Disease burden of patients with antibiotic-resistant bacteria (Extended-Spectrum Beta-Lactamase or Carbapenem-Resistant Enterobacteriaceae) in Korea

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Background and Objectives

- Infections due to antibiotic-resistant bacteria pose a great threat to the global public healthcare.
- In the Global Burden of Disease region of High-income Asia Pacific, South Korea has the 2nd lowest age-standardized mortality across 4 countries.[1,2]
- But, the number of antimicrobial resistance deaths in Korea is higher than deaths from diabetes and kidney diseases, respiratory infections and chronic respiratory diseases.[1]
- Despite the importance of infections caused by antibiotic-resistant bacteria, the results of related studies are scarce.
- We aimed to
  i) describe the characteristics of patients with Extended-Spectrum Beta-Lactamase(ESBL), Carbapenem-Resistant Enterobacteriaceae(CRE)-blood stream infection for K.pneumoniae and E.coli.
  ii) identify the clinical and economic burden among Resistant(R), Susceptible(S) and Control(N) group.

Methods

- We conducted a retrospective cohort study on patients with ESBL-producing or CRE(K. pneumoniae or E. coli) bacteremia and matched controls with susceptible infection group and without infection(control) group(occurred between January and June 2020).
- Data were collected from 10 nationwide hospitals in South Korea over 11-months period between April, 2021 to March, 2022.
- Patients were classified as 3 groups and matched at a 1:1:1 ratio. (Figure 1) After propensity score matching, total 795 patients were included in analysis.
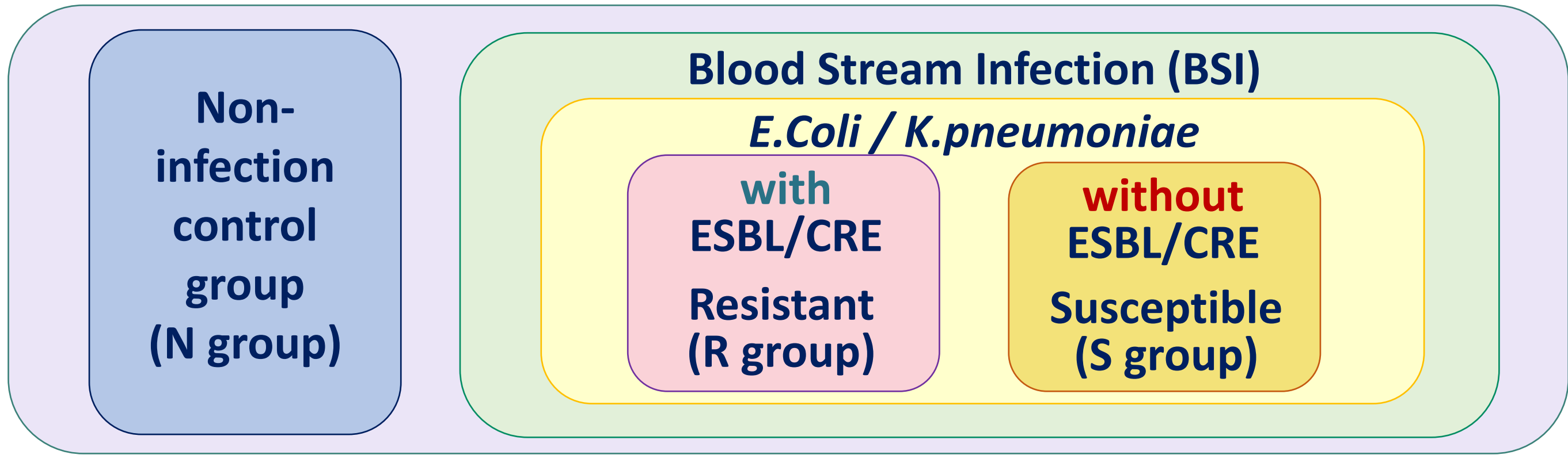

Figure 1. Patient group classification

Results

- The proportions of hospital-acquired and healthcare-associated infections were higher in the R group than S group. In CRE, the length of ICU stay and the duration of antibiotics administration were longer in the R group than S group. The time to appropriate antibiotic therapy was longer in the R group than S group (ESBL-E: 2,193 vs. 260, p<0.001, CRE 3,446 vs. 344, p=0.016). (Table 1)
- In ESBL-E, the LOS for the R group was significantly longer 1.5 times and 2.2 times than S and N group. The 90-day mortality rates for ESBL-E and CRE in the R group were more than 2 times higher than the S group. In ESBL-E and CRE, the R group incurred the highest total costs and the total economic burden for the R, S, and N group is significantly different($11,151 vs. $8,712 vs. $6,063, p=0.004; $40,464 vs. $8,748 vs. $7,279, p= 0.024). (Table 2)

Table 1. Baseline characteristics of R group and mached S group

Variables	ESBL-E			CRE[†]		
	R (n = 237)	S (n = 237)	P	R (n = 28)	S (n = 28)	P
Age, yr	72.2 ± 11.5	71.8 ± 11.8	0.256	67.2 ±13.7	67.8 ± 13.9	0.237
Female	144 (60.8)	145 (61.2)	0.317	15 (53.6)	15 (53.6)	–
ICU stay, days*	1.5 ± 6.4	1.4 ± 3.4	0.851	8.4 ± 15.0	2.2 ± 4.6	0.045
Hospital days to bacteremia	8.1 ± 31.3	2.6 ± 13.3	0.014	12.7 ± 16.0	10.6 ± 36.4	0.785
Hospital-acquired infection	66 (27.9)	36 (15.2)	0.001	18 (64.3)	2 (7.1)	<0.001
Healthcare-associated infection	137 (57.8)	92 (38.8)	<0.001	22 (78.6)	8 (28.6)	<0.001
History of surgery	6 (4.4)	5 (5.4)	>0.999	0 (0.0)	0 (0.0)	–
Positive follow-up blood culture	31 (13.1)	15 (6.3)	0.020	8 (28.6)	1 (3.6)	0.016
Duration of bacteremia, days	4.1 ± 3.6	4.5 ± 4.2	0.272	10.1 ± 14.2	3.5 ± 1.7	0.122
Metastatic infection	9 (3.8)	3 (1.3)	0.083	3 (10.7)	0 (0.0)	0.083
Charlson comorbidity index	6.5 ± 2.7	6.6 ± 3.0	0.509	7.2 ± 2.9	6.4 ± 3.1	0.237
SOFA score	3.6 ± 3.3	3.8 ± 3.6	0.547	5.9 ± 4.0	3.6 ± 4.7	0.057
Time to appropriate antibiotics, minutes	2,193 ± 2,179	260 ± 487	<0.001	3,446 ± 5,488	344 ± 588	0.016
Duration of antibiotics administration, days	13.4 ± 9.3	14.3 ± 9.7	0.322	18.7 ± 13.0	11.8 ± 6.4	0.019

[†]Including both extended-spectrum beta-lactamase producing and carbapenem-resistant Enterobacteriaceae.
*The value of zero was also included in the analyses.
Values are presented as number (%) or mean ± standard deviation. –: statistical analysis is not applicable.
ESBL-E: extended-spectrum beta-lactamase producing Enterobacteriaceae;
CRE: carbapenem-resistant Enterobacteriaceae;
ICU: intensive care unit;
SOFA: sequential organ failure assessment

Table 2. Clinical and economic burden of R, S and N group

Variable	ESBL-E					CRE[†]				
	R (n = 237)	S (n = 237)	N (n = 237)	P[a]	P[b]	R (n = 28)	S (n = 28)	N (n = 28)	P[a]	P[b]
Length of stay(LOS), days	22.5 ± 32.7	14.7 ± 15.6	10.3 ± 28.8	0.001	0.094	38.6 ± 31.1	20.3 ± 37.8	24.1 ± 68.0	0.059	0.384
30-day mortality	24 (10.3)	10 (4.3)	7 (3.0)	0.016	0.002	7 (25.0)	3 (12.0)	0 (0.0)	0.414	0.066
90-day mortality	28 (12.1)	13 (5.6)	8 (3.4)	0.019	0.001	8 (28.6)	3 (12.0)	0 (0.0)	0.257	0.034
Total economic burden($)	11,151 ± 12,908	8,712 ± 9,138	6,063 ± 7,268	0.014	0.004	40,464 ± 52,819	8,748 ± 6,954	7,279 ± 5,905	0.003	0.024

P[a] values between the R and S groups; P[b] values calculated by the Friedman test (Cochran's Q test) for the R, S, and N groups.

Conclusion

Patients with antibiotic-resistant bacteria showed higher mortality and caused more medical expenses compared to the antibiotic-susceptible bacteremia and cases without infection. In consideration of the high clinical and economic burden of patients with ESBL-producing and CRE bacteremia, appropriate infection control measures should be prepared to prevent the spread of antibiotic-resistant bacteria and appropriate policies to reduce the disease burden of patients with ESBL-producing and CRE bacteremia.

1. https://www.healthdata.org/sites/default/files/files/Projects/GRAM/S_Korea_0.pdf 2. World Health Organization (WHO). TrACSS 2021-2022; https://amrcountryprogress.org/download/AMR-self-assessment-surveyresponses-2020-2021.xlsx