

Drivers of Empiric Carbapenem Use: How Important is History of Extended-spectrum Beta-lactamase (ESBL) Infection?

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Background

- Carbapenems are first-line agents for serious infections caused by ESBL-producing isolates
- In patients with a history of ESBL-positive culture, empiric therapy with a carbapenem has become common practice in hospitals
- Actual likelihood of developing a subsequent ESBL infection is unknown

Objective

- Evaluate the microbiology of subsequent infections among patients with history of ESBL-positive culture and determine risk factors associated with ESBL-positive subsequent infection that may justify an empiric carbapenem

Methods

- Retrospective, observational study conducted at Wake Forest Baptist Health (WFBH)
- The electronic medical record (EMR) was used to generate a report of all *E. coli* or *K. pneumoniae* ESBL-positive cultures during calendar year 2017. An analogous report was generated representing ESBL-negative *E. coli* or *K. pneumoniae* cultures (inpatient and outpatient cultures were included)
- Initial cultures during the study period were termed index cultures
- Patients were randomly selected until 100 patients were enrolled from each report (200 patients total)
- The EMR was reviewed to determine study eligibility and collect patient and culture data up to 1 year after the index culture

Methods (cont.)

- Data analyzed using Chi-square or Fisher's exact test (categorical data) and Student's *t*-test (continuous data)
- Risk factors associated with ESBL-positive subsequent infection were analyzed using univariate comparisons

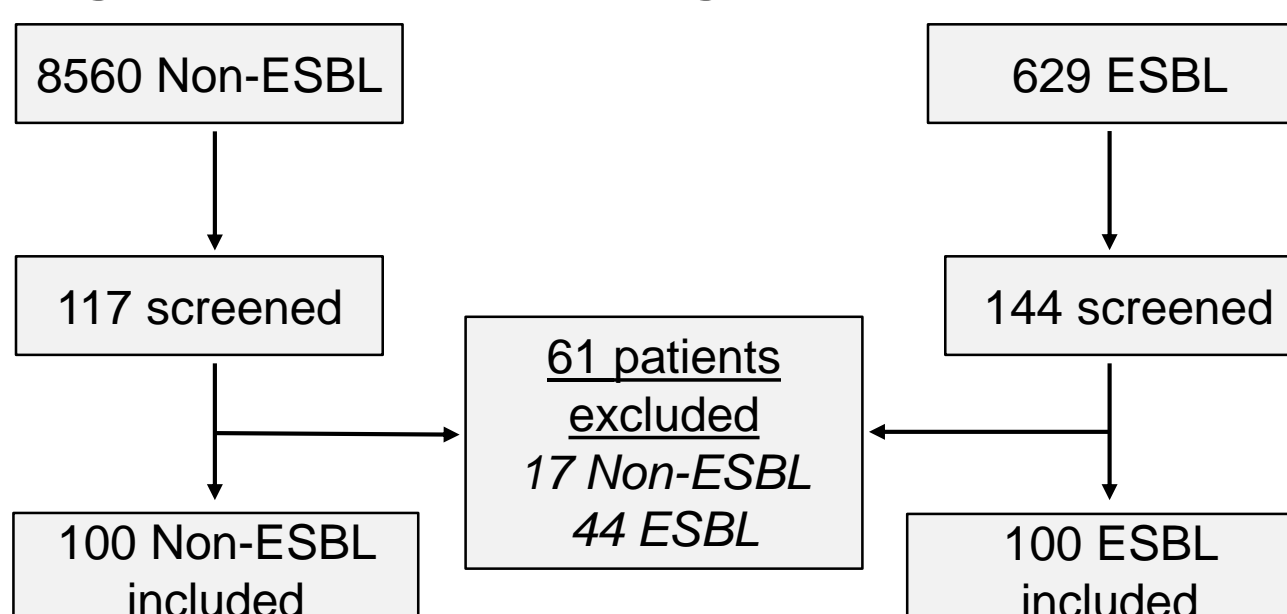
Table 1. Inclusion and Exclusion Criteria

Inclusion	Exclusion
Age ≥ 18 years	
Inpatients and outpatients receiving medical care in the WFBH system	Patients with a culture positive for <i>E. coli</i> or <i>K. pneumoniae</i> within 1 year prior to index culture
Positive culture for <i>E. coli</i> or <i>K. pneumoniae</i> during calendar year 2017	

PRIMARY OUTCOME
Proportion of patients who developed a subsequent ESBL infection
SECONDARY OUTCOMES
Risk factors associated with ESBL-positive subsequent infection

Results

Figure 1. Patient Screening



Results (cont.)

Table 2. Patient Characteristics

	ESBL Index Culture (n = 100)	Non-ESBL Index Culture (n = 100)
Age (years), mean ± SD	63.1 ± 18.5	55.5 ± 21.6
Female gender, n (%)	78 (78)	89 (89)
Outpatient	58 (58)	80 (80)
Index culture site		
- Urine	79 (79)	93 (93)
- Sputum	7 (7)	3 (3)
- Blood	7 (7)	1 (1)
- Wound	4 (4)	2 (2)
- Other	3 (3)	1 (1)
Index culture species		
- <i>E. coli</i>	83 (83)	88 (88)
- <i>K. pneumoniae</i>	17 (17)	12 (12)
Charlson comorbidity index score, mean ± SD	4.3 ± 3.2	2.6 ± 2.9
Immunocompromised	7 (7)	1 (1)

- Overall, the mean age was 58 years, 84% of patients were female and 69% of patients were outpatients
- Within 1 year of index culture, 100 patients (50%) developed subsequent infection
- Among subsequent infections, 22 were ESBL-positive, 43 were ESBL-negative, and 35 had no or negative culture
- The mean time since index culture for ESBL-positive subsequent infection and non-ESBL subsequent infection was 85 (26-226) days and 140 (15-363) days, respectively (p=0.014)
- When comparing time to subsequent infection, 21 (95%) ESBL-positive and 26 (61%) non-ESBL occurred < 6 months after index culture (p=0.003)

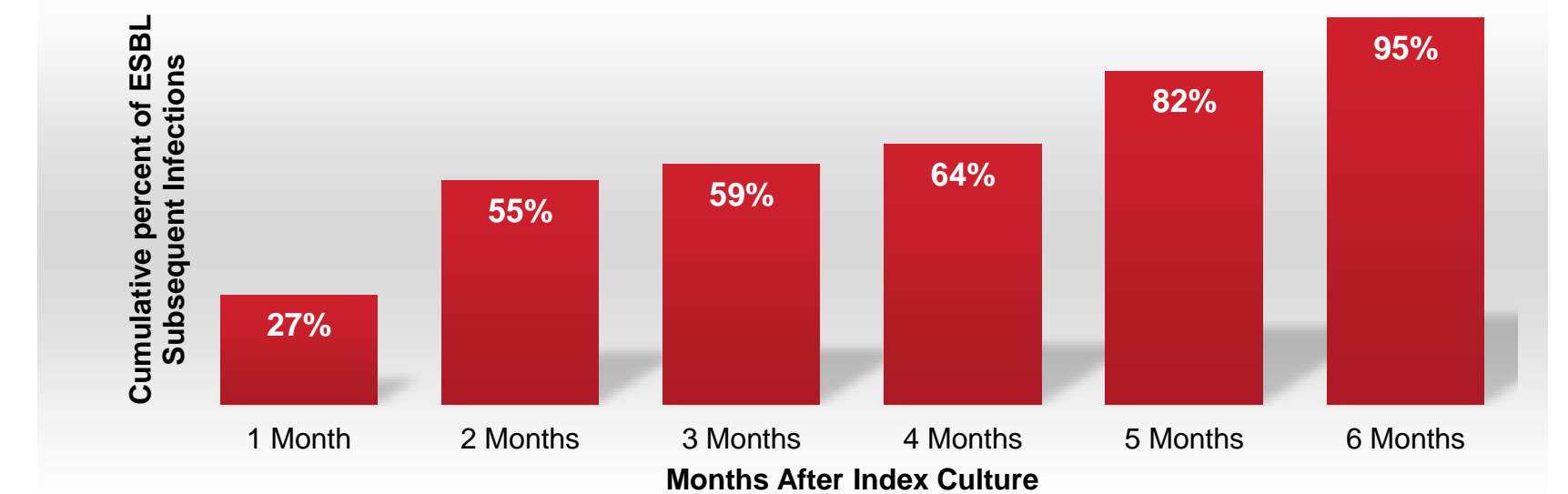
Results (cont.)

Table 3. Characteristics of Patients with Culture-positive Subsequent Infections

Data presented as n (%) unless indicated otherwise

Factor	Culture Positive Subsequent Infection		p-value
	ESBL-positive (n=22)	ESBL-negative (n=43)	
Age (years), mean (SD)	67 (16.2)	60 (23.3)	0.091
Male	7 (32)	3 (7)	0.009
Immunocompromised	0 (0)	3 (7)	0.700
Charlson Comorbidity Index Score, mean (SD)	3.5 (3.1)	2.58 (2.4)	0.098
ESBL-positive Index Culture	22 (100)	18 (42)	<0.001
Days between index culture and subsequent infection, mean (SD)	85 (64.6)	140 (103.9)	0.014

Figure 2. Cumulative rate of ESBL-positive Subsequent Infection



Conclusions

- History of positive culture for ESBL-producing *E. coli* or *K. pneumoniae* is associated with subsequent infection caused by ESBL-positive *E. coli* or *K. pneumoniae*
- Patients presenting < 6 months after ESBL-producing index culture are at increased risk for ESBL-producing subsequent infection, justifying empiric carbapenem therapy