



## Note

## Comparison of knowledge to antimicrobial stewardship institution policies targeting *Staphylococcus aureus* bacteremia and candidemia between medical doctors and pharmacists in an academic teaching hospital in Japan

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## ABSTRACT

*Staphylococcus aureus* bacteremia (SAB) and candidemia have significant impacts on mortality. Both have important implications for antimicrobial stewardship programs (ASPs). However, there are limited data regarding who should be educated and what components should be considered for the ASPs. Hence, we investigated the possibility of the key elements for implications of SAB and candidemia managements for ASPs.

We conducted a cross-sectional study on the knowledge of antimicrobial stewardship institution policies targeting SAB and candidemia for all medical doctors (MDs) and pharmacists to using an E-learning system. To compare the differences in proportions of appropriate knowledge between junior residents and other MDs, and all MDs and pharmacists, we performed bivariate analyses using Fisher's exact test and  $\chi^2$  test with odds ratios (ORs) with 95% confidence intervals (CIs).

In total, all 395 MDs (71 junior residents, 137 senior residents and fellows, and 187 attending doctors) and all 63 pharmacists including 4 antimicrobial stewardship teams pharmacists responded to survey. MDs other than junior residents responded significantly inappropriately to the questions on the candidemia than junior residents (OR = 0.6, 95% CI: 0.4–1.0). Pharmacists had a significantly lower proportion of appropriate knowledge to the candidemia than MDs (OR = 0.4, 95% CI: 0.2–0.8). The major pitfall was failure to consult an ophthalmologist (82.5%).

Next step, we will conduct educational intervention about institution policies, and evaluate whether to improve the knowledges and practices by pre-post test and chart review.

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*Staphylococcus aureus* bacteremia (SAB) and candidemia have significant impacts on mortality [1,2]. Both SAB and candidemia have important implications for antimicrobial stewardship programs (ASPs) and pharmacists are expected to play an important role in ASPs and antimicrobial stewardship teams (ASTs) [3,4].

Previous studies have shown that interventions of ASPs for SAB and candidemia managements targeting only medical doctors (MDs) could improve mortality from SAB and candidemia [5,6].

However, regarding these managements in antimicrobial stewardship, there are limited data regarding who should be educated and what components should be considered. Accordingly, we investigated the effective and efficient elements for implications of SAB and candidemia for ASPs.

We conducted a cross-sectional study in May 2017 on the knowledge of all MDs and pharmacists to ASPs institution policies targeting SAB and candidemia at our hospital, which has

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approximately 780 inpatient beds and serves as a tertiary referral hospital for metropolitan Tokyo. These institution policies are made base on the IDSA guidelines [1,2]. We composed a questionnaire regarding institution policies and performed the survey using an E-learning system. The questionnaire consisted of each component of the institution policies, focused on appropriate antibiotic and antifungal treatment duration, follow-up blood culture, and ophthalmologist consultation (only for candidemia) [2,7]. Regarding questions for the SAB, the appropriate knowledge was "Follow-up blood cultures are taken and treatment duration is decided based on the results." The inappropriate knowledges were "Treatment is continued for 1 week without follow-up blood cultures" and "Treatment is continued for 3 weeks without follow-up blood cultures". Regarding questions on candidemia, the appropriate knowledge was "Follow-up blood cultures are taken, an ophthalmologist is consulted, and treatment duration is decided based on the results." The inappropriate knowledges were "Although follow-up blood cultures are taken and treatment duration is decided based on the results, an ophthalmologist is not consulted", "Treatment is continued for 1 week without follow-up blood cultures and an ophthalmologist consult", and "Treatment is continued for 2 weeks without follow-up blood cultures and consulting an ophthalmologist". We compared the differences in proportions of appropriate knowledge between junior residents and other MDs, and all MDs and pharmacists. These univariate analyses were performed using Fisher's exact test and  $\chi^2$  test with odds ratios (ORs) and 95% confidence intervals (CIs). Two-sided *P* values <0.05 were considered. All statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). All study participants provided informed consent.

In total, all 395 MDs (71 junior residents, 137 senior residents and fellows, and 187 attending doctors) and all 63 pharmacists including 4 ASTs pharmacists in our hospital responded to this survey. The proportions of depend on the results of follow blood cultures, 1-week treatment without follow blood cultures, and 3-weeks treatment without follow blood cultures about the SAB institution policy for all participants were 84.7%, 6.1%, and 10.9%, respectively. The proportions of follow blood cultures and consultation to ophthalmologist appropriate, follow blood culture but no consultation to ophthalmologist, 1-week treatment without follow blood cultures and consultation to ophthalmologist, and 2-weeks treatment without follow blood cultures and consultation to ophthalmologist about the candidemia institution policy for all participants were 31.4%, 68.1%, 11.4%, and 10.5%, respectively (Table 1).

We conducted the stratified analysis at department level among MDs other than junior residents and pharmacist with and without

ASTs (Table 2). The proportions of appropriate knowledge between SAB and candidemia are below: Internal Medicine; 90.5% (133/147) and 39.5% (58/147), Surgery; 77.4% (65/84) and 26.2% (22/84%), Others; 83.9% (78/93) and 23.7% (22/93), Non-ASTs Pharmacists; 81.0% (51/63) and 17.5% (11/63), ASTs Pharmacists; 100% (4/4) and 50.0% (2/4).

**Table 2**

The appropriate knowledges of survey of SAB and candidemia institution policies, stratified by department (n = 387).

	Total	No. (%) of participants with:	
		SAB	Candidemia
Internal medicine	147	133 (90.5)	58 (39.5)
Infectious Diseases	37	34 (91.9)	17 (45.9)
Gastroenterology	23	21 (91.3)	11 (47.8)
Respiratory	21	18 (85.7)	4 (19.0)
Diabetes, Endocrinology and Metabolism	17	15 (88.2)	6 (35.3)
Cardiology	13	12 (92.3)	7 (53.8)
General Internal Medicine	9	9 (100)	1 (11.1)
Nephrology	9	8 (88.9)	5 (55.6)
Rheumatology	9	9 (100)	3 (33.3)
Neurology	4	2 (50)	2 (50.0)
Hematology	3	3 (100)	1 (33.3)
Palliative Care	2	2 (100)	1 (50.0)
Surgery	84	65 (77.4)	22 (26.2)
General Surgery	20	18 (90.0)	3 (15.0)
Oral and maxillofacial Surgery	11	4 (36.4)	2 (18.2)
Otolaryngology	11	10 (90.9)	3 (27.3)
Orthopedics	9	8 (88.9)	5 (55.6)
Dermatology	7	5 (71.4)	1 (14.3)
Neurosurgery	7	7 (100)	3 (42.9)
Cardiovascular Surgery	5	5 (100)	0 (0)
Ophthalmology	4	3 (75.0)	2 (50.0)
Thoracic Surgery	4	2 (50.0)	2 (50.0)
Urology	4	1 (25.0)	0 (0)
Plastic Surgery	2	2 (100)	1 (50.0)
Others	93	78 (83.9)	22 (23.7)
Pediatrics	18	16 (88.9)	7 (38.9)
Emergency Medicine	16	15 (93.8)	4 (25.0)
Obstetrics and Gynecology	15	12 (80.0)	1 (6.7)
Radiology	13	10 (76.9)	3 (23.1)
Psychiatry	6	5 (83.3)	4 (66.7)
Administer of hospital	6	6 (100)	0 (0)
Pathology	6	4 (66.7)	1 (16.7)
Anesthesiology	5	4 (80.0)	0 (0)
Rehabilitation	4	3 (75.0)	1 (25.0)
Laboratory	4	3 (75.0)	1 (25.0)
Pharmacists	63	51 (81.0)	11 (17.5)
Non-ASTs Pharmacists	59	47 (79.7)	9 (15.3)
ASTs Pharmacists	4	4 (100)	2 (50.0)

Unless otherwise stated, data are presented as n (%).

SAB, *Staphylococcus aureus* bacteremia; ASTs, antimicrobial stewardship teams.

**Table 1**

Characteristics of survey of SAB and candidemia institution policies between medical doctors and pharmacists (n = 458).

	No. (%) of participants with:				
	All participants (n = 458)	Junior residents (n = 71)	Senior residents and fellows (n = 137)	Attending doctors (n = 187)	Pharmacists (n = 63)
SAB					
Depend on the results of follow blood cultures	388 (84.7)	61 (85.9)	118 (86.1)	158 (84.5)	51 (80.9)
1-week treatment without follow blood cultures	28 (6.1)	7 (9.9)	5 (3.6)	11 (5.9)	5 (7.9)
3-weeks treatment without follow blood cultures	50 (10.9)	8 (11.3)	14 (10.2)	19 (10.2)	9 (14.2)
Candidemia					
Follow blood cultures and consult to ophthalmologist	144 (31.4)	31 (43.7)	47 (34.3)	55 (29.4)	11 (17.5)
Follow blood culture but no consult to ophthalmologist	312 (68.1)	39 (54.9)	90 (65.7)	131 (70.1)	52 (82.5)
1-week treatment without follow blood cultures and consult to ophthalmologist	52 (11.4)	8 (11.3)	9 (6.6)	16 (8.6)	19 (30.1)
2-weeks treatment without follow blood cultures and consult to ophthalmologist	48 (10.5)	8 (11.3)	13 (9.5)	9 (4.8)	18 (28.6)

Unless otherwise stated, data are presented as n (%).

All questions are allowed multiple answers.

SAB, *Staphylococcus aureus* bacteremia.

**Table 3**  
Univariate analysis of appropriate knowledges to SAB and candidemia institution policies between medical doctors and pharmacists.

	No. (%) of patients with:		OR (95% CI)	P value	No. (%) of patients with:		OR (95% CI)	P value
	Junior residents (n = 71)	Other medical doctors <sup>a</sup> (n = 324)			All medical doctors (n = 395)	Pharmacists (n = 63)		
SAB	61 (85.9)	276 (85.1)	1.1 (0.5–2.2)	0.875	337 (85.3)	51 (81)	0.7 (0.4–1.5)	0.371
Candidemia	31 (43.7)	102 (31.5)	0.6 (0.4–1.0)	0.049	133 (33.7)	11 (17.5)	0.4 (0.2–0.8)	0.010

Unless otherwise stated, data are presented as n (%).

SAB, *Staphylococcus aureus* bacteremia; OR, odds ratio; CI, confidence interval.

<sup>a</sup> Senior residents and attending physicians.

Regarding the proportions of appropriate knowledges about the SAB institution policy, there was no significant difference between junior residents and other MDs (OR = 1.1, 95% CI: 0.5–2.2,  $P = 0.875$ ), and all MDs and pharmacists (OR = 0.7, 95% CI: 0.4–1.5,  $P = 0.371$ ). MDs other than junior residents responded significantly inappropriately to the questions on the candidemia institution policy than junior residents (OR = 0.6, 95% CI: 0.4–1.0,  $P = 0.049$ ). Compared to MDs, pharmacists had a significant less proportion of appropriate knowledges to the questions on the candidemia institution policy (OR = 0.4, 95% CI: 0.2–0.8,  $P = 0.010$ ) (Table 3).

Our results showed that there were differences in knowledge to the SAB and candidemia institution policies between MDs and pharmacists, particularly with more years of experience among MDs. Although previous studies have reported on knowledge to these managements, data regarding differences between occupations and years of experience are limited [5,8].

Regarding candidemia, junior residents had significantly more proportions of appropriate knowledges than other MDs, and MDs had significantly higher proportions of appropriate knowledges compared to pharmacists. The major pitfall identified was failure to consult an ophthalmologist among all participants (31.3%). A previous study reported that the proportion of failure to consult an ophthalmologist was 46.4% [5]. Evaluating endophthalmitis was pointed out as a key element in the management of candidemia [2]. We believe that the results of differences with occupations and years of experience may reflect differences in knowledge. We provided lectures on infectious diseases once a week for junior residents from 2013, which may be why junior residents had higher appropriate proportions, compared to other MDs. We think pharmacists had fewer opportunities to learn the candidemia compared to MDs. However, ASTs pharmacists are expected to play importance roles of ASPs [3,4]. Although the number was small, ASTs pharmacists had appropriate knowledge than non-ASTs pharmacists. In our hospital, some pharmacists participate ASTs from 2016 and monitor the duration and amount of broad-spectrum antibiotics. If primary care team use carbapenem more than 3 days, they communicate with primary care team directly about possibility of de-escalation. In case with difficulty of de-escalation, they consult to infectious disease doctors.

Regarding SAB, there was no significant difference in the knowledges between junior residents and other MDs, and MDs and pharmacists. The proportion of appropriate knowledges among all participants was higher (84.7%) than those reported in other studies (47.5–79.3%) [8]. However, more effort is needed to achieve 100% education in the ASPs.

Our study had several limitations. Firstly, our study was based on an E-learning system, meaning that there may have been differences between the results of our study and practices to the institution policies. Secondly, our questionnaire did not fulfill the all components of SAB and candidemia institution policies, such as evaluating endocarditis for SAB, removal central venous catheters and step down from intravenous antifungal drugs to oral antifungal drugs for candidemia. Lastly, our study was a single-center study.

However, our hospital is the clinical reference center on antimicrobial resistance which were launched to implement the National Action Plan on antimicrobial resistance 2016–2020 in Japan [9]. Through dissemination of our findings with the clinical community, we expect good practices regarding SAB and candidemia in the ASPs in Japan.

In conclusion, we found that pharmacists have little knowledge of candidemia than physicians, and senior physicians have little knowledge of candidemia than junior physicians. To reveal important elements of ASPs for SAB and candidemia, who should be involved and what components should be considered for the ASPs, we will conduct educational intervention about institution policies, and evaluate whether to improve the knowledges and practices by pre-post test and chart review.

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#### Potential conflicts of interest

All authors declare no conflicts of interest from this study.

#### ICMJE statement

All authors meet the ICMJE authorship criteria.

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#### References

- [1] Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:e18–55.
- [2] Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2016;62:e1–50.
- [3] Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;44:159–77.
- [4] Smith JR, Frens JJ, Snider CB, Claeys KC. Impact of a pharmacist-driven care package on *Staphylococcus aureus* bacteremia management in a large community healthcare network: a propensity score-matched, quasi-experimental study. *Diagn Microbiol Infect Dis* 2018;90:50–4.
- [5] Takesue Y, Ueda T, Mikamo H, Oda S, Takakura S, Kitagawa Y, et al. Management bundles for candidaemia: the impact of compliance on clinical outcomes. *J Antimicrob Chemother* 2015;70:587–93.

- [6] Nguyen CT, Gandhi T, Chenoweth C, Lassiter J, Dela Pena J, Eschenauer G, et al. Impact of an antimicrobial stewardship-led intervention for *Staphylococcus aureus* bacteraemia: a quasi-experimental study. *J Antimicrob Chemother* 2015;70:3390–6.
- [7] Holland TL, Arnold C, Fowler Jr VG. Clinical management of *Staphylococcus aureus* bacteremia: a review. *J Am Med Assoc* 2014;312:1330–41.
- [8] Nagao M, Yamamoto M, Matsumura Y, Yokota I, Takakura S, Teramukai S, et al. Complete adherence to evidence-based quality-of-care indicators for *Staphylococcus aureus* bacteremia resulted in better prognosis. *Infection* 2017;45:83–91.
- [9] The Government of Japan. National Action Plan on Antimicrobial Resistance (AMR) 2016–2020. Available from: <http://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000138942.pdf>. [accessed 01.05.18].