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# Multidrug-resistant bacteria in geriatric clinics, nursing homes, and ambulant care – Prevalence and risk factors

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ABSTRACT

Colonization/infection with multidrug-resistant bacteria (MDRB) such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae, is an increasing problem not only in hospitals but also in long-term care facilities. The aim of this study was to determine the prevalence as well as the risk factors of colonization/infection with MRSA, VRE, and ESBL producing Enterobacteriaceae in geriatric clinics, nursing homes, and ambulant care in Frankfurt am Main, Germany. 288 patients from 2 geriatric clinics ($n = 46$), 8 nursing homes ($n = 178$), and 2 ambulant care facilities ($n = 64$) as well as 64 staff members were screened for MDRB in the time period from October 2006 to May 2007. 58 patients (20.1%) and 4 staff members (6.2%) were colonized with MDRB. Among patients, 27 (9.4%) were colonized with MRSA, 11 (3.8%) were screened positive for VRE, and 25 (8.7%) were found to be colonized with ESBL producing Enterobacteriaceae. Prevalence of MDRB in geriatric clinics, nursing homes, and ambulant care facilities were 32.6%, 18.5%, and 15.6%, respectively. Significant risk factors for MDRB were immobility (OR: 2.7, 95% CI: 1.5–4.9; $p = 0.002$), urinary catheter (OR: 3.1, 95% CI: 1.7–5.9; $p < 0.001$), former hospitalization (OR: 2.1, 95% CI: 1.1–4.0; $p = 0.033$), and wounds/decubiti (OR: 2.3, 95% CI: 1.5–4.9; $p = 0.03$). Finally, the high level of MDRB in geriatric clinics, nursing homes, and ambulant care points to the importance of these institutions as a reservoir for dissemination.



## Introduction

The importance of long-term care facilities especially nursing homes as reservoirs of multidrug-resistant bacteria (MDRB) primarily methicillin-resistant *Staphylococcus aureus* (MRSA) has been addressed by various studies (Manzur et al., 2008; Pop-Vicas et al., 2008; Woltering et al., 2008; Baldwin et al., 2009; Benenson et al., 2009; Greenland et al., 2011; Reynolds et al., 2011). Colonization with MDRB may last for an extended period of time, hence, patients in long-term care facilities represent a major route for the introduction or reintroduction of MDRB to acute-care facilities (Oteo et al., 2006; Manzur and Gudiol, 2009; Gastmeier, 2010; Shurland et al., 2010). This is of socio-economic relevance since infections due to MDRB are associated with increased morbidity, mortality, and costs (Cosgrove et al., 2005; DiazGranados et al., 2005; Schwaber and Carmeli, 2007).

To control the spread of MDRB there is an ongoing need for information regarding the epidemiology of MRSA, vancomycin-resistant enterococci (VRE), and extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae in long-term care facilities. The present study aimed to determine the prevalence and risk factors for colonization/infection with MRSA, VRE, and ESBL producing Enterobacteriaceae in geriatric clinics, nursing homes, and ambulant care facilities in Frankfurt am Main, Germany.

## Materials and methods

### *Patients/settings/study design*

There exist 3 registered geriatric clinics, 40 nursing homes, and approx. 100 ambulant care facilities in Frankfurt am Main. The local health authority asked selected institutions to participate in the

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**Table 1**
Prevalence for MDRB in geriatric clinics, nursing homes, and ambulant care.

| | Total ($n=12$) | | Geriatric clinics ($n=2$) | | Nursing homes ($n=8$) | | Ambulant care facilities ($n=2$) | |
|---|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | *n* | % |
| Patients | 288 | 100 | 46 | 100 | 178 | 100 | 64 | 100 |
| Patients with MDRB | 58 | 20.1 | 15 | 32.6 | 33 | 18.5 | 10 | 15.6 |
| Patients with MRSA | 27 | 9.4 | 8[a] | 17.4 | 16[b] | 9 | 3 | 4.7 |
| Patients with ESBL | 25 | 8.7 | 2 | 4.3 | 20[b] | 11.2 | 3 | 4.7 |
| Patients with VRE | 11 | 3.8 | 7[a] | 15.2 | 0 | 0 | 4 | 6.3 |
| Staff | 64 | 100 | 14 | 100 | 50 | 100 | n.a. | n.a. |
| Staff with MDRB | 4 | 6.3 | 2 | 14.3 | 2 | 4 | n.a. | n.a. |
| Staff with MRSA | 2 | 3.1 | 0 | 0 | 2 | 4 | n.a. | n.a. |
| Staff with ESBL | 2 | 3.1 | 2[c] | 14.3 | 0 | 0 | n.a. | n.a. |
| Staff with VRE | 1 | 1.6 | 1[c] | 7.1 | 0 | 0 | n.a. | n.a. |

n.a., not analysed.
[a] Two patients were colonized with MRSA and VRE.
[b] Three patients were colonized with MRSA and ESBL.
[c] One staff was colonized with VRE and ESBL.

period prevalence study between October 2006 and May 2007. Staff members of participating institutions were allowed to join in on a voluntary basis.

Patients/residents/people, henceforth referred to as patients, of the participating institutions, or their legal guardian, were individually approached for written consent to take swabs from nose, throat, rectum, and if present wounds as well as to access their medical records. Data were collected using a standardized questionnaire. Medical records were examined for details of hospital admissions, illnesses, and other potential risk factors.

### *Detection and characterization of MDRB*

Swabs (Hain Diagnostika, Nehren, Germany) were screened on blood agar (Heipha, Eppelheim, Germany) and mannitol salt agar (Heipha) for the presence of *S. aureus* incl. MRSA, on VRE-selective agar (Becton Dickinson, Heidelberg, Germany) for the presence of VRE, and on BLSE agar (AES Chemunex, Bruz Cedex, France) as well as on Endo agar (Heipha) with a 10 μg cefuroxime disc for the presence of ESBL producing Enterobacteriaceae.

Species verification of *S. aureus* isolates was performed by means of colony morphology, gram-stain, positive catalase reaction and positive tube coagulase test (Becton Dickinson). Methicillin-resistance in *S. aureus* was determined by the agar diffusion test following guidelines set by Clinical and Laboratory Standards Institute (CLSI, National Committee for Clinical Laboratory Standards, 2006) and further proven by amplification of the *mecA* gene as described previously (Wichelhaus et al., 1999). Clonal identity and relatedness of MRSA isolates were analysed by pulsed-field gel electrophoresis after *Sma*I restriction of whole chromosomal DNA as well as by *spa* typing as described previously (Wichelhaus et al., 1999; Harmsen et al., 2003). Spa types were assigned using the Ridom StaphType software (Ridom GmbH, Würzburg, Germany) as described previously (Harmsen et al., 2003).

Species verification of colonies growing on VRE-agar as *Enterococcus faecium* and *Enterococcus faecalis* was performed by means of Api20Strep (bioMèrieux, Marcy Étoile, France). Vancomycin and/or teicoplanin resistance was determined by the Etest-method following interpretation guidelines of MIC values set by CLSI and further proven by amplification of the *vanA* and *vanB* gene as described previously (Werner et al., 2008). Clonal identity and relatedness of VRE isolates were analysed by pulsed-field gel electrophoresis after *Sma*I restriction of whole chromosomal DNA as described previously (Werner et al., 2008).

Species verification of colonies that grew on BLSE agar or within the cefuroxime disc zone on Endo agar as Enterobacteriaceae was performed by means of Api20E (bioMèrieux). All isolates were tested for ESBL production by the double disc synergy test as well as double disc approximation method following CLSI-guidelines. The presence of ESBL-encoding genes ($bla_{TEM}$, $bla_{SHV}$, $bla_{CTX\text{-}M}$) was investigated by PCR and sequencing (Pfeifer et al., 2009). Clonal identity and relatedness of ESBL producing Enterobacteriaceae were analysed by pulsed-field gel electrophoresis after *Xba*I restriction of whole chromosomal DNA according to the Tenover criteria (Tenover et al., 1995).

### *Statistical analysis*

Categorical data, i.e. age ≥ 85 years, hospital stay within the previous two years, immobility, urinary catheter, stoma (e.g. tracheostoma, ileostoma), percutaneous endoscopic gastrostomy tube, wound/decubitus, diabetes, presence of a care level, history of MRSA, were compared using the Fisher's exact test. Odds ratios (OR) and 95% confidence intervals (CI) are given. All tests were performed two-tailed, and a $p$-value < 0.05 was considered to be significant. In addition multiple logistic regression analysis with backward elimination (criterion: $\alpha = 0.05$) was applied. Statistical analysis was performed using BiAS software, version 10.02.

## Results

### *Prevalence and characterization of MDRB*

We screened 288 patients from 2 geriatric clinics ($n=46$), 8 nursing homes ($n=178$), and 2 ambulant care facilities ($n=64$) as well as 64 staff members for presence of MDRB in the time period from October 2006 to May 2007. Age of patients (years, mean ± SD) in geriatric clinics, nursing homes, and ambulant care facilities were 83 ± 7.7, 83 ± 9.3, and 74 ± 15.8, respectively.

A total of 58 patients (20.1%) and 4 staff members (6.2%) were colonized with MDRB. 27 patients (9.4%) and 2 staff members (3.1%) were colonized with MRSA, 11 patients (3.8%) and one staff member (1.6%) were screened positive for VRE, and 25 patients (8.7%) and 2 staff members (3.1%) were found to be colonized with ESBL producing Enterobacteriaceae (Table 1). Of 58 patients culture positive for any MDRB, 5 (8.6%) were colonized by more than one MDRB (Table 1). Prevalence of MDRB in geriatric clinics, nursing homes, and ambulant care facilities among patients were 32.6% (95% CI: 19.5–48.0), 18.5% (95% CI: 13.1–25.0), and 15.6% (95% CI: 7.8–26.9), respectively (Table 1).

With regard to MRSA there are two methods to determine the prevalence, i.e., MRSA to patient ratio, as usually applied in long-term care facilities, or MRSA to *S. aureus* ratio, as usually applied in acute care facilities. In this study 146 out of 288 patients (50.7%) were tested positive for *S. aureus*. Hence, with regard to MRSA to

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**Table 2**
Molecular characteristics of MDRB.

| MRSA ($n=29$) | | VRE ($n=12$) | | ESBL ($n=27$) | |
|---|---|---|---|---|---|
| Spa type | $n$ | Type | $n$ | Type | $n$ |
| t003 | 28 | *E. faecium* | | *E. coli* | |
| | | VanA | 3 | CTX-M-1 | 1 |
| | | VanB | 8 | CTX-M-14 | 1 |
| | | | | CTX-M-15 | 21 |
| | | | | TEM-52 | 1 |
| t032 | 1 | *E. faecalis* | | *K. pneumoniae* | |
| | | VanB | 1 | CTX-M-2 | 1 |
| | | | | CTX-M-15 | 1 |
| | | | | SHV-12 | 1 |

patient ratio the MRSA prevalence is 9.4% whereas with regard to MRSA to *S. aureus* ratio the MRSA prevalence is 18.5%.

Strain typing revealed the predominance of MRSA isolates with clonal relatedness to spa type t003, ST225/CC5 ("Rheinhessen subtype" epidemic strain; $n=28$), whereas only one MRSA isolate was clonally related to the spa type t032; ST22/CC22 ("Barnim" epidemic strain) (Table 2).

Among VRE isolates, 11 were identified as *E. faecium* and one as *E. faecalis*. Three *E. faecium* isolates were tested positive for the presence of the *vanA* gene whereas other VRE's were demonstrated to carry the *vanB* gene (Table 2). Molecular typing by means of PFGE revealed 8 different genotypes among vancomycin-resistant *E. faecium* isolates applying a similarity cut-off of 82% and visual inspection of the related patterns (data not shown).

Enterobacteriacea producing ESBL were identified as *Escherichia coli* ($n=24$) and *Klebsiella pneumoniae* ($n=3$). The ESBL enzyme predominantly identified was CTX-M-15 ($n=22$) as shown in Table 2. *Xba*I macrorestriction analysis of the 24 ESBL-*E. coli* isolates revealed 11 different genotypes. The clonal transfer of 4 different CTX-M-15 producing *E. coli* strains, i.e., strain 1 in two patients, strain 2 in one patient and one staff, strain 3 in three patients, strain 4 in ten patients, could be confirmed. The three *K. pneumoniae* isolates harboured different ESBL genes and were not genetically related (data not shown).

### *Risk factors associated with MDRB*

Statistical analysis identified risk factors associated with the presence of MDRB, MRSA, VRE as well as ESBL producing Enterobacteriaceae as summarized in Table 3. Multiple logistic regression analysis revealed the most important independent risk factors for being positive for (i) MDRB, i.e., immobility, urinary catheter; for (ii) MRSA, i.e., stoma, decubitus/wound, diabetes; for (iii) VRE, i.e., immobility; as well as for (iv) ESBL, i.e., previous hospital stay, urinary catheter.

## Discussion

Antibiotic and especially multi-drug resistance among human pathogens is a cause of major concern (Spellberg et al., 2011). Infections due to MDRB appear as a global challenge not only with respect to mortality but also with respect to an increasing demand on healthcare resources (Walker et al., 2009).

Patients of long-term care facilities represent a population at increased risk for being colonized or infected with MDRB because of age associated morbidities and accordingly a higher rate of hospital admissions (Gastmeier, 2010). Long-term care facilities therefore represent a turntable capable of distributing MDRB across hospitals, other healthcare institutions, and the community (Rooney et al., 2009; Gastmeier, 2010).

The present study elucidates the prevalence of MRSA, VRE, and ESBL producing Enterobacteriaceae in geriatric clinics, nursing homes, and ambulant care in one of Germany's larger metropolitan areas, Frankfurt am Main. To the best of our knowledge, this is the first point prevalence analysis so far encompassing this broad spectrum of MDRB combined with this large number of long-term care facilities. We screened 288 patients from 12 long-term care facilities and identified 58 patients (20.1%; 95% CI: 15.7–25.2) as MDRB positive. With regard to MRSA isolates identified among patients, 26 (96.3%) were clonally related to the Rheinhessen subtype epidemic strain, i.e., spa type t003, that is highly prevalent in hospitals in this area (Robert Koch-Institut, 2009). Interestingly this strain replaced the Southern German epidemic strain, i.e., spa type t041, that was frequently identified in hospitals in the 90s (Wichelhaus et al., 1997) and that was also proven to be highly prevalent in long-term care facilities within the Frankfurt area by a comparable study from the year 2000/2001 focusing solely on MRSA (Wichelhaus et al., 2001). In comparison to this earlier study, where 185 patients from geriatric clinics, 319 residents from nursing homes, and 92 people accessing ambulant care were screened for the presence of MRSA, MRSA prevalence has risen from 2.7% to 17.4% in geriatric clinics, 0.3% to 9.0% in nursing homes, and 2.7% to 4.7% in ambulant care. This increase in MRSA prevalence clearly documents further dissemination of MRSA outside the hospital in the Frankfurt area. We assume that existing hygiene recommendation concerning MRSA are sufficient, however, staff members and patients should receive better education on how to implement these guidelines in routine practice in order to avoid spread of MRSA (Baldwin et al., 2010). Moreover, reduced staffing levels have been identified as barriers to compliance with infection control standard precautions and need to be addressed (Vicca, 1999; Baldwin et al., 2010).

Of further interest is the finding that no community associated (CA) or lifestock-associated (LA) MRSA was identified. This is in line with another study in nursing homes from northern Germany that comparable to our study identified a MRSA prevalence of 7.6%

**Table 3**
Risk factors associated with MDRB.

| | MDRB | | MRSA | | ESBL | | VRE | |
|---|---|---|---|---|---|---|---|---|
| | OR (95 CI) | $p$-Value | OR (95 CI) | $p$-Value | OR (95 CI) | $p$-Value | OR (95 CI) | $p$-Value |
| Age ≥ 85 years | 1.69 (0.94–3.01) | 0.079 | 1.27 (0.57–2.79) | 0.686 | 1.82 (0.79–4.19) | 0.208 | 0.96 (0.29–3.2) | 1 |
| Previous hospital stay | 2.06 (1.06–3.97) | **0.033** | 1.16 (0.5–2.69) | 0.835 | 4.65 (1.36–15.92) | **0.008** | 2.66 (0.56–12.57) | 0.338 |
| Immobility | 2.67 (1.45–4.89) | **0.002** | 1.63 (0.73–3.65) | 0.312 | 3.02 (1.22–7.47) | **0.02** | 11.47 (1.45–90.83) | **0.004** |
| Urinary catheter | 3.13 (1.67–5.85) | **<0.001** | 1.92 (0.81–4.51) | 0.144 | 4.62 (1.99–10.72) | **<0.001** | 2.11 (0.6–7.45) | 0.264 |
| Stoma | 2.08 (0.68–6.33) | 0.193 | 5.68 (1.78–18.09) | **0.008** | 1.67 (0.36–7.87) | 0.378 | 0.74 (0.35–1.57) | 0.43 |
| Percutaneous endoscopic gastrostomy | 2.01 (0.81–4.9) | 0.125 | 1.99 (0.63–6.29) | 0.271 | 2.2 (0.69–6.99) | 0.252 | 1.05 (0.13–8.59) | 1 |
| Decubitus/wound | 2.27 (1.45–4.91) | **0.033** | 4.71 (1.97–11.25) | **0.001** | 0.53 (0.12–2.35) | 0.549 | 3.95 (1.10–14.19) | **0.047** |
| Diabetes | 0.83 (0.41–1.67) | 0.729 | 3 (1.33–6.79) | **0.014** | 0.6 (0.2–1.83) | 0.464 | 0.73 (0.15–3.44) | 1 |
| Presence of a care level | 1.25 (0.63–2.47) | 0.615 | 1.23 (0.48–3.18) | 0.818 | 1.10 (0.42–2.88) | 1 | 1.58 (0.33–7.48) | 0.482 |
| History of MRSA | 2.08 (0.68–6.33) | 0.193 | 5.68 (1.78–18.09) | **0.008** | 0.74 (0.09–5.88) | 1 | 0.74 (0.35–1.57) | 0.43 |

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and found neither CA-MRSA nor LA-MRSA (Pfingsten-Würzburg et al., 2011). Similar findings of clonal spread of epidemic healthcare associated HA-MRSA in nursing homes were described by other investigators in Germany and Europe (Smith et al., 2008; Pfingsten-Würzburg et al., 2011).

Acquired vancomycin resistance in enterococci mainly is a feature of *E. faecium* as also demonstrated in this study. The predominance of the *vanB* genotype in VRE isolates reflects the situation found in the Frankfurt university hospital (Englert et al., 2011) and is in line with a changing trend in many German health care institutions showing a tremendous increase in *vanB* genotype VRE prevalence (Wendt et al., 1999; Werner et al., 2008; Klare et al., 2010). Molecular typing revealed 8 different PFGE-types and therewith a high degree of genotypical heterogeneity among VRE isolates indicating primarily the successful horizontal spread of the *vanB* gene in *E. faecium*.

ESBL producing Enterobacteriaceae in this study were predominantly identified as *E. coli* producing ESBL-type CTX-M-15 which is widespread not only in Germany but worldwide (Pitout and Laupland, 2008; Dhanji et al., 2011). Molecular typing of the ESBL-*E. coli* isolates revealed presence of various strains whereby clonal dissemination of four CTX-M-15 producing *E. coli* strains was observed between several patients of three nursing homes and one geriatric clinic. A recent study from Northern Ireland addressing the prevalence of ESBL producing and ciprofloxacin-resistant *E. coli* in nursing homes revealed a prevalence rate of 40.5% whereas the present study determined a prevalence rate of 11.2% (Rooney et al., 2009). This difference might be explained by special circumstances within an individual nursing home such as staffing level or implementation of infection control measures and probably is the reason for the broad range of prevalence rates already identified within a single study, i.e., 0–75% in Northern Ireland (Rooney et al., 2009) and 0–20% in Frankfurt am Main.

Data on the prevalence of MDRB in long-term care facilities among staff members are scarce making a comparison difficult. MDRB were identified in 6.3% of staff members that participated in this study which is comparable with MRSA prevalence rates among staff of 7.5% and 5.8% reported by others (Baldwin et al., 2009; Monaco et al., 2009).

The present study confirmed immobility, urinary catheter, former hospitalization, and wounds/decubiti as significant risk factors for colonization/infection with MDRB (Mody et al., 2008; Benenson et al., 2009; Rooney et al., 2009).

There may be at least one limitation that needs to be acknowledged and addressed regarding the present study. Since patients were individually approached for written consent to participate in the study, some patients refused participation. Whereas participation rate was high among patients from geriatric clinics, it was less high among patients from nursing homes and ambulant care. Hence, it remains speculative whether patients that were sensitized to the subject MRSA primarily participated in the study – with the chance for free MRSA tests – giving reason to suspect false high MRSA prevalence rates among patients from nursing homes and ambulant care. This potential recruitment bias for MRSA can be excluded regarding ESBL and VRE, as none of the participants or their caregivers have been aware of these microorganisms before.

Finally, the high numbers of MDRB like MRSA, VRE, and ESBL-producing Enterobacteriaceae in geriatric clinics, nursing homes, and ambulant care, as shown in the present study, point to the importance of these facilities as reservoirs for dissemination.

## Conflict of interest statements

T.A.W. and C.B. have accepted speaking invitations from various pharmaceutical companies, though none poses a conflict of interest with the work presented here.

I.G., U.H., C.I., G.W., Y.P., H.A., and S.B. declare that they have no competing interests.

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