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Difference in Baseline Antimicrobial Prescription Patterns of Hospitals According to Participation in the National Antimicrobial Monitoring and Feedback System in Korea

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ABSTRACT

This study aimed to evaluate the differences in the baseline characteristics and patterns of antibiotic usage among hospitals based on their participation in the Korea National Antimicrobial Use Analysis System (KONAS). We obtained claims data from the National Health Insurance for inpatients admitted to all secondary- and tertiary-care hospitals between January 2020 and December 2021 in Korea. 15.9% (58/395) of hospitals were KONAS participants, among which the proportion of hospitals with > 900 beds (31.0% vs. 2.6%, $P < 0.001$) and tertiary care (50.0% vs. 5.2%, $P < 0.001$) was higher than that among non-participants. The consumption of antibiotics targeting antimicrobial-resistant gram positive bacteria (33.7 vs. 27.1 days of therapy [DOT]/1,000 patient-days, $P = 0.019$) and antibiotics predominantly used for resistant gram-negative bacteria (4.8 vs. 3.7 DOT/1,000 patient-days, $P = 0.034$) was higher in KONAS-participating versus -non-participating

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Disclosure

The authors have no potential conflicts of interest to disclose.

Data Availability Statement

The data sets used and/or analyzed during this study are available upon reasonable request from the corresponding author.

Author Contributions

Conceptualization: Kim DS, Kim B. Data curation: Shin J, Chae J. Formal analysis: Shin J, Chae J, Kim DS, Kim B. Funding acquisition: Choi JY. Investigation: Shin J, Park JY, Chae J, Kim HS, Moon SM, Heo E, Park SY, Seo DM, Chun HJ, Kim YC, Lee MJ, Huh K, Park HJ, Yun IJ, Jeong SJ, Choi JY, Kim DS, Kim B. Methodology: Kim DS. Project administration: Kim DS, Kim B. Resources: Shin J, Park JY, Chae J, Kim HS, Moon SM, Heo E, Park SY, Seo DM, Chun HJ, Kim YC, Lee MJ, Huh K, Park HJ, Yun IJ, Jeong SJ, Choi JY, Kim DS, Kim B.

hospitals. The current KONAS data do not fully represent all secondary- and tertiary-care hospitals in Korea; thus, the KONAS results should be interpreted with caution.

Keywords: Antimicrobial Stewardship; Anti-Infective Agents; Prescription

Like many countries, the Korean government announced a national action plan on antimicrobial resistance in August 2016.[1] As part of this plan, the Development of National Antimicrobial Monitoring System project was launched in 2019, and the Korea National Antimicrobial Use Analysis System (KONAS), a national monitoring system in Korea was established in 2022.[2] KONAS provides the results of quantitative analyses of the antimicrobial prescriptions from each participating hospital, in order to allow hospitals to easily comprehend their antimicrobial prescription status and help implement an antimicrobial stewardship program (ASP).[2,3] Due to the lack of appropriate rewards and obligations regarding the implementation of ASPs, many medium-to-small-sized Korean hospitals have yet to establish ASP in their hospitals and are hesitant to participate in KONAS.[4] Reflecting on this situation, only 15.9% (58/365) of secondary- and tertiary-care hospitals participated in the KONAS in 2022, its first year.[5] Therefore, concerns about the representativeness of the KONAS have been raised, and caution is necessary when interpreting its data.

This study aimed to evaluate the differences in the baseline characteristics and patterns of antibiotic usage among Korean hospitals based on their participation in KONAS. We analyzed these differences based on the existence of a dedicated ASP team as well.

We obtained National Health Insurance (NHI) claims data for inpatients admitted to all secondary- and tertiary-care hospitals in Korea between January 2020 and December 2021 from the Health Insurance Review and Assessment Service (HIRA). The data obtained included the following: hospital information (number of hospital beds, hospital type, status of infection prevention and control fee receipt, surgical prophylactic antibiotic assessment grade, number of inpatients, and number of patient days); age; primary discharge diagnosis code; sub-discharge diagnosis code; surgical treatment; and prescribed antibiotics. The discharge diagnoses were coded according to the International Classification of Diseases, Tenth Revision, and any comorbidities were calculated using the disease categories specified in the Charlson Comorbidity Index (CCI).[6] To determine whether KONAS-participating hospitals had dedicated ASP teams, defined as official hospital organizations responsible for ASP activities such as antibiotic interventions, monitoring, reporting, and education, we contacted KONAS managers from each hospital via email between October and December 2022 to gather this information.

Antibiotics were defined as drugs corresponding to the J01 and A07AA09 (oral vancomycin) code of the Anatomical Therapeutic Chemical classification of the WHO.[7] Antibiotic consumption was measured in terms of days of therapy (DOT) and standardized per 1,000 patient days. Antibiotic classes were defined by KONAS, with a few categories added after discussion with the research group (**Supplementary Table 1**).[3,8]

To compare the differences among each group, the *t*-test (or, in cases of non-normality, the Wilcoxon rank sum test) and the χ^2 test (or, the expected frequencies < 5, Fisher's exact test) were used. All statistical comparisons were two-sided, and a *P* value < 0.05 was considered statistically significant. To minimize the effects of confounding,[9] propensity score matching was used. The propensity score was calculated from multivariable logistic regression models

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with the following factors: hospital size; age; and CCI. Propensity scores were then integrated into the inverse probability of treatment weighting (IPTW) method. The distribution of covariates after weighting was evaluated, with an absolute value of the standardized differences < 0.1 considered acceptable. The linear regression model was performed to assess the trends of antibiotic consumption associated with participation in KONAS or the presence of a dedicated ASP team. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

A total of 365 hospitals (45 tertiary- and 320 secondary-care) were included in this study, of which 58 (15.9%) were KONAS participants. The proportion of hospitals with > 900 beds (31.0% vs. 2.6%, respectively; $P < 0.001$) and tertiary-care hospitals (50.0% vs. 5.2%, $P < 0.001$) was higher in KONAS-participating hospitals than in non-participating hospitals. The KONAS-participating hospitals showed a higher infection prevention and control fee receipt rate (98.3% vs. 71.3%, $P < 0.001$), higher proportion of surgical prophylactic antibiotic assessment grades 1 or 2 (87.9% vs. 35.2%, $P < 0.001$), and higher number of annual operations per 100 patients (51.3 ± 12.0 vs. 37.5 ± 17.0, $P < 0.001$). As for patient characteristics, the mean age of patients was lower (53.5 ± 3.5 vs. 55.3 ± 6.0, $P = 0.003$) in KONAS-participating hospitals than in non-participating hospitals, and there was no significant difference in mean CCI score. The mean proportion of patients with cancer (8.0 ± 3.0 vs. 6.0 ± 4.5, $P < 0.001$) was higher in KONAS-participating than in non-participating hospitals (**Table 1**).

Regarding the number of antibiotic prescriptions after application of IPTW, the amount of antibiotics predominantly used to treat infections with antibiotic-resistant gram-positive bacteria (GramPos) (33.7 vs. 27.1 DOT/1,000 patient-days, $P = 0.019$) and antibiotics predominantly used to treat extensive infections with antibiotic-resistant gram-negative bacteria (GramNeg) (4.8 vs. 3.7 DOT/1,000 patient-days, $P = 0.034$) were higher in the KONAS-participating versus -non-participating hospitals. In comparison, a lower number of narrow-spectrum beta-lactam antibiotics was prescribed by the KONAS-participating versus the KONAS-non-participating hospitals (237.4 vs. 272.6 DOT/1,000 patient-days, $P = 0.031$).

When analyzed by general classification, glycopeptide (34.1 vs. 26.0 DOT/1,000 patient-days, $P = 0.003$) and macrolide (17.2 vs. 13.8 DOT/1,000 patient-days, $P = 0.048$) were prescribed more often, while carbapenem (32.7 vs. 39.0 DOT/1,000 patient-days, $P = 0.029$), fluoroquinolone (85.5 vs. 109.5 DOT/1,000 patient-days, $P < 0.001$), and aminoglycoside (13.9 vs. 18.8 DOT/1,000 patient-days, $P = 0.011$) were prescribed less often at KONAS-participating versus -non-participating hospitals. Overall, decreasing trends were observed for the majority of antibiotic classes, except for GramNeg, carbapenem, and metronidazole (**Supplementary Tables 2** and **3**).

Of the 58 KONAS-participating hospitals, 7 (10.3%) had a team dedicated to ASP. The overall parameters were similar, except for annual operations per 100 patients (61.0 ± 8.7 vs. 50.0 ± 11.8, $P = 0.021$) between hospitals with dedicated ASP teams and those without (**Table 2**).

Regarding the number of antibiotic prescriptions after application of IPTW, no differences were observed in most of antibiotic classes defined by KONAS between hospitals with ASP teams and those without. GramNeg were prescribed significantly less in hospitals with ASP teams compared with those without (3.8 vs. 7.8 DOT/1,000 patient-days, $P = 0.002$). When analyzed by general classification, no antibiotic classes showed significant differences in the number of prescriptions among the two groups. Regarding the monthly antibiotic

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Table 1. Antibiotic prescription patterns of secondary- and tertiary-care hospitals in Korea according to KONAS participation status

Variables	Before IPTW			After IPTW			SMD
	Participation in KONAS (n = 58)	Others (n = 307)	*P* value	Participation in KONAS (n = 60)	Others (n = 306)	*P* value	
Hospital characteristics							
No. of hospital beds (%)							
≥ 900	18 (31.0)	8 (2.6)	< 0.001	4 (6.6)	21 (7.0)	0.940	0.029
600–899	23 (39.7)	30 (9.8)	-	8 (12.8)	44 (14.4)		
< 600	17 (29.3)	269 (87.6)	-	48 (80.6)	241 (78.6)		
Hospital type (%)							
Tertiary-care	29 (50.0)	16 (5.2)	< 0.001	8 (12.9)	33 (11.0)	0.660	
Secondary-care	29 (53.5)	291 (55.3)	-	52 (87.1)	273 (89.0)		
Receiving infection prevention and control fee (%)	57 (98.3)	219 (71.3)	< 0.001	32 (53.4)	162 (53.0)	0.962	0.007
Higher grade[a] from surgical prophylactic antibiotic assessment by HIRA (%)	51 (87.9)	108 (35.2)	< 0.001	25 (42.5)	133 (43.4)	0.899	0.018
Annual operation[b] number/100 patients, mean ± SD	51.3 ± 12.0	37.5 ± 17.0	< 0.001	39.8 ± 13.0	39.6 ± 17.5	0.914	0.014
Characteristics of patients							
Age, mean ± SD	53.5 ± 3.5	55.3 ± 6.0	0.003	54.7 ± 4.2	55.0 ± 6.0	0.607	0.064
Charlson's comorbidity index of patients, mean ± SD	1.2 ± 0.2	1.2 ± 0.4	0.171	1.1 ± 0.2	1.2 ± 0.3	0.205	
Proportion of cancer patients, mean ± SD	8.0 ± 3.0	6.0 ± 4.5	< 0.001	5.8 ± 2.0	6.6 ± 4.9	0.059	
Antibiotic prescription, DOT/1,000 patient-days							
KONAS classification							
Total antibiotics	986.3	965.6	0.658	949.6	968.2	0.732	
BSHO	303.2	277.1	0.230	308.1	278.0	0.169	
BSCA	274.2	272.9	0.931	248.9	273.4	0.099	
GramPos	35.2	26.6	0.002	33.7	27.1	0.019	
NSBL	245.5	272.1	0.089	237.4	272.6	0.031	
GramNeg	3.8	3.7	0.860	4.8	3.7	0.034	
General classification							
Carbapenem	33.6	39.0	0.052	32.7	39.0	0.029	
Fluoroquinolone	95.4	109.3	0.060	85.5	109.5	< 0.001	
Metronidazole	48.2	52.4	0.326	48.0	52.5	0.281	
Glycopeptide	34.1	26.0	0.003	32.8	26.5	0.022	
3rd and 4th generation cephalosporin	205.2	185.1	0.096	183.4	185.1	0.888	
Aminoglycoside	11.4	19.0	< 0.001	13.9	18.8	0.011	
Macrolide	15.5	14.1	0.383	17.2	13.8	0.048	

IPTW = inverse probability of treatment weighing, SMD = standardized mean difference, KONAS = Korea National Antimicrobial Use Analysis System, SD = standard deviation, HIRA = Health Insurance Review and Assessment Service, BSHO = broad-spectrum antibiotics predominantly used for hospital-onset infections, BSCA = broad-spectrum antibiotics predominantly used for community-acquired infections, GramPos = antibiotics predominantly used for resistant gram-positive bacteria, NSBL = narrow-spectrum beta-lactam agents, GramNeg = antibiotics predominantly used for extensive antibiotic-resistant gram-negative bacteria.
[a]Including grade 1 or 2.
[b]Operations included in the surgical prophylactic antibiotic assessment program included craniotomy, shoulder surgery, hip replacement surgery, cholecystectomy, colorectal surgery, knee replacement surgery, breast surgery, hysterectomy, prostatectomy, cesarean section, spine surgery, lung surgery, hernia surgery, laryngeal surgery, fracture surgery, pacemaker implantation surgery, appendectomy, and vascular surgery.

prescription patterns, discrepancies in the trends of some antibiotic classes were observed among the different groups (**Supplementary Table 4**).

The consumption of antibiotics targeting antimicrobial-resistant pathogens, such as GramPos, GramNeg, and carbapenems, was higher in KONAS-participating versus -non-participating hospitals during the study period. Given that the distribution of antimicrobial-resistant pathogens is similar between KONAS-participating hospitals and other hospitals nationwide,[5] this difference might be attributable to patient characteristics that are not fully measurable in the NHI claims data, such as disease severity. Additionally, the complexity of the surgical procedures and their complications may have contributed to this trend. Thus, further analyses are required to identify a more plausible explanation.

Overall antibiotic consumption patterns were not significantly different, except for GramNeg infections, between KONAS-participating hospitals with versus without dedicated ASP teams.

Table 2. Antibiotic prescription patterns among KONAS-participating hospitals according to dedicated antimicrobial stewardship program status

Variables	Before IPTW			After IPTW			SMD
	ASP team (n = 7)	Others (n = 51)	*P* value	ASP team (n = 30)	Others (n = 29)	*P* value	
Hospital characteristics							
No. of hospital beds (%)							
> 900	5 (71.4)	13 (25.5)	0.050	22 (72.2)	15 (52.6)	0.120	
600–899	2 (28.6)	21 (41.2)	-	8 (27.8)	14 (47.4)		
< 600	0 (0.0)	17 (33.3)	-	0 (0.0)	0 (0.0)		
Hospital type (%)							
Tertiary-care	6 (85.7)	23 (45.1)	0.102	23 (100.0)	29 (100.0)		
Secondary-care	1 (14.3)	28 (54.9)	-	0 (0.0)	0 (0.0)		
Receiving infection prevention and control fee (%)	7 (100.0)	48 (94.1)	1.000	30 (100.0)	29 (100.0)	1.000	
Higher grade[a] from surgical prophylactic antibiotic assessment by HIRA (%)	7 (100.0)	44 (86.3)	0.581	30 (100.0)	29 (100.0)	1.000	
Annual operation[b] number/100 patients, mean ± SD	61.0 ± 8.7	50.0 ± 11.8	0.021	56.0 ± 19.6	56.3 ± 9.0	0.950	0.031
Characteristics of patients							
Age, mean ± SD	51.9 ± 2.2	53.7 ± 3.7	0.077	51.7 ± 6.5	53.3 ± 3.5	0.277	
Charlson's comorbidity index of patients, mean ± SD	1.2 ± 0.2	1.2 ± 0.2	0.743	1.2 ± 0.3	1.3 ± 0.2	0.169	
Proportion of cancer patients, mean ± SD	11.4 ± 4.7	7.4 ± 2.3	0.063	10.2 ± 8.7	9.3 ± 2.8	0.617	
Antibiotic prescription, DOT/1,000 patient-days							
KONAS classification							
Total antibiotics	961.3	1,171.2	0.852	1,318.8	1,326.3	0.953	
BSHO	416.0	395.1	0.490	408.7	451.0	0.226	
BSCA	285.6	319.4	0.296	335.7	346.4	0.821	
GramPos	55.7	52.0	0.708	72.7	65.6	0.312	
NSBL	268.9	268.0	0.975	303.1	274.5	0.422	
GramNeg	3.2	5.8	0.002	3.8	7.8	0.002	
General classification							
Carbapenem	36.8	44.6	0.363	47.5	55.2	0.249	
Fluoroquinolone	100.2	109.1	0.292	108.3	120.5	0.240	
Metronidazole	37.9	51.2	0.137	45.1	55.7	0.285	
Glycopeptide	53.8	50.2	0.711	70.0	63.4	0.336	
3rd and 4th generation cephalosporin	213.5	243.3	0.377	256.7	262.5	0.894	
Aminoglycoside	8.6	12.8	0.167	13.2	14.4	0.740	
Macrolide	12.1	13.8	0.583	15.0	13.3	0.654	

IPTW = inverse probability of treatment weighing, SMD = standardized mean difference, ASP = antimicrobial stewardship program, KONAS = Korea National Antimicrobial Use Analysis System, SD = standard deviation, HIRA = Health Insurance Review and Assessment Service, BSHO = broad-spectrum antibiotics predominantly used for hospital-onset infections, BSCA = broad-spectrum antibiotics predominantly used for community-acquired infections, GramPos = antibiotics predominantly used for resistant gram-positive bacteria, NSBL = narrow-spectrum beta-lactam agents, GramNeg = antibiotics predominantly used for extensive antibiotic-resistant gram-negative bacteria.

[a]Including grade 1 or 2.

[b]Operations included in the surgical prophylactic antibiotic assessment program included craniotomy, shoulder surgery, hip replacement surgery, cholecystectomy, colorectal surgery, knee replacement surgery, breast surgery, hysterectomy, prostatectomy, cesarean section, spine surgery, lug surgery, hernia surgery, laryngeal surgery, fracture surgery, pacemaker implantation surgery, appendectomy, and vascular surgery.

Even hospitals with ASP teams could only employ one full-time clinical pharmacist for ASP, whereas others had to handle additional responsibilities beyond ASP (data not shown). Moreover, infectious disease (ID) physicians had limited engagement with ASP teams during the coronavirus disease 2019 pandemic in Korea.[10] Unfortunately, support and/or manpower for ASPs are still insufficient in many Korean hospitals,[11] although in this regard, KONAS plays an important role in supporting ASPs.[3] Given that national policy legislation to support the institutionalization of ASPs has been discussed, sufficient personnel for ASP (ID physicians, clinical pharmacists, etc.) with computerized support systems for antibiotic prescriptions as well as tracking and monitoring are expected to be established in Korean hospitals soon, with the role of KONAS emphasized accordingly.

This study had the following limitations. First, many confounding factors that could have influenced antibiotic prescription patterns, such as disease severity, presence of

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antimicrobial-resistant pathogens, and specific ASP activities, were not considered owing to the limitations of the study's data sources. Second, there are discrepancies between antibiotic consumption data from NHI claims and prescription data extracted from electronic health records. For instance, the total annual antibiotic consumption appears much higher than in other countries, likely because discharge antibiotics cannot be distinguished from antibiotics prescribed during hospitalization in the NHI claim data (**Supplementary Table 5**).[12] Third, the study period coincided with the coronavirus disease 2019 pandemic. In this study, a decreasing tendency in the number of antibiotics prescribed was observed, as seen in a previous study, which might have been influenced by the pandemic situation.[13] Finally, we could not compare the temporal trends before and after the implementation of the KONAS project. The analysis was performed for data before the initiation of the KONAS project, which provided the baseline characteristics of the participating hospitals.

In conclusion, the consumption of antibiotics targeting antimicrobial-resistant pathogens, such as GramPos, GramNeg, and carbapenem, was higher in KONAS-participating hospitals. Therefore, the current KONAS data do not fully represent all secondary- and tertiary-care hospitals in Korea; thus, these results should be interpreted with caution.

Ethics statement

The protocol for this study was reviewed and approved by the HIRA Institutional Review Board (IRB No. 2023-014-001). Due to the retrospective nature of the study, the requirement for written informed consent was waived. The need for informed consent was waived due to the retrospective nature of this study and the use of anonymous data.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1
Classification of antibiotic classes

Supplementary Table 2
Monthly antibiotic prescription pattern in secondary- and tertiary-care hospitals in Korea

Supplementary Table 3
Monthly antibiotic prescription pattern in secondary- and tertiary-care hospitals in Korea: a comparison between Korea according to participation in Korea National Antimicrobial Use Analysis System (KONAS)-participating hospitals and the others

Supplementary Table 4
Monthly antibiotic prescription pattern in Korea according to participation in Korea National Antimicrobial Use Analysis System (KONAS)-participating hospitals in Korea: a comparison between hospitals with dedicated team for antimicrobial stewardship program and the others

Supplementary Table 5

The estimation of amount of discharge antibiotics in this study

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