive care unit

1. INTRODUCTION

Growing antimicrobial resistance among bacteria has become an urgent public health problem as it increases treatment costs and mortality rate (Busani et al., 2017; Thabit et al., 2015). Nationwide reports from hospitals in Thailand in 2010 revealed that the number of patients who died from *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*,

Klebsiella pneumoniae, and *Escherichia coli* infections were 22,567, 10,791, 9,698, 7,855, and 3,104, respectively (Suttajit et al., 2013). Therefore, choosing an appropriate antimicrobial can reduce unfavorable treatment outcomes (Morata et al., 2012; Santimaleeworagun et al., 2011).

The antibiogram provides important information on drug resistance trends in healthcare settings (Joshi, 2010) and can guide drug selection during empirical therapy. However, in Thailand, data regarding duplicate isolates from the same patient are not eliminated while constructing antibiograms, and antibiograms stratified by specimen type or ward are not generally used. A study conducted by Horvat et al. (2003) at a medical center in Kansas, USA revealed that duplicate methicillin resistant *S. aureus* (MRSA) isolates had been obtained from 88% of the patients and the rate of MRSA decreased when duplicate isolates were eliminated from the antibiogram analysis. Moreover, Kuster et al. (2008) have shown that stratified antibiograms providing unit-specific and anatomical site-specific data are preferable for selecting empirical antibiotic treatment compared with conventional antibiograms. Therefore, we compared conventional antibiograms with stratified antibiograms classified by specimens or wards and evaluated the effects of eliminating duplicate isolates from a patient in a given year on the antibiograms for nosocomial pathogens such as *E. coli*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, and *P. aeruginosa*. We hypothesized that the stratified antibiograms would more accurately enable antimicrobial selection.

2. MATERIALS AND METHODS

2.1 Study design

This retrospective study included antimicrobial susceptibility data of bacteria isolated from patients admitted to the Hua Hin hospital in the year 2015. The facility is a 340-bed tertiary care and referral center for coronary heart disease and traumatic patients that is located in Hua Hin, Prachuap Khiri Khan province, western Thailand. Antibiotic susceptibility results from surveillance specimens, from the out-patient department, and the emergency room were excluded. Antimicrobial susceptibility testing was performed using the standard disk diffusion method, as recommended by the Clinical and Laboratory Standards Institute (2016).

2.2 Data analysis

Susceptibility rate of bacteria among the conventional antibiogram that included susceptibility data from all isolates, regardless of specimen type or ward (conventional antibiogram); the stratified antibiogram that categorized isolates by hospitalization ward of the patient at the time of specimen collection (intensive care unit (ICU)/non-ICU); and the anatomical site from which it was isolated (blood, urine, or sputum) was compared. For comparing the effect of duplicate isolates, antimicrobial susceptibility data were sorted in chronological order by patient identification number, date of testing, and specimen number, for facilitating subsequent analyses. The results for the first isolate per patient in a given year, regardless of susceptibility profile or specimen were obtained and compared with results from all isolates, including those from the same patient. Hence, all isolates that showed divergent resistance patterns in follow-up isolates collected during 14 days after the first isolate and to more than two antibiotic agents were excluded.

2.3 Statistical analysis

Percentage antimicrobial susceptibility in each type of antibiogram (conventional vs. stratified antibiogram, or all isolates vs. eliminated duplicate isolates) was compared using the Chi-square or Fisher's exact tests. All statistical analyses were performed using PSPP version 8.0.2. All tests were two-tailed, and a p-value of < 0.05 was considered statistically significant.

3. RESULTS

During the study period, 2,323 bacterial isolates were evaluated, which included 757 isolates of *E. coli* (32.6%), 363 isolates of *S. aureus* (15.6%), 358 isolates of *K. pneumoniae* (15.4%), 372 isolates of *A. baumannii* (16.0%), and 473 isolates of *P. aeruginosa* (20.4%).

Antibiotic susceptibility for each isolate, calculated either from all samples or only the first sample (without duplicates), did not significantly differ between the conventional and stratified antibiograms (Table 1). In the stratified antibiogram by ward or type of specimen, overall antibiotic susceptible rates were similar to those obtained in the conventional antibiogram. However, significant difference in susceptibility rate of *P. aeruginosa* against ciprofloxacin, gentamicin, and amikacin between isolates obtained from ICU and non-ICU patients was detected (Table 2). Further, the proportion of urinary *P. aeruginosa* isolates susceptible to ceftazidime, ciprofloxacin, gentamicin, amikacin, and imipenem was lower than that of all *P. aeruginosa* strains, regardless of the source of the specimen (Table 3).

Table 1 Percentage susceptibility of isolates to antimicrobial agents in antibiograms including all isolates (AI) and antibiogram without duplicate isolates (rDI)

Organisms	Type of antibiogram (number of isolates)	AMK	CFP/SUL	CAZ	CRO	CIP	CLI	CST	SXT	GEN	IPM	MEM	OXA	VAN	ETP
E. coli	AI [757]	98.7	-	56.9	47.4	32	-	-	35.7	59.8	99.5	9.5	-	-	98.1
	rDI [671]	98.7	-	56.9	47.4	32.9	-	-	36.3	60.9	99.6	9.7	-	-	98.2
S. aureus	AI [363]	-	-	-	-	-	58.9	-	98.6	63.1	-	-	61.7	100	-
	rDI [306]	-	-	-	-	-	59.4	-	98.7	64.1	-	-	62.7	100	-
K. pneumoniae	AI [358]	94.1	-	60.9	60.4	31.2	-	-	37.9	77.9	95.3	95	-	-	92.4
	rDI [313]	94.2	-	59.4	58.8	31.5	-	-	37.4	77	95.2	94.9	-	-	91.9
A. baummanii	AI [372]	38.8	30.2	26.6	-	24.3	-	100	-	1.2	29.3	29.3	-	-	-
	rDI [333]	41	31.6	27.9	-	25.9	-	100	-	2.4	30.9	30.9	-	-	-
P. aeruginosa	AI [473]	84.1	65.4	75.9	-	80.1	-	100	-	3.5	64.5	64.3	-	-	-
	rDI [426]	84.5	66	77	-	80.4	-	100	-	4	65.3	65	-	-	-

Note: AMK = amikacin; CFP/SUL = cefoperazone/sulbactam; CAZ = ceftazidime; CRO = ceftriaxone; CIP = ciprofloxacin; CLI = clindamycin; COL = colistin; GEN = gentamicin; IPM = imipenem; MEM = meropenem; OXA = oxacillin; ETP = ertapenem; SXT = trimethoprim-sulfamethoxazole; VAN = vancomycin

Table 2 Percentage susceptibility of isolates to antimicrobial agents in samples from intensive care unit (ICU) and non-ICU patients

Organisms	Ward	Susceptibility to antimicrobial agent (% [number of isolates])													
		AMK	**CFP/SUL**	**CAZ**	**CRO**	**CIP**	**CLI**	**CST**	**SXT**	**GEN**	**IPM**	**MEM**	**OXA**	**VAN**	**ETP**
E. coli	ICU	100 [96]	-	56.3 [96]	41.7 [96]	33.9 [59]	-	-	27.1 [59]	46.9 [96]	100 [96]	100 [96]	-	-	91.7 [96]
	Non-ICU	99.1 [527]	-	56.2 [527]	47.6 [527]	33.4 [287]	-	-	36 [283]	62 [527]	99.6 [527]	99.4 [527]	-	-	98.8 [510]
S. aureus	ICU	-	-	-	-	-	61.2 [49]	-	94.2 [52]	59.6 [52]	-	-	59.6 [52]	100 [15]	-
	Non-ICU	-	-	-	-	-	54.7 [254]	-	99.3 [263]	58.6 [263]	-	-	57.0 [263]	100 [75]	-
K. pneumoniae	ICU	85.5 [69]	-	62.3 [69]	62.3 [69]	62.5 [8]	-	-	50 [8]	82.6 [69]	89.9 [69]	89.9 [69]	-	-	86.8 [68]
	Non-ICU	95.7 [254]	-	58.7 [254]	56.3 [254]	31.8 [66]	-	-	33.8 [68]	74.8 [254]	96.5 [254]	96.1 [254]	-	-	93.6 [251]
A. baummanii	ICU	33.7 [95]	26.3 [95]	23.2 [95]	-	20 [95]	-	100 [44]	-	25.3 [95]	25.3 [95]	26.0 [95]	-	-	-
	Non-ICU	40.4 [265]	31.3 [265]	27.8 [265]	-	25.7 [265]	-	100 [111]	-	33.5 [266]	30.8 [266]	30.5 [266]	-	-	-
P. aeruginosa	ICU	78.9 [90]	58.6 [87]	75.6 [90]	-	73.6 [87]	-	100 [87]	-	76.7 [90]	55.6 [90]	55.0 [90]	-	-	-
	Non-ICU	85 [361]	66.9 [359]	75.6 [361]	-	81.6 [359]	-	100 [358]	-	84.8 [361]	65.7 [361]	65.7 [361]	-	-	-

Note: AMK = amikacin; CFP/SUL = cefoperazone/sulbactam; CAZ = ceftazidime; CRO = ceftriaxone; CIP = ciprofloxacin; CLI = clindamycin; COL = colistin; GEN = gentamicin; IPM = imipenem; MEM = meropenem; OXA = oxacillin; ETP = ertapenem; SXT = trimethoprim-sulfamethoxazole; VAN = vancomycin **– 3**

Table 3 Percentage susceptibility of isolates to antimicrobial agents when stratified by specimen type (blood, sputum, urine) and compared to all specimens

Organisms	Specimen	Susceptibility to antimicrobial agent (% [number of isolates])													
		AMK	CFP/SUL	CAZ	CRO	CIP	CLI	CST	SXT	GEN	IPM	MEM	OXA	VAN	ETP
E. coli	Blood	100 [132]	-	72 [132]	67.4 [132]	-	-	-	-	67.4 [132]	100 [132]	100 [132]	-	-	100 [128]
	Sputum	98.5 [65]	-	50.8 [65]	32.3 [65]	-	-	-	-	56.9 [65]	100 [65]	98.5 [65]	-	-	98.5 [65]
	Urine	98.4 [441]	-	56.5 [441]	46.7 [441]	32 [441]	-	-	35.8 [436]	59.4 [441]	99.1 [441]	99.5 [441]	-	-	97.2 [430]
	Total specimen	98.7 [757]	-	56.9 [757]	47.4 [757]	32 [441]	-	-	35.8 [436]	59.8 [757]	99.5 [757]	99.5 [757]	-	-	98.1 [739]
S. aureus	Blood	-	-	-	-	-	75 [64]	-	100 [64]	76.6 [64]	-	-	79.7 [64]	100 [5]	-
	Sputum	-	-	-	-	-	38.1 [134]	-	97.8 [134]	42.5 [134]	-	-	38.8 [134]	100 [56]	-
	Urine	-	-	-	-	-	-	-	92.3 [13]	23.1 [13]	-	-	23.1 [13]	100 [8]	-
	Total specimen	-	-	-	-	-	58.9 [350]	-	98.6 [363]	63.1 [363]	-	-	61.7 [363]	100 [93]	-
K. pneumoniae	Blood	95.1 [61]	-	70.5 [61]	73.8 [61]	0 [1]	-	-	-	83.6 [61]	95.1 [61]	95.1 [61]	-	-	93.4 [61]
	Sputum	94.4 [142]	-	58.5 [142]	58.5 [142]	-	-	-	-	76.8 [142]	97.2 [142]	96.5 [142]	-	-	95 [142]
	Urine	94.6 [92]	-	50 [92]	48.9 [92]	31.5 [92]	-	-	38 [92]	71.7 [92]	94.6 [92]	94.6 [92]	-	-	90.1 [91]
	Total specimen	94.1 [358]	-	60.9 [358]	60.4 [358]	31.2 [93]	-	-	38 [95]	77.9 [358]	95.3 [358]	95 [358]	-	-	92.4 [353]

Table 3 Percentage susceptibility of isolates to antimicrobial agents when stratified by specimen type (blood, sputum, urine) and compared to all specimens (continued)

Organisms	Specimen	Susceptibility to antimicrobial agent (% [number of isolates])													
		AMK	**CFP/SUL**	**CAZ**	**CRO**	**CIP**	**CLI**	**CST**	**SXT**	**GEN**	**IPM**	**MEM**	**OXA**	**VAN**	**ETP**
A. baummannii	Blood	68.2 [22]	59.1 [22]	54.5 [22]	-	59.1 [22]	-	100 [22]	-	63.6 [22]	59.1 [22]	54.5 [22]	-	-	-
	Sputum	-	30.6 [235]	27.2 [235]	-	23.4 [235]	-	100 [105]	-	28.5 [235]	28.5 [235]	29.4 [235]	-	-	-
	Urine	37 [27]	22.2 [27]	11.1 [27]	-	11.1 [27]	-	100 [13]	-	29.6 [27]	18.5 [27]	18.5 [27]	-	-	-
	Total specimen	38.8 [372]	30.2 [372]	26.6 [372]	-	24.3 [372]	-	100 [159]	-	31.2 [372]	29.3 [372]	29.3 [372]	-	-	-
P. aeruginosa	Blood	84.2 [19]	92.9 [14]	89.5 [19]	-	85.7 [14]	-	100 [19]	-	84.2 [19]	89.5 [19]	89.5 [19]	-	-	-
	Sputum	-	66.2 [272]	78.7 [272]	-	80.9 [272]	-	100 [271]	-	85.7 [272]	61.4 [272]	61 [272]	-	-	-
	Urine	60.6 [71]	52.1 [71]	54.9 [71]	-	57.7 [71]	-	100 [71]	-	59.2 [71]	52.1 [71]	52.1 [71]	-	-	-
	Total specimen	84.1 [473]	65.4 [468]	75.9 [473]	-	80.1 [468]	-	100 [467]	-	83.5 [473]	64.5 [473]	64.3 [473]	-	-	-

Note: AMK = amikacin; CFP/SUL = cefoperazone/sulbactam; CAZ = ceftazidime; CRO = ceftriaxone; CIP = ciprofloxacin; CLI = clindamycin; COL = colistin; GEN = gentamicin; IPM = imipenem; MEM = meropenem; OXA = oxacillin; ETP = ertapenem; SXT = trimethoprim-sulfamethoxazole; VAN = vancomycin

4. DISCUSSION

Antibiograms are useful for choosing empirical therapy, especially in nosocomial infections, and antibiograms stratified by location or specimens, without data from duplicate isolates, can especially assist healthcare professionals in designing more appropriate recommendations of antibacterial use in each setting (Saxena et al., 2016). Here, we did not observe any difference between the antibiogram obtained after eliminating duplicate isolates and the conventional antibiogram, even for those obtained from the same patients, and this observation may be due to the fact that less than 18% of the data was duplicated in the antibiogram analysis. While Horvat et al. (2003) and Lee et al. (2004) have assessed the impact of duplicate isolates on antibiograms used for selecting more appropriate empirical therapy, data duplicities in those studies are 27% and 60%, respectively. Thus, the percentage of data duplication in our study was lower than that in the previous studies; specifically, there was a lower proportion of *S. aureus* isolates among the pathogens evaluated. In addition, treatment-monitoring practices also differed. *Staphylococcus aureus* infections may occasionally persist for more than 7 days, thus requiring repeated cultures from the same patient. However, how such difference in the magnitude of duplication of susceptibility data affect the antibiogram analysis require further investigation, especially with respect to parameters such as individual protocols on the amount of sample sent each time for bacterial culture and follow-up cultures from infected patients.

The antibiogram stratified by specimen type or ward showed that the percentage susceptibility of urinary *P. aeruginosa* isolates to ceftazidime, ciprofloxacin, gentamicin, amikacin, and imipenem was lower (<60%) than that of *P. aeruginosa* isolates obtained from all specimens (>80%). In addition, *P. aeruginosa* isolated from ICU patients had a lower susceptibility to ciprofloxacin, gentamicin, and amikacin than those from non-ICU patients. Therefore, such stratified antibiograms can help improve empirical therapy.

The disk diffusion method is frequently used for antimicrobial susceptibility testing; therefore, it was used here as well. However, errors with some antimicrobial disks, such as those for cefoperazone-sulbactam, vancomycin, oxacillin, and colistin were present, and susceptibility results for these agents required careful interpretation.

Thus, in the future, the elimination of duplicate isolates of bacterial cultures and the use of a stratified antibiogram can improve an institution's antibiogram profile and facilitate superior empirical antibiotic selection. Such strategies may also be nationally adopted in all institutions, and comparisons among antibiograms derived from institutional and regional data could reflect real-time differences in antimicrobial resistance, which can then help selecting antibiotics for treatment.

5. CONCLUSION

Our findings did not reveal any difference between antibiograms with and without duplicate isolates. However, a stratified antibiogram categorized by specimen type and ward may be useful for selecting a more appropriate empirical therapy.

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