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RISK FACTORS AND OUTCOMES FOR BLOODSTREAM INFECTIONS WITH EXTENDED-SPECTRUM β-LACTAMASE-PRODUCING *KLEBSIELLA PNEUMONIAE;* FINDINGS OF THE NOSOCOMIAL SURVEILLANCE SYSTEM IN HUNGARY

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Risk factors for and outcomes of bloodstream infections (BSIs) caused by ESBL-producing and by ESBL-non-producing *Klebsiella pneumoniae* were compared in a four-year multicenter study in Hungary. One hundred ESBL-positive and one hundred ESBL-negative patients were included as cases and controls. Investigated risk factors were related to demographics, comorbid conditions, treatments, invasive procedures, surgery prior bacteremia, presence of additional nosocomial infections and preceding hospital admission within a year. Measured outcomes were crude mortality, mortality related to infection and delay in introducing appropriate therapy (DAT). Though some risk factors for infection (admission to intensive care units, having central venous and/or urinary catheter, mechanical ventilation) were shared by both groups, in other respects cases and controls were found to differ substantially. 36 percent of patients with BSIs with ESBL-producing Klebsiella died versus 23 percent of controls (odds ratio [OR]: 2.5; 95% confidence interval [CI]: 1.0–5.4; p = 0.02). 18 percent of deaths in cases versus 9% in controls could be attributed to infection (OR: 5.0; 95% CI: 1.5–16.2; p = 0.006). Cases more often received previous antibiotic therapy than controls (OR: 2.7; 95% CI: 1.1–6.7; p = 0.02) and delay in the introduction of appropriate antibiotic treatment was observed in 44% of cases versus 19% of controls (OR: 3.4; 95% CI: 1.6–7.3; p = 0.001). The results demonstrate that BSIs caused by ESBL-producing *K. pneumoniae* are related to previous antibiotic therapy and are associated with a high rate of mortality that is often linked to delay in the introduction of

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appropriate antibiotic therapy. This confirms that besides infection control measures the early identification and antibiotic resistance profiling of the infecting pathogen is salient in the control of BSIs caused by ESBL-producing *K. pneumoniae*.

Keywords: risk factors, outcome, ESBL Klebsiella bacteremia

Introduction

The prevalence of extended-spectrum-β-lactamases (ESBL) has been increasingly reported worldwide since their first description in 1983 [1]. ESBL-producing Enterobacteriaceae pose an increasing problem in hospital environments and have become one of the most important causes of nosocomial infections in Europe [2]. Co-selection with other resistances, especially those with fluoroquinolones, aminoglycosides and sulfonamides further limits therapeutic options in infections with ESBL-producing pathogens. Moreover, the control of ESBL-producing Gram-negative bacteria is costly and requires tremendous infection control efforts [3].

A number of studies investigated the risk factors and patient outcomes of infections caused by ESBL-producing Enterobacteriaceae [3–10]. Fewer studies focus exclusively on *K. pneumoniae* or *Klebsiella spp*. [11–13]. Identified risk factors for the acquisition of infection with ESBL-producing pathogens were prior administration of antibiotics – especially that of cephalosporins –, invasive procedures, a stay in an intensive-care unit (ICU), immunosuppression, severe underlying diseases and extended stay in hospital. In addition, infections with ESBL-producing organisms are associated with higher rates of mortality and increased treatment costs [3, 14].

Klebsiella pneumoniae is the most common ESBL-producing pathogen in Hungary comprising 65% to 75% of all ESBL-producing Enterobacteriaceae [15]. In invasive isolates of *K. pneumoniae* resistance rate to third generation cephalosporins, mainly due to production of ESBL, proved to be 28% in 2008, which is a substantial increase from 2003, when the rate was 10% [16].

In order to obtain national, standardized and representative epidemiological data on nosocomial infections a national surveillance system has been launched by the National Center for Epidemiology (NCE) in 2004. The surveillance system covered the following areas: surgical site infection, ICU device-associated infections, hospital-wide surveillance of nosocomial bloodstream infections (BSIs), infections caused by multidrug resistant organisms (MDROs) including ESBL-producing *K. pneumoniae*, and nosocomial outbreaks in hospitals

[17]. Data collected in the surveillance system showed that after methicillin-resistant *Staphylococcus aureus* (MRSA), ESBL-producing *K. pneumoniae* is the most common MDRO in Hungary.

To our understanding no multicenter study on risk factors for and outcomes of infections with ESBL-producing *K. pneumoniae* has been performed in Hungary so far. The aims of this study were to investigate risk factors for and outcomes of BSIs caused by ESBL-producing and ESBL-non-producing *K. pneumoniae.*

Materials and Methods

Study design

Hospital-wide nosocomial surveillance of BSIs and MDROs is a part of the National Nosocomial Surveillance (NNS): a confidential, standardized, electronic reporting system. Software is offered freely for participating hospitals. Training on surveillance definitions, methodology and software use is provided by NCE on regular basis.

BSIs were defined according to Center for Diseases Control and Prevention criteria available on the NCE's website (http://www.oek.hu) for participating hospitals. Participating hospitals had to report all nosocomial BSIs and infections caused by MDROs.

For risk factor analysis of each case of BSI, an individual questionnaire had to be completed covering age, gender, dates of admission, discharge and infection, date of blood culture, isolated pathogen(s), antibiotic resistance profiles of isolated bacteria, general status at discharge, death related to infection; comorbidities (diabetes, cardiovascular, pulmonary, renal, hepatic, central nervous system diseases, malignancy), treatment and invasive procedures prior to BSI (immunosuppressive therapy, antibiotic therapy, stay in ICU, central venous catheter, mechanical ventilation, urinary catheter, dialysis, surgery, parenteral nutrition); specifics of antibiotic therapy (choice, start of administration, duration of administration of antibiotics) and other relevant information (hospitalized in the previous year, presence of an additional nosocomial infection).

Statistical analysis of bloodstream infections caused by ESBL-producing and by ESBL-non-producing *Klebsiella pneumoniae* was performed on data obtained in NNS between January 2005 and December 2008. The number of ESBL-producing and ESBL-non-producing *K. pneumoniae* BSIs was 114 and 172, respectively. 100 cases of ESBL-producing *K. pneumoniae* BSIs and 100 cases of

ESBL-non-producing *K. pneumoniae* BSIs were randomly selected. Risk factors for acquisition of ESBL-producing Klebsiella were calculated with Fisher's exact test for all the risk factors mentioned above. Outcomes studied were in-hospital mortality, mortality related to infection and delay in appropriate therapy. Mortality related to infection was defined as active infection at the time of death and no apparent alternative cause of death. Delay in appropriate therapy was defined as the absence of treatment with an antibiotic possessing in vitro activity against the isolated pathogen within 48 hours of drawing blood culture. In line with CLSI guidelines, treatment with penicillins and cephalosporins were considered inappropriate for all ESBL-producing *K. pneumoniae* isolates, while all other treatments were evaluated individually, based on the susceptibility test results for each isolate.

Laboratory methods

The isolation, identification and antibiotic resistance profiling of the Klebsiella strains was performed by hospital laboratories. Identification was carried out by standard procedures and/or by a variety of automatic and semi-automatic identification systems (VITEK (bioMérieux, Marcy l'Etoile, France), or Micronaut E system (Genzyme Virotech GmbH, Ruesselsheim, Germany). Antibiotic susceptibility tests were performed by the Kirby–Bauer disc diffusion method according to CLSI guidelines [18] or by automatic systems for antibiotic susceptibility testing. The production of an ESBL was confirmed by Etest ESBL (AB Biodisk, Solna, Sweden) and/or ESBL combined disk test (MAST Diagnostics, Merseyside, UK) according to manufacturers' instruction. *E. coli* ATCC 25922 and *K. pneumoniae* ATCC 700603 were included as quality control strains in all sessions.

Statistical analysis

Statistical package SAS version 9.1 (SAS Institute Ins., Cary, North Carolina, USA) was used for statistical analyses. Contingency tables were prepared for the main study variables by ESBL and non-ESBL production. Categorical variables were compared via Fisher's exact test. The medians and interquartile ranges were calculated for the continuous variables. Normally distributed continuous variables were compared via Student's t test, and non-normally distributed contin-

uous variables were compared via the Wilcoxon rank sum test. In the next step, univariate analyses were performed for each of the three outcomes evaluated by logistic regression modeling.

Multivariable regression models were constructed using a stepwise procedure, incorporating variables found to be significant on univariate testing, with the exception of ESBL production, to determine additional risk factors for in-hospital mortality, mortality related to infection, and delay in appropriate treatment (DAT). Logistic regression models were used to calculate the adjusted odds ratios (OR) and 95% confidence intervals (95% CI). For ease of comparison between adjusted and unadjusted effects, odds ratios rather than relative risks were reported in the univariate analyses of mortality, mortality related to infection, and DAT. For all statistical analyses, a p value of ≤ 0.05 was considered significant.

Results

Fourhundred eighty-seven infections caused by ESBL-producing *K. pneumoniae* were reported in NNS between January 2005 and December 2008. The 487 cases were comprised of the following infections: urinary tract infections: 141 (28.9%), bloodstream infections: 114 (23.4%), pneumonia and lower respiratory tract infections: 108 (22.1%), surgical site infections: 91 (18.6%) and other infections including skin and soft tissue infections: 33 (6.8%). The number of reported ESBL-non-producing *K. pneumoniae* BSIs was 172 during the same period.

Data on 100 cases of BSI caused by ESBL-producing and 100 cases of BSI caused by ESBL-non-producing *K. pneumoniae* (controls) were processed and are summarized in Table 1. The median age proved to be 63 years for cases (interquartile range [IQR] 48–74), and 57 years for controls (IQR 46–71). Males made up 62% of cases and 72% of controls. Demographics showed no significant differences between the two groups. Median length of stay in hospital prior to acquiring BSI was 10.5 days for cases and 10 days for controls. Median length of hospital stay subsequent to having a Klebsiella positive blood culture was 11.5 (interquartile range [IQR] 6.5–16.5) days for cases versus 14 (IQR 7–23) days for controls.

Rates for some risk factors (treatment in ICU, having a central venous catheter, having a urinary catheter, previous surgical procedure, mechanical ventilation) proved to be very high in both cases and controls (Table I).

Table I

Baseline characteristics and comparison of patients with ESBL-producing and ESBL-non producing *K. pneumoniae*

Characteristic	Bacteremia type				Comparison
	ESBL (N=100)		Non-ESBL (N=100)		
	No.	%	No.	%	p-value*
Demographics					
Age (median, IQR#)	63	48-74	57	46-71	0.22**
Gender (male %)	62	62.0	72	72.0	0.17
Comorbidity, therapy, procedure					
Diabetes	15	15.0	9	9.0	0.28
Cardiovascular disease	39	39.0	29	29.0	0.18
Pulmonary disease	25	25.0	9	9.0	0.004
Renal disease	7	7.0	4	4.0	0.54
Central nervous system disease	8	8.0	3	3.0	0.21
Malignancy	32	32.0	15	15.0	0.007
Hepatic disease	5	5.0	1	1.0	0.21
More than 2 comorbidities	15	15.0	2	2.0	0.001
Immunosuppressive therapy	16	16.0	5	5.0	0.02
Central venous catheter	82	82.0	77	77.0	0.48
Mechanical ventilation	59	59.0	52	52.0	0.78
Urinary catheter	70	70.0	86	86.0	0.9
Dialysis	7	7.0	6	6.0	1.00
Surgery	55	55.0	60	60.0	0.1
Intensive care unit	76	76.0	65	65.0	1.00
Parenteral nutrition	25	25.0	17	17.0	0.22
Hospitalized in previous year	43	43.0	10	10.0	<0.0001
Recent antibiotic therapy	82	82.0	68	68.0	0.03
Other nosocomial infection					
Pneumonia	29	29.0	19	19.0	<0.0001
Surgical site infection	16	16.0	3	3.0	<0.0001
Urinary tract infection	14	14.0	3	3.0	0.9
Death	36	36.0	23	23.0	0.02***
Death related to infection	18	18.0	9	9.0	0.006***
Delay in appropriate therapy	44	14.0	19	19.0	0.001***

* calculated with Fisher's exact test
** calculated with Wilcoxon rank sum test
*** multivariable analysis results
# IQR = interquartile range

Table I summarizes variables for both groups studied. Cases more often harbored comorbidities: chronic pulmonary disease ($p = 0.004$) and malignancies ($p = 0.007$). In addition, they significantly more frequently suffered of two comorbidities ($p = 0.001$). More cases than controls received immunosuppressive therapy ($p = 0.02$); and were hospitalized within a year ($p < 0.0001$) and received antibiotic therapy ($p = 0.03$) prior to infection. The frequency of use of invasive

devices were similar in both groups, but the use of urinary catheters and the frequency of recent surgical procedures was more common among controls.

Since the two groups differed substantially, controlling for confounding was performed by univariate and then by multivariable analysis for each studied outcome.

Table II summarizes the univariate analysis for each of the three outcomes evaluated by regression modeling.

In univariate analysis BSI caused by ESBL-producing *K. pneumoniae* proved to be a significant risk factor for mortality (OR, 1.9; 95% CI,1.0–3.5; p = 0.04), for mortality related to infection (OR, 2.2; 95% CI, 0.9–5.2; p = 0.007) and for significant delay in initiating appropriate therapy (OR, 3.4; 95% CI, 1.8–6.3; p = 0.0002). Additional variables were also found to be significant risk factors for death in univariate analysis: age above 70 years (OR, 3.1; 95% CI, 1.4–7.2; p = 0.007), chronic pulmonary disease (OR, 3,4; 95% CI, 1.6–7.3; p = 0.001), insertion of central venous catheter (OR, 2.4; 95% CI, 0.9-5.7; p = 0.05), mechanical ventilation (OR, 2.8; 95% CI, 1.5–5.2; p = 0.002), insertion of urinary catheter (OR, 3.3; 95% CI, 1.3–8.2; p = 0.01), previous stay in ICU (OR, 2.3; 95% CI, 1.2–4.7; p = 0.02) and parenteral nutrition (OR, 2.1; 95% CI, 1.1–4.3; p = 0.03). In univariate analysis concomitant presence of another nosocomial infection, namely pneumonia (OR, 2.3; 95% CI 1.1–4.7; p = 0.03) and surgical site infection (OR, 3.8; 95% CI, 1.4–10.5; p = 0.008) were also significant factors for mortality.

Early death after infection (within 5 days of testing blood culture) was analyzed in both patient groups. Early death occurred significantly more often in the ESBL-producing group (p = 0.02).

In multivariable analysis, after adjusting to avoid confounding variables (Table III) ESBL-producing *K. pneumoniae* remained a significant risk factor of mortality. Further predictors of death were age above 70 years, chronic pulmonary disease, and presence of pneumonia or surgical site infection in addition to BSI.

Univariate analysis of death related to infection detected the following significant risk factors: neurological disease (OR, 4.1; 95% CI 1.1–15.2; p = 0.03); mechanical ventilation (OR, 3.2; 95% CI, 1.3–8.1; p = 0.01); previous antibiotic therapy (OR, 4.8; 95% CI, 1.1–21.0; p = 0.04). Presence of pneumonia and surgical site infection also proved to be significant risk factors (p = 0.003 and p = 0.0003 respectively).

In multivariate analysis, after controlling for all confounders, significant risk factors of death related to infection remained ESBL-production, neurological disease, presence of pneumonia and surgical site infection.

Table II

Univariate analysis of death, death-related infection and delay in appropriate therapy of patients with BSIs with *K. pneumoniae*

Characteristic	Death				Death-related infection (DRI)				Delay in appropriate therapy			
	Death (%) (N=59)	OR	95% CI	p	DRI (%) (N=27)	OR	95% CI	p	DAT (%) (N=63)	OR	95% CI	p
Exposure – ESBL	36 (61.0)	1.9	1.0–3.5	0.04	18 (66.7)	2.2	0.9–5.2	0.007	44 (69.8)	3.4	1.8–6.3	0.0002
Gender (male)	44 (74.6)	1.7	0.8–3.3	0.14	20 (74.1)	1.5	0.6–3.7	0.40	38 (60.3)	0.6	0.3–1.2	0.17
Age												
–49	11 (18.6)	ref			7 (25.9)	ref			17 (27.0)	ref		
50–70	23 (39.0)	1.6	0.7–3.7	0.23	8 (29.6)	0.8	0.3–2.3	0.64	26 (41.3)	1.1	0.5–2.3	0.80
71–	25 (42.4)	3.1	1.4–7.2	0.007	12 (44.4)	1.9	0.7–5.1	0.23	20 (31.7)	1.2	0.6–2.7	0.59
Diabetes	6 (10.2)	0.8	0.3–2.0	0.61	3 (11.1)	0.9	0.3–3.3	0.88	13 (20.6)	3.0	1.3–7.1	0.01
Cardiovascular disease	25 (42.4)	1.7	0.9–3.1	0.11	12 (44.4)	1.7	0.7–3.8	0.22	28 (44.4)	1.9	1.0–3.6	0.03
Pulmonary disease	18 (30.5)	3.4	1.6–7.3	0.001	3 (11.1)	0.6	0.2–2.0	0.39	10 (15.9)	0.9	0.4–2.0	0.77
Renal disease	3 (5.1)	1.1	0.3–4.4	0.87	0 (0.0)	–			5 (7.9)	0.5	0.2–1.8	0.31
Central nervous system disease	6 (10.2)	3.1	0.9–10.5	0.07	4 (14.8)	4.1	1.1–15.2	0.03	7 (11.1)	4.2	1.2–14.8	0.03
Malignancy	11 (18.6)	0.7	0.3–1.4	0.30	5 (18.5)	0.7	0.3–2.0	0.51	12 (19.1)	0.7	0.3–1.4	0.31
Hepatic disease	2 (3.4)	1.2	0.2–6.7	0.83	1 (3.7)	1.3	0.1–11.5	0.82	2 (3.2)	1.1	0.2–6.1	0.92
More than 2 comorbidities	7 (11.9)	1.8	0.6–4.9	0.27	2 (7.4)	0.8	0.2–3.9	0.83	10 (15.9)	3.5	1.3–9.7	0.01
Immunosuppression	4 (6.8)	0.5	0.2–1.6	0.27	2 (7.4)	0.6	0.1–2.9	0.57	3 (4.8)	0.3	0.1–1.2	0.08
Central venous catheter	52 (88.1)	2.4	0.9–5.7	0.05	23 (85.2)	1.6	0.5–4.8	0.43	51 (80.9)	1.1	0.5–2.4	0.73
Mechanical ventilation	40 (67.8)	2.8	1.5–5.2	0.002	20 (74.1)	3.2	1.3–8.1	0.01	31 (49.2)	0.9	0.5–1.7	0.80
Urinary catheter	53 (89.8)	3.3	1.3–8.2	0.01	27 (100.)	–			52 (82.5)	1.5	0.7–3.2	0.29
Dialysis	7 (11.9)	0.3	0.1–1.0	0.06	4 (14.8)	0.3	0.1–1.1	0.07	7 (11.1)	0.4	0.1–1.1	0.08
Surgery	32 (54.2)	1.5	0.8–2.7	0.22	15 (55.6)	1.5	0.6–3.3	0.37	35 (55.6)	1.6	0.9–2.9	0.12
Intensive care unit	46 (78.0)	2.3	1.2–4.7	0.02	22 (81.5)	2.6	0.9–7.1	0.07	40 (63.5)	0.9	0.5–1.6	0.68
Parenteral nutrition	18 (30.5)	2.1	1.1–4.3	0.03	7 (25.9)	1.4	0.5–3.5	0.50	16 (25.4)	1.5	0.7–2.9	0.30
Hospitalized in previous year	13 (22.0)	1.0	0.5–2.2	0.90	5 (18.5)	0.8	0.3–2.3	0.68	18 (28.6)	1.8	0.9–3.6	0.10
Recent antibiotic therapy	46 (78.0)	1.3	0.6–2.6	0.53	25 (92.6)	4.8	1.1–21.	0.04	54 (85.7)	2.6	1.2–5.7	0.02
Other nosocomial infection												
No other infection	26 (44.1)	ref			7 (25.9)	ref			35 (55.6)	ref		
Pneumonia	19 (32.2)	2.3	1.1–4.7	0.03	11 (40.7)	4.6	1.7–12.8	0.003	14 (22.2)	1.0	0.5–2.0	0.90
Surgical site infection	10 (17.0)	3.8	1.4–10.5	0.008	7 (25.9)	9.1	2.7–30.3	0.0003	9 (14.3)	2.1	0.8–5.6	0.14
Urinary tract infection	4 (6.8)	1.1	0.3–3.5	0.92	2 (7.4)	2.1	0.4–10.9	0.39	5 (7.9)	1.0	0.3–2.9	0.95

Table III

Multivariable analysis of outcomes: mortality, death related to infection, delay in appropriate therapy

Hiányzik a * lábjegyzet

Crude mortality – ESBL: Odds Ratio Estimates*				
Effect – p-value		Point Estimate	95% Wald	
			Confidence	Limits
ESBL	0.02	2.469	1.129	5.401
Age: 50–70	0.50	1.407	0.526	3.767
Age:71–	0.04	2.793	1.026	7.599
Pulmonary disease	0.03	2.625	1.091	6.315
Mechanical ventilation	0.45	1.441	0.553	3.756
Urinary catheter	0.55	1.419	0.444	4.537
Intensive care unit	0.46	1.451	0.538	3.910
Parenteral nutrition	0.24	1.713	0.691	4.244
Pneumonia	0.04	2.132	0.918	4.956
Surgical site infection	0.004	5.753	1.721	19.233
Urinary tract infection	0.89	0.915	0.242	3.456

Death related to infection – ESBL: Odds Ratio Estimates				
Effect – p-value		Point Estimate	95% Wald	
			Confidence	Limits
ESBL	0.006	5.068	1.581	16.241
Central nervous s. disease	0.03	4.849	1.115	21.087
Mechanical ventilation	0.39	1.822	0.465	7.137
Intensive care unit	0.45	1.789	0.390	8.215
Recent antibiotic therapy	0.20	2.865	0.561	14.630
Pneumonia	0.004	5.489	1.722	17.493
Surgical site infection	<0.0001	24.949	5.097	122.122
Urinary tract infection	0.25	2.889	0.472	17.690

Delay in appropriate therapy – ESBL: Odds Ratio Estimates				
Effect – p-value		Point Estimate	95% Wald	
			Confidence	Limits
ESBL	0.001	3.436	1.614	7.317
Diabetes	0.06	2.955	0.958	9.117
Cardiovascular disease	0.29	1.461	0.723	2.953
Central nervous system disease	0.08	3.336	0.860	12.947
More than 2 comorbidities	0.80	1.195	0.299	4.775
Recent antibiotic therapy	0.02	2.760	1.129	6.747
Hospitalized in previous year	0.21	0.564	0.229	1.389

Delay in appropriate therapy occurred in 44% of cases versus 19% in controls (OR, 3.4; 95% CI, 1.8–6.3; p = 0.0002), ESBL production and previous antibiotic therapy (OR, 2,7; 95% CI 1.1–6.7; p = 0.02) proved to be significant predic-

tors for delay in appropriate therapy. In multivariate analysis, ESBL production and previous antibiotic therapy both remained significant risk factors for delay in appropriate therapy.

Discussion

This study identified risk factors and outcomes for BSIs caused by ESBL-producing *K. pneumoniae*. Baseline comparison of cases and controls revealed significant risk factors for the acquisition of ESBL-producing K. pneumoniae: pulmonary disease ($p = 0.004$), malignancy ($p = 0.007$), more than two comorbidities ($p = 0.001$), immunosuppressive therapy ($p = 0.02$), recent antibiotic therapy ($p = 0.03$) and hospitalization within a year ($p < 0.0001$). Known risk factors can increase clinicians' suspicion for ESBL-producing infections, promoting active surveillance culture draw for pathogen identification and the starting of early appropriate therapy.

Some reports suggest that prior antibiotic therapy, admission to ICU, use of invasive devices (central venous- and urinary catheter, mechanical ventilation) were significant risk factors for the acquisition of ESBL-producing pathogens [5, 12, 19, 20]. These risk factors were identified in the univariate analysis of this study, as well, but did not prove to be significant in multivariable analysis.

Some additional studies failed to detect any independent risk factors for the acquisition of ESBL-producing pathogens [4, 13].

According to the multivariable analysis presented here, BSIs caused by ESBL-producing *K. pneumoniae* were associated with a 2.5-fold risk of in-hospital mortality, a 5.0-fold risk of death related to infection and a 3.4-fold risk of delay in appropriate therapy versus BSIs caused by ESBL-non-producing *K. pneumoniae,* which is consistent with earlier reports [3–10]. Further independent risk factors for death were: age above 70 years, chronic pulmonary disease and presence of other nosocomial infection (pneumonia) or surgical site infection. Independent risk factors for death-related infection were neurological disease and the presence of pneumonia or surgical site infection.

A number of studies demonstrated that infection with ESBL-producing pathogens was associated with an extended stay in hospital [3, 9, 11]. A surprising result of this study was the lack of significant difference in the length of hospital stay subsequent to infection between the two groups. A significantly higher rate of early mortality (within 5 days) in our BSI group with ESBL-producing pathogens can account for this observation. This is also in line with previous findings. A significant association with mortality in patients with ESBL-producing nosocomial

pathogens has been reported by a number of studies [3, 4, 6, 19, 21, 22]. One study demonstrated an overall mortality four times greater than in patients infected with ESBL-non-producing organisms [22].

A multidisciplinary approach is required to control the rise in infections caused by ESBL-producing *K. pneumoniae* in Hungary. It is of utmost importance that microbiology laboratories rapidly and reliably detect ESBL-producing pathogens allowing the early initiation of adequate antibiotic therapy and the introduction of appropriate infection control measures. The awareness of factors governing the acquisition and mortality of BSIs caused by ESBL-producing *K. pneumoniae* helps to identify vulnerable patients and should contribute both to the prevention of infections and to an improved patient care.

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