Multidrug-resistant bacteria in travellers hospitalized abroad: prevalence, characteristics, and influence on clinical outcome☆

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ARTICLE INFO

SUMMARY

Background: Worldwide, the burden of multidrug-resistant bacteria (MDR) is increasing, especially in the hospital setting.

Aim: To explore characteristics and clinical relevance of MDR obtained from travellers transferred from hospitals abroad.

Methods: This retrospective study included patients transferred from hospitals abroad to the University Hospital Zurich, Switzerland, who routinely underwent admission screening for possible colonization with meticillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase-producing bacteria (ESBL) and multidrug-resistant Gram-negative bacteria (MR Gram negative).

Findings: Forty-six (17%) of 259 subjects were found to be colonized with MDR and nine (3.5%) patients to be infected. Thirty-three (12%) patients were colonized with one bacterial species, 12 (4.6%) with two, and three (1.2%) were colonized with three different bacterial species. In total, 36 ESBL, 21 MR Gram-negative and three MRSA isolates were detected. *Escherichia coli* ($N = 18$, 30%), *Klebsiella pneumoniae* ($N = 14$, 23%) and *Acinetobacter baumannii* ($N = 14$, 23%) were most frequently isolated. The most common sites of detection were skin (97%) and respiratory tract (41%). Being colonized contributed to an increased length of ICU stay [median (range): 8 (1—35) vs 3.5 (1—78) days; $P = 0.011$]. In-hospital mortality in patients colonized with MDR (10.9%) was higher than in uncolonized patients (2.3%, $P = 0.018$). Being colonized with MDR was associated with death (adjusted odds ratio: 5.176; 95% confidence interval: 1.325—20.218).

Conclusions: A substantial proportion of patients transferred from abroad are colonized with MDR, a fact which is associated with poor clinical outcome.

Introduction

Multidrug-resistant bacteria (MDR) are globally on the rise, albeit with strong regional differences. For example, extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* are detected in 79% of surgical wound infections in India, which is in

marked contrast to New Zealand with <5%.[1] Meticillin-resistant *Staphylococcus aureus* (MRSA) are highly prevalent in the USA (34%), but the prevalence in The Netherlands is <2%.[2] These differences are thought to be associated with local differences in antibiotic policies.[3] Whereas acquired resistance mechanisms such as ESBL or meticillin resistance are generally assumed to be triggered by high quantities of antibiotics in the environment, the steady rise of previously less perceived MDR bacteria such as *Acinetobacter baumannii* is associated with the selection of these bacteria by potent broad-spectrum antibiotics.[4] Thus, *A. baumannii* is not clustered in different regions but rather associated with hospitals and other healthcare facilities, where broad-spectrum antibiotics are frequently used.[5] With ever-rising numbers of travellers the number of patients transferred from hospitals abroad back to their home country is increasing. As a result, the patients' exposure to pathogens with different resistance profiles and the chance of acquisition of these bacteria increases, possibly triggering spread of resistance to previously unaffected hospitals and geographical regions.[6]

Consequently, every patient transferred from abroad to the University Hospital of Zurich undergoes pre-emptive contact isolation or droplet isolation (in cases of respiratory symptoms) and is being screened for colonization with MDR. In the current study, we aimed to evaluate the prevalence of colonized patients among subjects transferred from hospitals abroad, the characteristics of the bacteria detected and the influence of MDR on clinical outcome.

Methods

In this retrospective study, patients who were transferred from abroad to the University Hospital Zurich between 1 January 2009 and 30 September 2011 were identified from the local infection control database, where every patient who undergoes infection control precautions is prospectively registered. Patients were included if they spent >24 h in a hospital abroad (i.e. outside Switzerland) within 14 days of admission to the University Hospital Zurich and if their length of stay (LOS) in our hospital was >24 h. Data on age, sex, hospital ward (surgical vs medical), country and geographical region (Europe, the Americas, Africa and the Middle East, and Asia and Australia), total LOS, ICU LOS, LOS on regular wards, duration of isolation precautions, in-hospital mortality, and microbiological information were collected on standardized data collection forms.

Ethical clearance was given by the Ethics Committee of the Kanton Zurich, Zurich, Switzerland.

Screening included nose and throat swabs, inguinal skin and wound swabs. In cases of respiratory symptoms, sputum was also cultured. Being colonized was defined as detection of MDR upon admission without apparent infection according to the clinical judgement of the attending clinicians and in the absence of specific antimicrobial treatment. Apparent infection was defined by the documented diagnosis of infection and the initiation of a specific antimicrobial treatment, respectively. The definitions were linked to the detection of bacteria. As a result, patients could be 'colonized' with one bacterial species and 'infected' with another.

ESBL bacteria and MRSA were defined according to laboratory standards.[7] Multidrug-resistant Gram-negative (MR Gram negative) bacteria were defined as those that were resistant to at least three different classes of antibiotics (classes were defined as: broad-spectrum beta-lactam/beta-lactamase inhibitor (piperacillin/tazobactam); third generation cephalosporins; carbapenems; aminoglycosides; and fluoroquinolones).

Comparability of groups was analysed by chi-square test or Fisher's exact test for categorical data and Student's *t*-test or Wilcoxon rank-sum test, respectively, for continuous data. Multivariable logistic regression analysis was performed to assess predictors of in-hospital death and the influence of the region of relocation on MDR colonization status. The model on in-hospital death contained sex, age, being colonized and being infected with bacteria. Sex was included because there were slightly more male patients in the study population. Age was included because of the obvious influence of older age on total risk of dying. Being infected was included to discern statistically the status 'colonized' from 'infected'.

For the model on region of relocation the reference region with the lowest colonization rate, Europe, was used. The other regions of relocation were controlled against.

Multivariate linear regression analysis was used to assess contribution of individual variables to ICU LOS. Sex, age, being colonized with bacteria, and being a surgical or medical patient was included in the model. All tests were two-tailed; $P < 0.05$ was considered statistically significant. Data were analysed using Statistical Package for Social Sciences (SPSS) version 15 for Windows (Chicago, IL, USA).

Results

Patient characteristics

Among 276 patients transferred from abroad between 1st January 2009 and 30th September 2011, 17 did not fulfil the inclusion criteria. Eight patients were not hospitalized for >24 h in the USA, eight patients were not hospitalized abroad and one patient was not from abroad at all. Among 259 patients who were analysed, 86 were women (33%) and 173 were men (66%), with a median (range) age of 56.2 (17.3–96.6) years. In total, 163 subjects (62%) were hospitalized on surgical wards and 96 (37%) on medical wards, respectively.

Microbiological results

Forty-six of 259 patients (17%) were considered colonized with MDR (ESBL, MRSA or MR Gram negative) (Table I). Thirty-three (12%) were colonized with one bacterial species, 12 (4.6%) with two different bacterial species and three (1.2%) were colonized with three different bacterial species. Nine (3.5%) patients had an apparent infection. Of those, three were additionally colonized as found upon admission screening. There was no difference in the proportion of patients colonized with MDR between surgical (12%) and medical wards (5.4%; $P = 0.4$, Fisher's exact test). Different bacterial species were analysed according to their antibiotic resistance profile and are listed in Table II.

Influence of region of origin

Because of low patient numbers from individual countries, travellers were subdivided according to the region from which