Hospital-acquired infections due to multidrug-resistant organisms in Hungary, 2005-2010

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Healthcare-associated infections caused by multidrug-resistant organisms are associated with prolonged medical care, worse outcome and costly therapies. In Hungary, hospital-acquired infections (HAIs) due to epidemiologically important multidrug-resistant organisms are notifiable by law since 2004. Overall, 6,845 case-patients (59.8% men; median age: 65 years) were notified in Hungary from 2005 to 2010. One third of case-patients died in hospital. The overall incidence of infections increased from 5.4 in 2005 to 14.7 per 100,000 patient-days in 2010. Meticillin-resistant *Staphylococcus aureus* (MRSA) was the most frequently reported pathogen (52.2%), but while its incidence seemed to stabilise after 2007, notifications of multidrug-resistant Gram-negative organisms have significantly increased from 2005 to 2010. Surgical wound and bloodstream were the most frequently reported sites of infection. Although MRSA incidence has seemingly reached a plateau in recent years, actions aiming at reducing the burden of HAIs with special focus on Gram-negative multidrug-resistant organisms are needed in Hungary. Continuing promotion of antimicrobial stewardship, infection control methodologies, reinforced HAI surveillance among healthcare and infection control practitioners, and engagement of stakeholders, hospital managers and public health authorities to facilitate the implementation of existing guidelines and protocols are essential.

Introduction

Healthcare-associated infections are infections arising from any aspect of healthcare management, most commonly during hospitalisation in acute care facilities (hospital-acquired infections, HAI) where the patient receives treatment for another medical or surgical condition. These infections are a significant cause of morbidity and mortality worldwide, primarily among immunocompromised and elderly people, especially if the causative organism has developed resistance to a number of antimicrobial agents. Patients infected with multidrug-resistant organisms usually have a significantly longer hospital stay, are more likely to be in need of intensive care, costly therapies and treatments, and have a worse prognosis [1]. While the burden of HAIs due to multidrug-resistant organisms may vary widely according to geographical region, healthcare setting, type of pathogen and antimicrobial substance, its relevance to patient safety and public health continues to increase both nationally and internationally. Therefore surveillance of HAIs caused by multidrug-resistant organisms, epidemiological, microbiological or both, has been established in most industrialised countries [2-6], and the need for a global approach has been recognised [7].

Data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) are worrisome. The proportion of strains of major pathogens isolated from blood or cerebrospinal fluid (CSF) with resistance to important antimicrobial agents exceeds 10% or even 25% in several countries, with the highest figures seen in southern and eastern Europe [8,9]. Recently, national efforts in infection control in the European Union (EU) have led in some countries to a plateau or even a reversal of the trend of increasing resistance to antimicrobial agents, for example for meticillin-resistant *Staphylococcus aureus* (MRSA), penicillin- and/or macrolide-resistant *Streptococcus pneumoniae* and aminoglycoside-resistant *Enterococci*; however, increasing trends are still being observed for multidrug-resistant *Escherichia coli* and *Klebsiella pneumoniae* [9].

Carbapenems are currently considered as last-line antibiotics for the treatment of many infections caused by certain multidrug-resistant organisms. In particular, carbapenem resistance among Gram-negative microorganisms such as *K. pneumoniae* [9,10], *Pseudomonas aeruginosa* [9] and *Acinetobacter baumannii* [11] has recently increased in Europe.

In Hungary (population ca. 10 million), HAIs due to epidemiologically important multidrug-resistant organisms are notifiable by law through the national surveillance system for nosocomial infections (Nemzeti Nosocomiális Surveillance Rendszer, NNSR) which was established in October 2004. Reporting is mandatory for all hospitals. We aimed at describing the patient population and infections due to multidrug-resistant

organisms reported to the relevant surveillance module of the NNSR, and assessing the epidemiological trends during the period from 2005 to 2010 and the recent situation of reported HAIs caused by multidrug-resistant organisms in Hungary.

Methods

Data source and reporting method

The NNSR, operated by the National Center for Epidemiology in Budapest, Hungary, is a national surveillance network and a database of nosocomial infections. Data on incident cases are collected, using surveillance methodology and HAI case definitions of the United States Centers for Disease Control and Prevention (US CDC) [12]. As of December 2010, the NNSR consisted of three compulsory modules (nosocomial outbreaks, HAI caused by multidrug-resistant

organisms/*Clostridium difficile*, and nosocomial bloodstream infections), four voluntary modules (surgical site infections, intensive care unit- and perinatal intensive care unit-based surveillance, device-associated infections) and a disinfectant database [13]. Reporting of the compulsory elements is continuous.

The relevant surveillance module of the NNSR contains records from patients with HAI caused by a given multidrug-resistant organism at one or more anatomical sites, acquired during a given hospital stay. HAI is defined as a localised or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s), with no evidence that the infection was present or incubating at the time of admission [12].

HAIs caused by the following multidrug-resistant organisms were included in the period studied: meticillin-resistant *S. aureus* (MRSA), vancomycin-resistant *Enterococcus* sp. (VRE), multidrug-resistant *Enterobacter* sp., multidrug-resistant *Escherichia coli*, multidrug-resistant *Klebsiella* sp., multidrug-resistant *A. baumannii*, multidrug-resistant *P. aeruginosa*, co-trimoxazole-resistant *Stenotrophomonas maltophilia*, and intermediate vancomycin-resistant *S. aureus* (VISA). The pathogens and key antibiotics to which resistance was monitored were selected through national expert consultations (Table 1). Throughout the period studied, resistance thresholds defined by the Clinical and Laboratory Standards Institute (CLSI) were used in laboratories in Hungary [14-19].

Variables required included information on patients' demographics (age, sex), lifestyle characteristics (smoking, alcohol consumption, drug abuse), medical history (concomitant diseases, recent surgeries), hospital stay (hospital ward, diagnosis upon admission, therapies or medical procedures applied as well as use of catheters before the recognition of HAI), outcome at discharge (recovered, transferred to another hospital, deceased), and healthcare-associated infection caused by a multidrug-resistant organism (pathogen, type of infection, date of microbiological confirmation). Data on admission diagnosis, concomitant diseases and lifestyle characteristics were gathered from International Classification of Diseases (ICD-10) diagnosis codes documented in the medical records. Case-based data were entered in the internet-based surveillance tool by infection control (IC) nurses and, if available, approved by IC doctors when the patient affected was discharged from the hospital or dies. No post-discharge data are collected.

Study design and study population

We conducted a descriptive study including all notified cases of HAI due to multidrug-resistant organisms in Hungary until 2010. We defined a case-patient as a patient who was infected with one or more multidrug-resistant organisms at one or more anatomical sites during a given hospital stay. Data from 2004 were

Table 1

Pathogens included in the module for hospital-acquired infections due to multidrug-resistant organisms of the national surveillance system for nosocomial infections in Hungary, 2005–10

Microorganism	Antibiotic resistance
Staphylococcus aureus (MRSA)	Meticillin/oxacillin
Klebsiella sp.	Third generation cephalosporins for ESBL-production, imipenem and/or meropenem
Acinetobacter baumannii	Imipenem and/or meropenem
Escherichia coli	Third generation cephalosporins for ESBL-production, imipenem and/or meropenem
Pseudomonas aeruginosa	Sensitive to maximum two of the following agents: piperacillin/tazobactam, ceftazidin, cefepim, imipenem, meropenem, ciprofloxacin, gentamicin, tobramycin, amikacin, aztreonam
Enterobacter sp.	Third generation cephalosporins for ESBL-production, imipenem and/or meropenem
Stenotrophomonas maltophilia	Cotrimaxazol (sumetrolim)
Staphylococcus aureus (VISA)[a]	Intermediate sensitivity to vancomycin
Enterococcus sp. (VRE)	Vancomycin

ESBL: extended spectrum beta-lactamase; MRSA: meticillin-resistant *Staphylococcus aureus*; VISA: intermediate vancomycin-resistant *S. aureus*; VRE: vancomycin-resistant *Enterococcus* sp.

[a] VISA was added to the surveillance module in 2008.

discarded because the surveillance system was established and launched in that year, and the reported data are incomplete. Furthermore we excluded case-patients for whom date of admission, date of discharge or microbiological tests were not available.

Descriptive and analytical methods

We estimated the yearly coverage of the surveillance system by means of three indicators: proportion of all hospitals included in the system (hospitals notifying at least one multidrug-resistant organism/all hospitals in Hungary), proportion of hospitalisations (hospitalisation in the notifying hospitals/hospitalisations in all hospitals in Hungary), and proportion of patient-days (patient-days in the notifying hospitals/patient-days in all hospitals in Hungary).

We described HAI case-patients in terms of the following variables: sex, age at admission, lifestyle characteristics, underlying medical conditions, type of healthcare institution, hospital ward, medical procedures and devices applies, outcome, type of infection and type of multidrug-resistant organism.

We classified healthcare institutions into five categories: primary (typically city hospitals with essential medical specialties), secondary (typically county hospitals and large hospitals in the capital city with highly differentiated clinical functions), tertiary (central referral hospitals and university clinics with highly differentiated clinical functions, specialised staff and technical equipment), specialised hospitals (single clinical specialty, possibly with sub-specialties) as well as chronic care/rehabilitation hospitals.

Distributions of categorical variables between patient groups (e.g. case-patients with versus those without prior operation) were compared using the chi-square test. A p-value of 0.05 was considered to be statistically significant. For continuous variables, interquartile ranges (IQR) were calculated.

Annual incidence densities of reported HAIs were calculated as: (number of HAIs notified to NNSR during a given year) / (patient-days from all hospitals notifying at least one HAI that year) x 100,000. Incidence densities were calculated overall and stratified by multidrug-resistant organism. Denominator data were retrieved from official annual reports on hospital beds and patient turnover issued by the National Health Insurance Fund in Hungary [20].

The analyses were performed using Stata v10 (StataCorp LP).

Results

Reporting hospitals

The proportion of hospitals that reported at least one patient with HAI due to a multidrug-resistant organism to the NNSR gradually increased from 27.8% (50

Table 2

Selected characteristics[a] of patients with reported hospital-acquired infection due to multidrug-resistant organism in Hungary, 2005–10 (n=6,845)

Patient characteristics	Number	Proportion of study population (%)
Sex		
Male case-patients	4,095	59.8
Female case-patients	2,750	40.2
Age group (age at admission)		
0–10 years	211	3.1
11–20 years	93	1.4
21–30 years	189	2.8
31–40 years	291	4.2
41–50 years	556	8.1
51–60 years	1,315	19.2
61–70 years	1,614	23.6
71–80 years	1,715	25.1
81–90 years	807	11.8
91–100 years	54	0.8
Lifestyle characteristics		
Smoking	597	8.7
Alcohol abuse	538	7.9
Concomitant diseases		
Cardiovascular disease	3,015	44.0
Chronic respiratory disease	1,072	15.7
Cancer	970	14.2
Chronic kidney disease	545	8.0

[a] Based on relevance and frequency.

of 180) in 2005 to 43.6% (75 of 172) in 2010. In 2005, reporting hospitals received 64.0% of hospitalisations and accounted for 58.5% of patient-days in Hungary, while in 2010 the corresponding figures were 87.8% and 78.7%.

Patient population

Overall, 8,673 case-patients were reported between 2004 and 2010. After applying exclusion criteria, 6,845 case-patients (59.8% men; median age at admission: 65 years, range: 1–98 years) were included in the analysis as study population (Table 2). The most frequently reported concomitant diseases were cardiovascular (44.0%) and chronic respiratory diseases (15.7%). The number of reported case-patients increased from 590 in 2005 to 1,807 in 2010. The median length of hospital stay was 25 days (IQR: 14–42 days) in the study population. The proportion of case-patients infected with more than one multidrug-resistant organism during the same hospital stay was around 18% each year; the median length of their hospital stay was 39 days

Table 3

Characteristics of hospital stay of case-patients with reported hospital-acquired infection due to multidrug-resistant organism in Hungary, 2005–10 (n=6,845)

Characteristics of hospital stay	Number	Proportion of study population (%)
Ward at admission		
Surgical ward	2,523	36.9
Intensive care unit	2,082	30.4
Medical ward	1,754	25.6
Rehabilitation ward	256	3.7
Obstetrics and gynaecology ward	47	0.7
Paediatrics ward	41	0.6
Psychiatry ward	39	0.6
Other/mixed	38	0.6
Missing	65	1.0
Medical interventions and devices		
Prior surgical intervention	3,762	55.0
Urinary catheter	3,888	56.8
Peripheral catheter	3,711	54.2
Central venous catheter	2,706	39.5
Endotracheal tube	2,029	29.6
Parenteral nutrition	1,671	24.4
Tracheostomy	1,007	14.7
Gastrostomy	150	2.2
External ventricular drain	143	2.1

(IQR: 24–61 days). The median number of days elapsed between date of admission and date of first microbiological confirmation of an HAI due to a multidrug-resistant organism was 12 (IQR: 6–21 days).

The number of case-patients notified by primary, secondary, tertiary, specialised and chronic care/rehabilitation hospitals was 1,163 (17.0%), 3,099 (45.3%), 2,433 (35.5%), 104 (1.5%) and 46 (0.7%), respectively. Fourteen hospitals accounted for more than half (3,560 of 6,845) of all reported case-patients. Almost one third of all case-patients (1,950 of 6,845) were reported from hospitals located in the capital city, Budapest.

In Table 3, data on hospital stay (ward at admission, medical procedures and devices applied) are reported. Among surgical specialties, the most frequently reported wards were general surgery (40.7%), traumatology (24.7%) and urology (11.5%), and among medical specialties general internal medicine (46.8%), haematology-oncology (12.1%) and infectious diseases (9.7%). Fifty-five per cent of case-patients underwent prior surgical intervention, most commonly gastro-intestinal and liver surgery (24.4%, excluding transplantations), orthopedic surgery (19.0%), neurosurgery (5.1%) and head and neck surgery (4.6%).

Case-patients with prior surgery had a lower prevalence of cardiovascular disease (41% versus 47%, p<0.001), chronic respiratory disease (11% versus 21%, p<0.001) and chronic kidney disease (5% versus 11%, p<0.001) compared to those without. No difference was found in age and sex distribution between the two groups. Among case-patients who underwent prior surgery the most common types of HAI were 54.6% surgical site infection (SSI), 9.7% bloodstream infection and 9.6% urinary tract infection (UTI). The most frequent types of infection among those without prior surgery were bloodstream infection (21.9%), UTI (17.2%) and pneumonia (13.9%).

Information on the outcome during the current hospital stay was available for 6,388 case-patients (93.3%). Of them, 2,772 (43.4%) recovered, 1,470 (23.0%) were transferred to another hospital, and 2,146 (33.6%) died. Patients infected with multidrug-resistant *P. aeruginosa* and *A. baumannii* had the highest case-fatality (43.8% and 40.2%, respectively); case fatality for MRSA infection was 32.6%. Patients infected with more than one multidrug-resistant organism had a case-fatality of 48.7%. Among all deaths, according to the reports, 14.2% were related directly or indirectly to the HAI.

Reported hospital-acquired infections

Of the 6,845 case-patients, 5,482 (80.1%) were infected with one multidrug-resistant organism at one anatomical site, 1,094 (16.0%) with one multidrug-resistant organism at more than one anatomical site, 129 (1.9%) with more than one multidrug-resistant organism at one anatomical site, and 140 (2.0%) with more than one multidrug-resistant organism at more than one anatomical site. The overall number of individual HAIs reported was 8,732. The overall incidence of HAI due to multidrug-resistant organisms increased from 5.4 in 2005 to 14.7 per 100,000 patient-days in 2010. The overall yearly incidence (per 100,000 patient-days) of HAI in primary, secondary, tertiary, specialised and chronic care/rehabilitation hospitals was 9.4, 9.1, 11.2, 7.5 and 3.2, respectively.

MRSA was the most frequent single cause of HAI during the study period (n=4,477, 52.2%), but while MRSA numbers stabilised after 2007 (annual notifications were 471 in 2005, 826 in 2007 and 824 in 2010), notifications of all the other multidrug-resistant organisms kept increasing during 2005 to 2010 from 247 to 1,468. As a result, MRSA represented 65.6% and 36.0% of all HAIs in 2005 and 2010, respectively. Incidence rates of reported HAIs by type of multidrug-resistant organism (excluding vancomycin-resistant *Enterococcus* sp., co-trimoxazole-resistant *S. maltophilia* and intermediate vancomycin-resistant *S. aureus*, which never exceeded an annual incidence rate of 0.1 per 100,000 patient-days in any given year) are shown in Figure 1.

SSI and bloodstream infection were the two most frequently reported sites during the whole study period;

Annual incidence rates of reported hospital-acquired infections due to multidrug-resistant organisms in Hungary, 2005–10 (n=8,732)
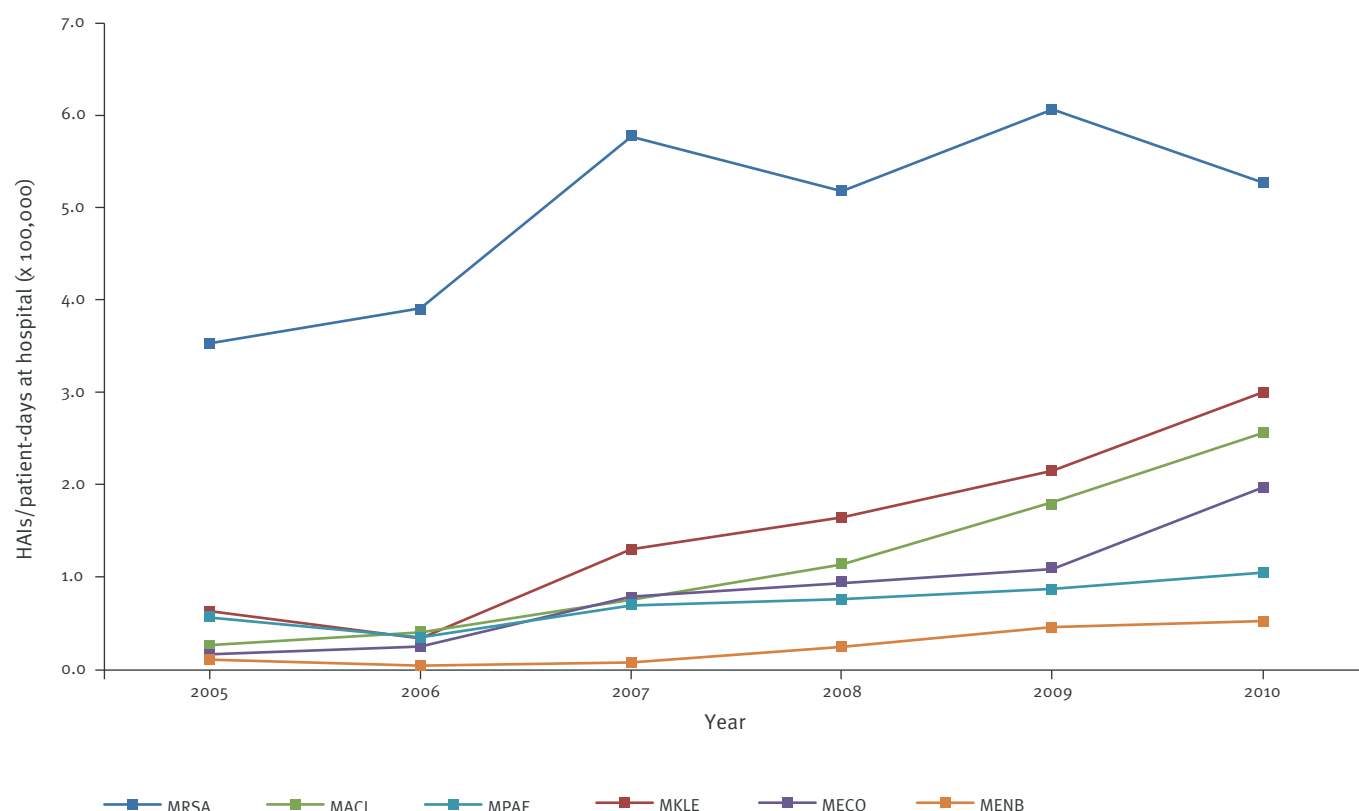
HAI: healthcare-associated infection; MACI: multidrug-resistant *Acinetobacter baumannii*; MECO: multidrug-resistant *Escherichia coli*; MENB: multidrug-resistant *Enterobacter* sp.; MKLE: multidrug-resistant *Klebsiella* sp; MPAE: multidrug-resistant *Pseudomonas aeruginosa*; MRSA: methicillin-resistant *Staphylococcus aureus*.

yet their proportion among all reported HAIs due to multidrug-resistant organisms decreased from 31.9% to 25.1% and from 25.9% to 21.7%, respectively, from 2005 to 2010. The proportion of reported urinary tract infections increased from 7.7% in 2005 to 19.3% in 2010.

Considerable differences were found in the distribution of the type of infections by multidrug-resistant organism (Figure 2). MRSA was the most frequently reported multidrug-resistant organism for all sites of infection in 2010 except for urinary tract and lower respiratory tract (Figure 3). However, the proportion of MRSA as cause of HAI decreased at each site of infection between 2005 and 2010, while an increase was seen in the proportion of multidrug-resistant *A. baumannii* (at all infection sites, except for urinary tract), *E. coli* (particularly bloodstream and urinary tract infections) and *Klebsiella* sp. (particularly surgical site and soft tissue infections).

Discussion

The coverage of Hungarian hospitals by the NNSR has constantly grown over the years. Although less than half of all hospitals notified at least one infection due to multidrug-resistant organisms in 2010, these healthcare institutions accounted for the vast majority of hospitalisations and patient-days in the country during that year. Efforts to further expand the coverage of the surveillance system should focus on those hospitals not currently reporting: mainly smaller facilities and chronic care hospitals.

The proportion of reports sent by primary, specialised and chronic care/rehabilitation hospitals was lower than their relative proportion of overall number of acute and chronic beds in Hungary. The opposite was observed for tertiary-level hospitals, while no difference was found for secondary-level hospitals. Varying compliance with reporting, case-mix of patients and presence or absence of high-risk specialties are the most plausible explanations for these differences.

Most frequent types of reported hospital-acquired infections due to multidrug-resistant organisms in Hungary in 2010 (n=2,252)
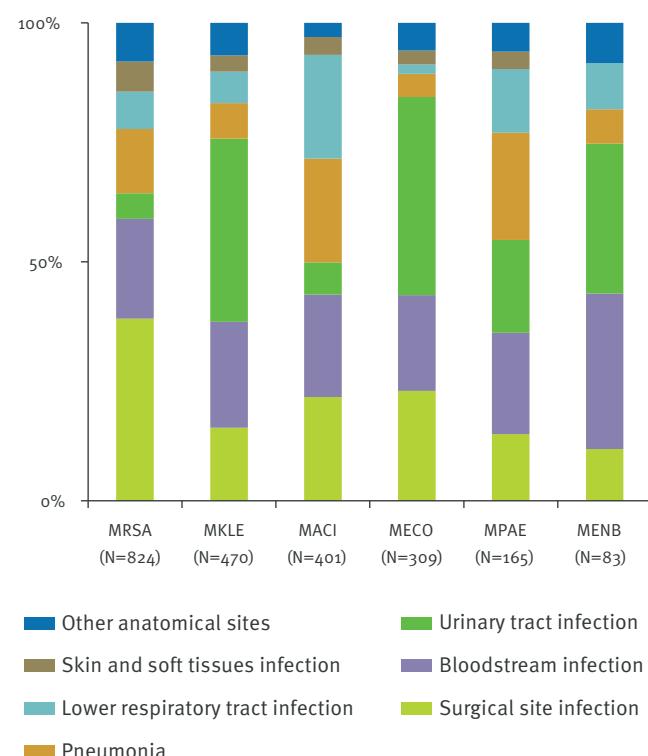
MACI: multidrug-resistant *Acinetobacter baumannii*; MECO: multidrug-resistant *Escherichia coli*; MENB: multidrug-resistant *Enterobacter* sp.; MKLE: multidrug-resistant *Klebsiella* sp; MPAE: multidrug-resistant *Pseudomonas aeruginosa*; MRSA: meticillin-resistant *Staphylococcus aureus*.

Surgical departments were the most frequent hospital wards concerned, and further investigations are needed to disentangle the possible impact of parallel surveillance activities linked to the SSI module of the NNSR, and specific issues in perioperative care. ICUs were the second in line which is likely due to the presence of high-risk patients, better patient monitoring, including higher frequency of sampling and more timely microbiological diagnosis. Similarly, an influence of the dedicated ICU surveillance module cannot be excluded. A more in-depth description should assess differences by region, individual hospitals and ward types.

The population of case-patients affected by HAI due to multidrug-resistant organisms was characterised by old age at admission, a high prevalence of comorbidities, and a large proportion of prior surgical interventions and indwelling medical devices. All these

are known risk factors for developing an HAI, either by impairing the immune system or by facilitating the entry of a multidrug-resistant organism through a medical procedure [21].

One third of the case-patients died during their hospitalisation. This figure is probably biased downwards considering that no information on final outcome is available for patients who were transferred to another hospital. According to the notification data, 14.2% of deaths could directly be ascribed to the HAI; however, no definition of HAI-related death exists in the NNSR to which reporting personnel must adhere.

MRSA was the most frequent cause of HAI at most anatomical sites except for UTIs and lower respiratory tract infections (LRTIs), exceeding 50% of all reported HAIs at surgical site as well as skin and soft tissues. Multidrug-resistant *A. baumannii* was the most frequent cause of LRTI, probably linked to ventilation and oral care practices. Extended-spectrum beta-lactamase (ESBL)-producing bacteria are increasingly causing UTI in inpatients and outpatients worldwide [22]. Also in Hungary, the proportion of reported UTIs due to multidrug-resistant organisms more than doubled over the study period; multidrug-resistant *K. pneumoniae* and multidrug-resistant *E. coli* accounted for approximately 70% of reports. This is most likely due to both the increased occurrence, spread and microbiological diagnoses of these pathogens. Improved awareness can also be a contributing factor since the issue has been extensively discussed at infection control meetings in Hungary since 2009, and a recommendation on the prevention of catheter-associated urinary tract infections was published in the same year.

The overall incidence of reported HAIs due to multidrug-resistant organisms in Hungary has shown a significant increase in recent years, but different tendencies are seen for Gram-positive and Gram-negative pathogens. Concerning Gram-positive pathogens, the incidence of MRSA infections has lately reached a plateau in some European countries [23] and in the United States [24]. Similarly in Hungary, MRSA incidence seemed to have stabilised around six infections per 100,000 patient-days over the last four years of the study period, when the reporting system was already established in major hospitals. In other words, at the beginning of surveillance, the continuously improving reporting of MRSA infections could have been the reason for the increase in observed incidence. After this initial period, we assume that the observed incidence approached the true incidence which has remained stable since then. Nonetheless, this figure is lower than those reported by most other European [3,25-27] and non-European countries [23,28,29]. For instance, the incidence of hospital-onset MRSA in Germany was 23 per 100,000 patient-days in 2009, approximately four times higher than the Hungarian result [3]. In Canada [28], the figure was 34.3 per 100,000 patient-days in 2007, around six times higher than in Hungary. The

Most frequently reported multidrug-resistant organisms by type of hospital-acquired infection in Hungary in 2010 (n=2,143)
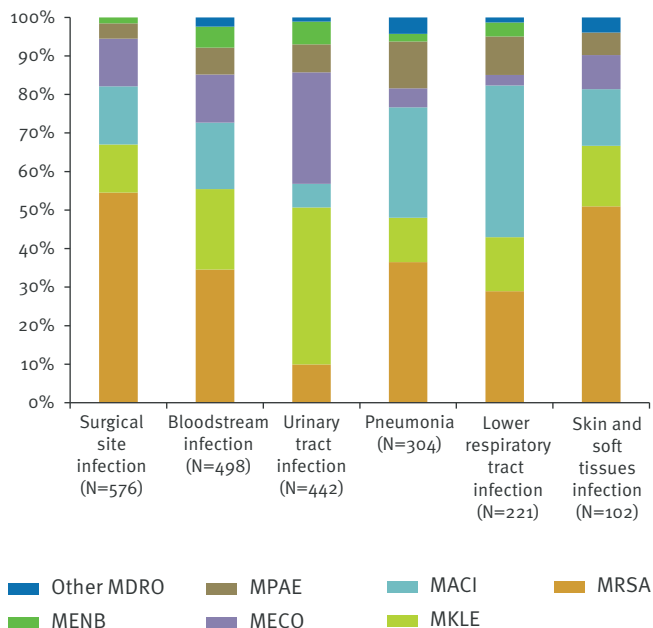
MACI: multidrug-resistant *Acinetobacter baumannii*; MECO: multidrug-resistant *Escherichia coli*; MENB: multidrug-resistant *Enterobacter* sp.; MKLE: multidrug-resistant *Klebsiella* sp; MPAE: multidrug-resistant *Pseudomonas aeruginosa*; MRSA: meticillin-resistant *Staphylococcus aureus*.

number of reported cases per 100,000 population in 2010 was 8.8 in Norway [27] and 16.8 and Sweden [26], to be compared with a value of 8.24 in Hungary. How much this is due to underreporting or true differences in incidence is hard to establish; differences in the frequency of microbiological sampling, availability of microbiological services, structure of surveillance systems and general compliance with reporting may also play an important role.

Prevention and control of infections caused by meticillin/oxacillin resistant *S. aureus* has been facilitated by a national guidance available in Hungary since 2001. Due to improved knowledge over time, not only infection control practitioners, but also healthcare workers have become familiar with necessary actions to be taken in case of MRSA in hospitals. Nonetheless it serves as a warning that the proportion of *S. aureus* resistant to meticillin isolated from blood is currently around 30% in Hungary, with a significant increase seen between 2007 and 2010 [9].

In contrast to the incidence pattern of Gram-positive MRSA, the incidence of infections caused by

multidrug-resistant Gram-negative organisms has continuously increased since the establishment of NNSR. The magnitude of this increase is striking (the ratio of incidences in 2010 versus 2005 is 11 for multidrug-resistant *E. coli*, 9 for multidrug-resistant *A. baumannii*, 6 for co-trimoxazole-resistant *S. maltophilia*, 5 for multidrug-resistant *Enterobacter* sp. and 5 for multidrug-resistant *Klebsiella* sp.), similarly to what has been observed in the EU [9] and also countries outside the EU [30-33] in the same time period. Therefore there appears to be a true increase in their incidence in Hungary, whereas the impact of improved reporting due to better awareness of the problem may obviously play a role, too. Recent surveillance results show that incidences of most multidrug-resistant organisms in 2011 are comparable to their respective values observed in 2010, except for multidrug-resistant *A. baumannii*, whose incidence further increased.

While extensive or inappropriate antimicrobial use may be the key factor in the striking emergence of multidrug-resistant Gram-negative organisms, their current successful spread, compared to MRSA, could also be attributed to particular microbiological characteristics (e.g. a successful decolonisation strategy is not available) and more efficient survival strategies through dissemination of acquired mechanisms of antibiotic resistance. Interestingly, Hungary is in the lower third of European countries regarding the quantity of outpatient antimicrobial consumption and had the lowest hospital use of antimicrobials for systemic use in 2009, nevertheless quality indicators of antibiotic use suggest issues need to be addressed both in ambulatory and hospital care [34-36]. We hypothesise that limited collecting of appropriate and early microbiological samples before initiating empiric antibiotic therapy, and therefore limited streamlining of antibiotic treatment based on culture results, may be the most relevant problem areas in practice.

A comprehensive evaluation of the National Nosocomial Surveillance System is planned in 2013 to assess its impact on the prevention and control of HAI in Hungary. At national level, surveillance results formed the basis for a decree issued by the Ministry of Health in 2009 (extended in its scope in 2012) on the prevention and control of HAI, surveillance of antimicrobial consumption and professional minimum requirements [37]. Governmental bodies and institutions with public health function were involved in the organisation of national campaigns linked to the European Antibiotic Awareness Day targeting both professionals and the public. National recommendations have already been issued for MRSA, VISA, ESBL-producing Gram-negative pathogens, VRE, and carbapenemase-producing *Enterobacteriaceae* [38-44]. However, partially as a reaction to the current epidemiological trends, a new comprehensive recommendation on prevention of infections caused by Gram-positive and emerging Gram-negative multidrug-resistant pathogens is being developed.

While national actions are essential, prevention efforts will have the desired effect only if existing guidelines and protocols are effectively and efficiently implemented in hospitals and followed in routine practice, tailored to the situation described by local surveillance results. Measures implemented at hospital level over the years also have to be reviewed and evaluated. Additional financial resources are needed for hospitals to be able to meet all legal requirements and provide continuous training for their personnel. Promotion of microbiological diagnosis would also be highly relevant. A number of obstacles should be addressed, for example healthcare reimbursement through diagnosis-related groups without separate budget for diagnostics and treatment, which may currently act as a disincentive to taking samples for microbiological tests.

In summary, our results highlight that, in addition to the efforts made until now, further actions are needed in Hungary, both at locally and nationally to reduce the burden of HAIs due to multidrug-resistant organisms.

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