Epidemiology and Susceptibility to Antimicrobials in Community, Hospital and Long-Term Care Facility Bacteremia in Northern Israel: a 6 Year Surveillance*

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ABSTRACT: **Background:** Identification of pathogens and their susceptibility to antimicrobials is mandatory for successful empiric antibiotic treatment.

Objectives: To compare the clinical characteristics of patients with bacteremia, as well as the bacterial distribution and antimicrobial susceptibility in community, hospital and long-term care facilities during two periods (2001–2002 and 2005–2006).

Methods: The study was conducted at the HaEmek Medical Center, a community 500-bed teaching hospital in northern Israel serving a population of ~500,000 inhabitants. All episodes of bacteremia (n=1546) during two 2 year periods (2001–2 and 2005–6) were prospectively recorded, evaluated and compared (755 in 2001–2 and 791 in 2005–6).

Results: In both periods the urinary tract was the main port of entry in community and long-term care facility bacteremia, while the urinary tract – primary and catheter-related – were similar in frequency as sources of hospital bacteremia. *Escherichia coli* was the most frequent pathogen isolate. No significant changes in the frequency of methicillin-resistant *Staphylococcus aureus* and extended-spectrum beta-lactamase-producing bacteria were seen between the two 2 year periods (2001–2 and 2005–6). The susceptibility of non-ESBL-producing *E. coli* decreased for some antibiotics while non-ESBL-producing *Klebsiella pneumoniae* susceptibility profile improved in the same period. A non-statistically significant trend of increased resistance in gram-negative isolates to quinolones, piperacillin and piperacillin-tazobactam was observed, but most isolates still remained highly susceptible to carbapenems. There was a small increase in mortality rate in hospital bacteremia during the second period.

Conclusions: Continuous surveillance is imperative for monitoring the local epidemiology and for developing local treatment guidelines.

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KEY WORDS: bacteremia, antimicrobials, susceptibility, resistance, epidemiology

Bacteremia is a leading cause of morbidity and mortality. In addition, the emergence and spread of multidrug-resistant pathogens complicate the treatment of serious infections, particularly among severely ill and high risk patients [1]. Infection by resistant strains has a poor prognosis with prolonged hospitalization and necessitates increased use of health care resources [1-4]. Therefore, identification of pathogens and assessing their susceptibility to antimicrobials according to sources is essential for implementing adequate clinical guidelines.

The aims of the present study were to compare the clinical and demographic characteristics of patients with bacteremia hospitalized at HaEmek Medical Center during two periods, 2001–2002 and 2005–2006. In addition, we evaluated the source, bacterial distribution and antimicrobial susceptibility of bacteremic isolates according to community, hospital and long-term care facility settings. Finally, we compared trends in antimicrobial susceptibility in both periods.

PATIENTS AND METHODS

The study was conducted at HaEmek Medical Center, a 500-bed community teaching hospital in northern Israel serving a population of ~500,000 inhabitants. From January 2001 to December 2006 all positive blood cultures, excluding those from the neonatal intensive care unit, were prospectively recorded. Only one isolate was included for each bacteremic episode. In the case of polymicrobial bacteremia, each isolate was separately included in the database. Two periods were evaluated and compared: 2001–2 and 2005–6. Continuous surveillance of microbiology laboratory records was conducted by the Infectious Disease team. Demographic, clinical and epidemiological data were obtained from patient charts. Two investigators (B.C. and N.T.) daily evaluated each episode to determine the source of infection and differentiate true

ESBL = extended-spectrum beta-lactamase

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bacteremia from contamination. Mortality was defined as the outcome when the patient died during hospitalization.

Blood cultures were processed using Bactec 9000 technology (USA). Microorganisms were identified using standard microbiological methods and their susceptibility to antibiotics was evaluated using the disk diffusion technique and Clinical Laboratory Standards Institute criteria. Minimal inhibitory concentration was measured using the Etest in patients with endocarditis and other serious infectious diseases or in those drug-bacteria combinations where the disk diffusion test is not recommended.

Blood cultures were classified as community bacteremia when obtained within the first 48 hours of admission, hospital bacteremia when obtained after the first 48 hours of admission, and long-term care facility bacteremia when obtained from a nursing home resident referred to our institution.

Statistical analysis was carried out by a standard chi-square test and Yates corrected test using the SPSS computer program. Results were considered statistically significant at $P < 0.05$.

RESULTS

Altogether, 1546 episodes of bacteremia were recorded: 755 in the first period (2001–2) and 791 in the second (2005–6). Three settings were evaluated and compared in each period: CB (435 vs. 423), HB (286 vs. 325) and LTCF-B (34 vs. 43) respectively.

No statistical differences were seen during both periods regarding gender, age, frequency of bacteremia (distribution among CB, HB, LTCF-B), bacteremia days (days from admission to positive blood culture), and mean length of hospitalization, with the exception of a mild increase in mortality rate in HB (21.0 to 25.2%, borderline significance $P = 0.055$) [Table 1].

Most bacteremic isolates were community (> 50%) or hospital acquired (~40%). LTCF-B (~5%) included elderly nursing home residents referred to our hospital because of fever or clinical deterioration. As expected, this group showed the shortest length of hospitalization (6.4 vs. 6.1 days) and the highest mortality rate (23.5% vs. 27.9% in 2001–2 and 2006–6 respectively, NS for all) [Table 1].

The urinary tract was the main port of entry in CB (49.0% vs. 45.2%) and LTCF-B (55.9% vs. 58.1%, 2001–2 vs. 2005–6, NS for all), while urinary tract (21.3% vs. 22.8%), primary bacteremia (15.0% vs. 22.2%) and catheter-related bacteremia (15.7% vs. 20.7%) showed similar frequency in hospital isolates. A significant increase in primary source (9.0% vs.

CB = community bacteremia
HB = hospital bacteremia
LTCF-B = long-term care facility bacteremia

Table 1. Clinical and demographic characteristics and source of pathogens

	Community bacteremia		Hospital bacteremia		Long-term care facility bacteremia	
	2001-2002	**2005-2006**	**2001-2002**	**2005-2006**	**2001-2002**	**2005-2006**
No. of patients	**435 (57.6%)**	**423 (53.4%)**	**286 (37.8%)**	**325 (41.0%)**	**34 (4.5%)**	**43 (5.4%)**
Gender male	46.7%	47.0%	54.2%	48.9%	52.9%	37.2%
Mean age (yrs)	58.2	59.8	59.5	59.7	75.7	81.0
Bacteremia day	0	1.37	11.5	13.4	1.4	1.7
Mean length of hospitalization (days)	10.0	8.7	27.5	24.1	6.4	6.1
Transferred to another hospital	6	18	6	40	0	1
Mortality rate died/alive	67/362 15.4%	50/355 11.8%	60/220 21.0% ^	82/203 25.2% ^	8/26 23.5%	12/30 27.9%
Source						
Primary	39 (9.0%) **	58(13.7%) **	43 (15.0%)	72 (22.2%)	1 (2.9)	6 (14.0%)
Urinary tract	213 (49.0%)	191 (45.2%)	61 (21.3%)	74 (22.8%)	19 (55.9)	25 (58.1%)
Respiratory	29 (6.7%) ~	44 (10.4%) ~	22 (7.7%)	30 (9.2%)	3 (8.8)	4 (9.3%)
Gastrointestinal	37 (8.5%)	38 (9.0%)	61 (21.3%) *	20 (6.2%) *	1 (2.9)	2 (4.7%)
Skin-soft tissue	35 (8.0%)	21 (5.0%)	26 (9.1%)	20 (6.2%)	3 (8.8)	4 (9.3%)
Infective endocarditis	14 (3.2%)	13 (3.1%)	7 (2.4%)	10 (3.1%)	0	0
Catheter related	6 (1.4%)	3 (0.7%)	45 (15.7%)	67 (20.7%)	3 (8.8)	0
Biliary tract	32 (7.4%)	37 (8.7%)	13 (4.5%)	24 (7.4%)	2 (5.9)	1 (2.3%)
Osteoarticular	9 (2.1%)	2 (0.5%)	3 (1.0%)	4 (1.2%)	2 (5.9)	1 (2.3%)

* $P < 0.0000$, ** $P = 0.03$, ^ $P = 0.055$.

13.7%, $P = 0.03$) in CB, and a decrease in gastrointestinal source in HB was found (2001–2 vs. 2005–6) [Table 1].

No major changes were observed in the distribution of most pathogens when comparing the two periods. *Escherichia coli* remained the most frequent pathogen except for 2001–2 HB, when *Staphylococcus aureus* and *E. coli* were the prevalent pathogens (17.5% vs. *E. coli* 16.8%) due to a sporadic nosocomial staphylococcal outbreak [Table 2].

In general, bacteremic isolates from community-acquired bacteremia were more susceptible to antimicrobial agents than hospital-acquired bacteremia and LTCF-B isolates [Table 3].

NON-ESBL *E. COLI* AND *KLEBSIELLA* SP. [TABLE 3]

A significant decrease in the susceptibility rate among non-ESBL *E. coli* to cephalotin (LTCF-B), amoxi-clavulanate, piperacillin (CB and HB) and piperacillin-tazobactam (HB) was observed. On the other hand, non-ESBL *Klebsiella* sp. showed a significant increase in susceptibility to second and third-generation cephalosporins (CB), and to aztreonam (CB and HB) (2001–2 vs. 2005–6) [Table 3].

Non-ESBL *E. coli* and *Klebsiella* sp. isolates showed high susceptibility rates to gentamicin in HB (≥ 80%), CB and LTCF-B (≥ 90%), with an even superior susceptibility profile to amikacin in all the settings in the second period (~95%) [Table 3].

ESBL = extended-spectrum beta-lactamase

ESBL PRODUCERS *E. COLI* AND *KLEBSIELLA* SP. [TABLE 3]

There were more ESBL-producing *Klebsiella* sp. than *E. coli;* the prevalence of *Klebsiella* sp. ESBL-positive was significantly higher in HB (30.9%) than in CB (6.25%) only during the first period ($P = 0.005$). No changes were observed in the frequency of *E. coli* ESBL producers and only a few ESBL producer isolates were recovered from LTCF settings [Table 3].

OTHER GRAM-NEGATIVE BACILLI (DATA NOT SHOWN)

A significant increase in susceptibility rate between the two periods was noted with cefuroxime (CB 91.1% vs. 96.2%, $P = 0.008$), ceftriaxone (CB 95.3% vs. 99.6%, $P = 0.003$; HB 83.0% vs.92.4%, $P = 0.03$) and ceftazidime (CB 95.3% vs. 99.6%, $P = 0.003$; HB 83.6% vs. 92.1%, $P = 0.03$), with a concomitant decrease in LTCF-B for cephalotin (94.4% vs. 50.0%, $P = 0.002$) (2001–2 vs. 2005–6 respectively).

The susceptibility to gentamicin was stable in CB (94.0% vs. 96.0%) and HB (87.5% vs. 87.9%) isolates, but decreased in LTCF-B (100% vs. 67%, $P = 0.005$, 2001–2 vs. 2005–6 respectively); amikacin revealed excellent antimicrobial activity against other gram-negative bacilli (> 97% in all settings and in both periods).

A non-significant decrease in the susceptibility rate for fluoroquinolones was noted in all the settings (CB 94.1 vs. 92.0%; HB 87.4 vs. 83.5%; and LTCF-B 100.0 vs. 65.2%; 2001–2 vs. 2005–6, NS for all)

Table 2. Distribution of pathogens

	Community bacteremia		Hospital bacteremia		Long-term care facility bacteremia	
Pathogens n (%)	**2001-2002**	**2005-2006**	**2001-2002**	**2005-2006**	**2001-2002**	**2005-2006**
E. coli	187 (43.0%)	174 (41.1%)	48 (16.8%)	56 (17.2%)	16 (47.1%)	13 (30.2%)
Klebsiella sp.	48 (11.0%)	35 (8.3%)	42 (14.7%)	33 (10.1%)	3 (8.8%)	5 (11.6%)
Other gram-negative	42 (9.7%)	50 (11.8%)	12 (4.0%)	19 (6.0%)	0	0
Staph. aureus	35 (8.0%)	22 (5.2%)	50 (17.5%)	45 (13.8%)	5 (14.7%)	4 (9.3%)
Strep. pneumoniae	31 (7.1%)	45 (10.6%)	4 (1.4%)	6 (1.8%)	1 (2.9%)	1 (2.3%)
Streptococcus sp.	24 (5.5%)	28 (6.6%)	6 (2.0%)	8 (2.4%)	1 (2.9%)	1 (2.3%)
Anaerobes	14 (3.2%)	16 (3.8%)	10 (3.4%)	10 (3.1%)	1 (2.9%)	0
P. aeruginosa	12 (2.8%)	9 (2.1%)	32 (11.2%)	33 (10.2%)	3 (8.8%)	3 (7.0%)
Enterobacter sp.	11 (2.5%)	8 (1.9%)	29 (10.1%)	19 (5.8%)	0	0
Proteus/Morganella sp.	10 (2.2%)	12 (2.9%)	8 (2.8%)	12 (3.7%)	3 (8.8%) **	13 (30.3%) b
Enterococcus sp.	8 (1.8%)	15 (3.5%)	14 (4.9%) *	33 (10.2%) *	1 (2.9%)	2 (4.7%)
Candida sp.	4 (0.9%)	0	4 (1.4%)	14 (4.3%)	0	0
Coagulase negative *Staphylococcus*	4 (0.9%)	4 (0.9%)	11 (3.8%)	13 (4.0%)	0	0
Serratia sp.	3 (0.7%)	2 (0.5%)	3 (1.0%)	3 (0.9%)	0	0
A. baumanii	2 (0.5%)	3 (0.7%)	13 (4.5%)	20 (6.2%)	0	0
Others			–	1 (0.3%)	–	1 (2.3%)
Total	435 (100%)	423 (100%)	286 (100%)	325 (100%)	34 (100%)	43 (100%)

* $P < 0.02$, ** $P = 0.04$.

Table 3. Susceptibility rates (%) of the most frequent isolates to the most common antibiotic drugs

	Community bacteremia				Hospital bacteremia				Long-term care facility bacteremia			
Pathogen and antimicrobial drug	**2001-2002**		**2005-2006**		**2001-2002**		**2005-2006**		**2001-2002**		**2005-2006**	
E. coli	**ESBL- (n=182)**	**ESBL+ (n=5)**	**ESBL- (n=166)**	**ESBL+ (n=8)**	**ESBL- (n=44)**	**ESBL+ (n=4)**	**ESBL- (n=52)**	**ESBL+ (n=4)**	**ESBL- (n=15)**	**ESBL+ (n=1)**	**ESBL- (n=13)**	**ESBL+ (n=0)**
Cephalotin	65.2	ND	56.4	ND	63.6	ND	45.1	ND	100.0 a	ND	46.2 a	ND
Cefuroxime	96.7	ND	99.4	ND	93.0	ND	90.4	ND	100.0	ND	91.7	ND
Ceftriaxone	99.5	ND	100.0	ND	100.0	ND	96.1	ND	100.0	ND	100.0	ND
Amoxi-clavulanate	83.0 ~~	40.0	74.4 ~~	12.5	86.4 ^	25.0	60.8 ^	25.0	100.0	ND	84.6	ND
Gentamicin	96.7	40.0	97.0	25.0	81.4	25.0	86.5	25.0	100.0	100.0	92.3	ND
Amikacin	99.5	80.0	99.4	75.0	100.0	25.0	98.0	75.0	100.0	100.0	100.0	ND
TMP-SXZ	68.9	20.0	74.4	12.5	63.3	0	56.9	0	50.0	0	75.0	ND
Piperacillin	71.4 ^^	ND	60.1 ^^	ND	78.4 **	ND	51.0 **	ND	86.7	ND	58.3	ND
Pip-tazobactam	97.7	80.0	95.1	62.5	97.7 ^^	50.0	84.0 ^^	0	80.0	100.0	91.7	ND
Fluoroquinolones	94	40.0	94.0	50.0	75.0	0	75.0	25.0	100.0	0	75.0	ND
Ertapenem	ND	ND	100.0	75.0	ND	ND	100.0	75.0	ND	ND	100.0	ND
Carbapenems	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	86.7	100.0	100.0	ND
***Klebsiella* sp.**	**ESBL- (n=45)**	**ESBL+ (n=3)**	**ESBL- (n=33)**	**ESBL+ (n=2)**	**ESBL- (n=29)**	**ESBL+ (n=13) #**	**ESBL- (n=26)**	**ESBL+ (n=7) #**	**ESBL- (n=2)**	**ESBL+ (n=1)**	**ESBL- (n=2)**	**ESBL+ (n=3)**
Cephalotin	75.6	ND	93.5	ND	69.0	ND	87.0	ND	100.0	ND	100.0	ND
Cefuroxime	77.8 ^^	ND	96.8 ^^	ND	75.9	ND	91.3	ND	100.0	ND	100.0	ND
Ceftriaxone	86.7 ^^	ND	100.0 ^^	ND	82.8	ND	100.0	ND	100.0	ND	100.0	ND
Ceftazidime	86.7 ^^	ND	100.0 ^^	ND	85.2	ND	100.0	ND	100.0	ND	100.0	ND
Amoxi-clavulanate	75.6	50.0	90.3	0	69.0	0	82.6	28.6	100.0	0	100.0	0
Gentamicin	86.4	100.0	93.5	50.0	86.2	ND	91.3	14.3	100.0	100.0	100.0	0
Amikacin	95.6	100.0	96.8	0	89.7	84.6	100.0	71.4	100.0	100.0	100.0	66.7
Aztreonam	84.4 ~	ND	100.0 ~	ND	79.3 ~	ND	100.0 ~	ND	100.0	ND	100.0	ND
TMP-SXZ	86.0	33.3	80.6	0	81.5	15.4	87.0	57.1	0	ND	50.0	ND
Piperacillin	74.2	ND	74.2	ND	76.0	ND	87.0	ND	0	ND	50.0	ND
Pip-tazobactam	86.4	33.3	90.3	50.0	88.9	23.1	95.7	28.6	100.0	ND	100.0	0
Fluoroquinolones	90.9	33.3	83.9	50.0	92.6	38.5	91.3	28.6	100.0	ND	100.0	33.3
Ertapenem	ND	ND	95.8	100.0	ND	ND	100.0	85.7	ND	ND	100.0	66.7
Carbapenems	100.0	100.0	100.0	100.0	89.7	100.0	100.0	100.0	100.0	100.0	100.0	100.0
P. aeruginosa	**(n=12)**		**(n=9)**		**(n=32)**		**(n=33)**		**(n=3)**		**(n=3)**	
Ceftazidime	ND		88.9		66.7		84.4		ND		100.0	
Gentamicin	83.3		75.0		90.6		78.8		66.7		66.7	
Amikacin	83.3		77.8		100.0		93.9		33.3		100.0	
Aztreonam	50.0		ND		64.5		50.0		50.0		ND	
Piperacillin	58.3		88.9		84.6		97.0		66.7		100.0	
Fluoroquinolones	83.3		77.8		90.3		81.8		50.0		66.7	
Carbapenems	100.0		100.0		86.8		93.9		33.3		66.7	
S. aureus	**(n=35)**		**(n=22)**		**(n=50)**		**(n=45)**		**(n=5)**		**n = 4**	
Oxacillin	88.6		72.7		76.0		66.7		60.0		50.0	
Clindamycin	97.1		86.4		91.5 ##		68.9 ##		100.0		50.0	
Erythromycin	ND		81.8		100.0		68.9		100.0		50.0	
Fusidic acid	91.2		90.5		93.9		100.0		66.7		100.0	
TMP-SXZ	94.3		100.0		95.8		97.8		100.0		100.0	
Gentamicin	91.4		77.3		75.0		70.5		66.7		25.0	
Vancomycin	100.0		100.0		100.0		100.0		100.0		100.0	
Rifampicin	100.0		100.0		96.0		97.8		100.0		100.0	
Fluoroquinolones	88.6		81.8		79.2		66.7		66.7		50.0	

Values are % of susceptible strains.

* $P < 0.000$, ** $P = 0.009$, ^ $P = 0.01$, ^^ $P = 0.03$, ~ $P = 0.04$, ~~ $P = 0.05$, #$P = 0.005$, ## $P = 0.006$.

ND = not done, ESBL = extended spectrum beta-lactamase.

Carbapenems = imipenem and meropenem, Fluoroquinolones = ciprofloxacin and ofloxacin.

- ***P. aeruginosa:*** We found a non-significant decrease in susceptibility to most antimicrobials (except for piperacillin and carbapenems) [Table 3].
- ***S. aureus:*** The frequency of *S. aureus* isolates decreased between 2001–2 and 2005–6, while the methicillin-resistant *Staphylococcus aureus* rate among all *S. aureus* isolates showed a non-significant increase (CB 11.4% to 27.2%, HB 24.0% to 33.3%, and LTCF-B 40% to 50%; 2001–2 vs. 2005–6 respectively) [Table 2].

Decreasing susceptibility was noted to most antimicrobials except for TMP-SXZ, vancomycin and rifampicin in all the settings and fusidic acid in HB and LTCF-B (2001–2 vs. 2005–6 respectively) [Table 3].

- ***Enterococcus* sp:** Most isolates were susceptible to penicillin and ampicillin; only two vancomycin-resistant *Enterococcus* strains were identified in HB in the second period (2005–6, data not shown).
- ***Acinetobacter baumanii:*** Only five blood cultures grew *A. baumanii* in the community setting, and none from LTCF. The susceptibility of hospital-acquired *A. baumanii* (13 and 20 isolates 2001–2 vs. 2005–6) to antimicrobials showed a non-significant increase: gentamicin 23.1% to 30.0%, amikacin 38.5% to 40.0%, piperacillin-tazobactam 20.0% to 26.3%, fluoroquinolones 27.3% to 30%, and carbapenems 54.5% to 60.0% (2001–2 vs. 2005–6 respectively).

SUSCEPTIBILITY TO QUINOLONES

We observed a statistically non-significant trend in the progressive increase of resistance to quinolones among non-ESBL *Klebsiella* sp., other gram-negative bacilli, *P. aeruginosa* and *S. aureus* in CB and HB, and among non-ESBL *E. coli* in LTCF-B [Table 3]. No fluoroquinolone-only resistant *E. coli* strains were isolated during the study period.

SUSCEPTIBILITY TO AMINOGLYCOSIDES

Gentamicin remained highly effective (≥ 90% sensitivity) against non-ESBL *E. coli* and *Klebsiella* sp. and other gram-negative rods in CB and LCTF-B, and against non-ESBL *Klebsiella* sp. in HB. Amikacin showed higher susceptibility rates (≥ 95%) against non-ESBL *E. coli* and *Klebsiella* sp. and other gram-negative rods in all settings (2005–6).

Finally, our findings showed that most isolates were highly sensitive to carbapenems, and KPC-type carbapenemases were not detected until the end of 2006.

DISCUSSION

In the present study we evaluated 1546 episodes of bacteremia during two study periods (2001–2 and 2005–6) in a community hospital. Three settings were evaluated and compared during each period: community bacteremia, hospital bacteremia and long-term care facility bacteremia. As expected, isolates from CB were, in general, more susceptible to antimicrobial agents than from HB [4].

A mild increase in mortality rate in HB (21.0% to 25.2%, borderline significance) was observed, probably related to co-morbidities and severity of disease. The urinary tract remained the main source of bacteremia, and *E. coli* persisted as the main pathogen isolated [1,5] during the study except for HB in the first period, when a mild predominance of *S. aureus* was detected (sporadic outbreak). Not surprisingly, primary and catheter-related bacteremias were sources of considerable importance in HB in our study [6].

In our hospital, gram-negative rods (~60%) remained a more frequent cause of bacteremia than gram-positive cocci (~29%), in contrast to the constant increase in gram-positive cocci among bacteremic isolates reported worldwide [7-9]. These differences are probably due to the characteristics of our hospital – being peripheral, community oriented, and lacking tertiary complexity (no neurocardiac surgery or hemato-oncology unit) – which are usually the cause of increasing predominance of gram-positive organisms.

Another interesting finding was the increase in susceptibility to TMP-SXZ observed among *Klebsiella* sp. isolates (HB) (15.4% vs. 57.1%, not significant); however, because *E. coli* susceptibility to TMP-SXZ remained less than 75% (in all settings), this agent is still under the level of susceptibility that allows its use as empiric treatment for suspected gram-negative infection [10].

Among non-ESBL *E. coli* a significant decrease was seen in the susceptibility rate for cephalotin (LTCF-B), amoxiclavulanate and piperacillin (CB and HB) and piperacillin-tazobactam (only in HB). The last finding is worrisome but not unexpected [7], raising doubt about the efficacy of piperacillin-tazobactam in the empiric treatment of hospital-acquired gram-negative bacteremia, even in patients without risk factors for ESBL producer strains [11].

In contrast, a more positive finding was the decrease in the resistance rates of non-ESBL *Klebsiella* sp. to second and third-generation cephalosporines and aztreonam in CB and HB in the second period.

ESBL-producing *E. coli and Klebsiella* sp. are now relatively common in health care settings and in the community as well [1,4,12,13]. We found a reduction in the prevalence of ESBL-producing *E. coli and Klebsiella* sp, with lower rates than previously reported in Israel [11].

The use of antimicrobials in general and broad-spectrum agents in particular is under strict supervision in our hospital. A detailed antibiotic formulary according to local protocols is part of our infection control policy and was applied without any changes during the entire study period. In addition, the use of ceftazidime (a strong ESBL inducer) is very limited; this fact may be one of the reasons for the low ESBL rates observed. On the other hand, we noted a statistically non-sig-

nificant trend of progressive resistance to quinolones among non-ESBL *Klebsiella* sp., other gram-negative rods and *P. aeruginosa* in CB and HB, and among non-ESBL *E. coli* and other gram-negative rods in LTCF-B. Similar findings were previously published [2,4,5,14,15]; but together these findings probably favor the empiric use of second and third-generation cephalosporines rather than quinolones in suspected gram-negative bacteremia in our study population, except in those cases where *P. aeruginosa* is suspected or the patient has risk factors for ESBL-producing Enterobacteriaceae [2,11-13].

In this study, we provided a comprehensive description and detailed analysis of all episodes of bacteremia occurring in two 2 year periods in our institution. The results, however, should be interpreted in the context of several limitations. First, we did not evaluate co-morbidities and severity of disease at admission, thus we cannot explain the increase in mortality in HB (2005–6). The second limitation was the lack of data on LTCF-B patients as a separate group when hospitalized, and the heterogeneity of these nursing home institutions in terms of number of beds, type of patients, policies of treatment and referral to hospital. Third, the fact that our hospital is located in a peripheral area of Israel and its lack of high complexity wards renders our findings as not representative of the situation in the whole country.

According to our data, we conclude that in our region gram-negative bacteria are the most prevalent isolate in blood cultures. It is noteworthy that the overall rate of resistant isolates (MRSA, ESBL-producing Enterobacteriaceae, vancomycin-resistant enterococcus) was relatively low and stable over the study period. Moreover, second and third-generation cephalosporins are still highly effective against non-ESBL *E. coli, Klebsiella* sp. and other gram-negative rods, in all settings, even more today than 6 years ago. In contrast, amoxycillin-clavulanate and piperacillin (both in CB and HB), and piperacillin-tazobactam (only in HB) emerged as a less attractive empiric choice for the treatment of *E. coli* infection. We are concerned about the increasing resistance to quinolones, even if at this time it did not achieve statistical significance. If the prevalence of resistant organisms will continue to rise as predicted, empiric antibiotic treatment would result in increased therapeutic failure and higher mortality, even in patients admitted from the community [12].

Antimicrobial susceptibility surveillance studies play a pivotal role in the fight to control resistant organisms [3]. Ongoing surveillance of the local epidemiology and antimicrobial resistance is indispensable for empirically treating infections, implementing resistance control measures and preventing the spread of antimicrobial-resistant microorganisms [4].

MRSA = multidrug-resistant *Staphylococcus aureus*

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"It takes two to speak the truth – one to speak, another to hear"

Henry Thoreau (1817-1862), American author, poet, naturalist, tax resister, development critic, surveyor, historian, philosopher, and leading transcendentalist.