Multidrug-resistant organisms in refugees: prevalences and impact on infection control in hospitals

Abstract

Introduction: The refugee crisis is a great challenge to the social and healthcare system in Europe, especially in Germany. An abundance of data has been published on the refugees' health problems (infections as well as physical diseases and psychiatric problems) and their prevention (i.e., sanitary and vaccination programs). However, data on prevalences of multidrug-resistant organisms (MDRO) in refugees are scarce, although it is known that most refugees are from or travelled through countries with high prevalences of MDRO. This paper presents current data on MDRO colonization of refugees admitted to hospitals, and the impact of screening upon admission and infection control in hospitals is discussed.

Methods: Anonymous data obtained by screening upon hospital admission were reported by hospitals in the Rhine-Main region of Germany to the local public health department. Screening and microbiological analyses were performed from December 2015 to March 2016 according to standardized and validated methods.

Results: 9.8% of the refugees screened (32/325) exhibited colonization with methicillin-resistant Staphylococcus aureus (MRSA), and 23.3% of the refugees (67/290) were colonized with Gram-negative bacteria with extended spectrum beta-lactamasases, and/or enterobacteria with resistance against 3 or 4 groups of antibacterials, so-called 3MRGN (multidrug-resistant Gram-negative bacteria with resistance against penicillins, cephalosporins and quinolones) and 4MRGN (with additional resistance against carbapenems). Carbapenem-resistant Gram-negative bacteria (CRGN) were detected in 2.1% (6/290) of the refugees.

Conclusion: The data confirms the studies published between 2014 and 2016, encompassing refugees tested in Germany, the Netherlands and Israel, with prevalences of MRSA and CRGN up to 13.5% and 5.6%. The MDRO prevalences are higher than those of "risk groups" for MRSA, such as hemodialysis patients and patients depending on outpatient home-nursing care or residing in nursing homes. Therefore, screening and special infection control in hospitals is strongly suggested when refugees are admitted to hospitals, in order to ensure best medical practice and safety for all hospital patients regardless of their country of origin.

Keywords: refugees, asylum seekers, multidrug-resistant organisms (MDRO), methicillin-resistant Staphylococcus aureus (MRSA), multidrug-resistant Gram-negative bacteria (MRGN), carbapenem-resistant Gram-negative bacteria (CRGN), screening, infection control

Zusammenfassung

Einleitung: Die Flüchtlingssituation ist eine große Herausforderung für das Gesundheitssystem in vielen Ländern Europas, besonders auch in Deutschland. Eine Vielzahl von Daten zur gesundheitlichen Situation...
von Flüchtlingen (Infektionen, körperliche Erkrankungen und psy-
chiatrische Probleme) und zu deren Prävention (Hygiene und Impf-
programme) sind publiziert. Jedoch sind Daten zu multiresistenen Erregern (MRE) bei Flüchtlingen vergleichsweise rar, obwohl viele Flüchtlinge aus Ländern mit hoher MRE-Prävalenz stammen und/oder auf ihrer Flucht durch Länder mit hoher MRE-Prävalenz gekommen sind. In der vorliegenden Arbeit werden aktuelle Daten zur MRE-Prävalenz von Flüchtlingen bei Aufnahme in Akutkrankenhäuser vorgestellt und die Bedeutung des Aufnahme-Screenings und des Hygiene-Managements in den Krankenhäusern diskutiert.

Methoden: Verschiedene Krankenhäuser in der Rhein-Main-Region teilten die Ergebnisse von Aufnahme-Screening-Untersuchungen von Flüchtlingen anonymisiert dem Gesundheitsamt mit. Die Screening-
Untersuchungen wurden zwischen Dezember 2015 und März 2016
nach standardisierten und validierten Methoden vorgenommen.

Ergebnisse: 9,8% der bei Klinikaufnahme gescreenten Flüchtlinge
(32/325) waren mit Methicillin-resistenter Staphylococcus aureus-
Stämmen kolonisiert und 23,3% der Flüchtlinge (67/290) wiesen
Gram-negative Erreger mit erweitertem Resistenzspektrum gegen
β-Laktam-Antibiota (ESBL) und/oder Enterobakterien mit Resistenz
gegen 3 oder 4 Antibiotikagruppen auf (3MRGN: multiresistente
Gram-negative Erreger mit Resistenz gegen Penicilline, Cephalosporine
und Fluorchinolone; 4MRGN mit Resistenz gegen die genannten Anti-
biotikagruppen und zusätzlicher Resistenz gegen Carbapeneme; Defi-
nition nach KRINKO 2012). Carbapenem-resistente Gram-negative Er-
reger (CRE) wurden bei 2,1% (6/290) der untersuchten Flüchtlinge ge-
funden.

Diskussion: Die Daten bestätigen zwischen 2014 und 2016 publizier-
nte Studien, in denen Flüchtlinge bei Krankenhausaufnahme in den Nieder-
landen, in Deutschland und in Israel gescreent worden waren mit MRSA-
und CRE-Prävalenzen bis zu 13,5% und 5,6%. Die MRE-Prävalenzen
sind höher als die bei sog. „Risikogruppen“ für MRSA, wie z.B. ambulante
Hämodialysepatienten, Patienten, die vom ambulanten Pflegedienst
betreut werden, oder bei Bewohnern von Altenpflegeheimen. Deshalb
ist das Aufnahmescreening und entsprechende Hygienemaßnahmen
dringend zu empfehlen, wenn Flüchtlinge in das Krankenhaus aufge-
nommen werden, um beste medizinische Versorgung für alle Kranken-
hauspatienten sicher zu stellen unabhängig von ihrem Herkunftsland.

Schlüsselwörter: Flüchtlinge, Asylsuchende, multiresistente Erreger
(MRE), Methicillin-resistenter Staphylococcus aureus (MRSA),
multiresistente Gram-negative Stäbchenbakterien (MRGN),
Carbapenem-resistente Gram-negative Erreger (CRE),
Aufnahmescreening, Hygienemaßnahmen

Introduction

With the refugee crisis, thousands of refugees are migra-
ting to Europe, many of them coming as asylum seekers
to Germany [1]. In 2015, more than 1,000,000 refugees
arrived in Germany, originating from various countries,
but chiefly from Syria, Afghanistan and East Africa
(Somaliland, Eritrea, Ethiopia). To date, about half have ap-
plied for official asylum [2].

To combat possible communicable disease risk imported
to Europe with the movement of these refugees, the
European Center for Disease Prevention and Control
(ECDC) has published a rapid risk assessment [1], arguing
for good hygiene in refugee camps in order to prevent
outbreaks of communicable diseases due to poor sanita-
tion or contaminated food, as well as for implementing
vaccination programs to preventing infections such as
measles, poliomyelitis, meningococcal disease, diphtheria
and influenza [1]. In 2014, a questionnaire-based survey
on screening among newly arrived migrants in Europe
showed that in most European countries, mandatory
screening upon arrival is conducted for tuberculosis, and
screening for hepatitis B and C, HIV and other infectious
diseases is done less than 30% of the countries [3]. In
some regions, screening for enteropathogenic bacteria
or parasites has been done as well [4], [5], but has
meanwhile been abandoned because of low rates of
colonization.
Rates of tuberculosis in refugees are a matter of concern, especially in those arriving from Somalia and East Africa, whereas the tuberculosis incidence of refugees originating from Asian countries are lower [6]. Some cases of louse-borne diseases, cutaneous diphtheria, malaria, and leishmaniasis have been published [1]; these are very seldom, however. More often, outbreaks of scabies or small pox have occurred [1, 7]. An abundance of data show that many refugees suffer from diseases such as the common cold, respiratory infections, diabetes etc., and especially from psychiatric disorders [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21]. However, regarding infections, refugees and migrants are not considered a threat to the general population; instead, they are to be perceived as a highly vulnerable group [22]. Compared to these issues, the potential risk of importing multidrug-resistant organisms (MDRO) has almost been neglected, although reports dating back to 2014 have shown high prevalences in Syrian war-injured children and adults [23], [24] obviously caused not only by the severely compromised health-care system but also by the availability of prescription-free antimicrobial drugs in Syria. Many refugees originate from countries with a high prevalence of multidrug-resistant organisms in the hospitals as well as in the community setting, such as Afghanistan, the Near East and the North and East African countries. Additionally, many of the refugees have travelled through countries with high prevalences of MDROs, such as Turkey, Greece, Libya, Italy etc. Thus, data on MDRO prevalence in refugees are necessary. The present paper reports on a multicenter study on screening refugees admitted to hospitals for MDRO, such as methicillin-resistant *Staphylococcus aureus* (MRSA) or multi-drug-resistant Gram-negative bacteria (MRGN).

**Materials and methods**

The enterobacteria and non-fermenting bacteria such as *Acinetobacter* spp. and *Pseudomonas* spp. are classified as 3MRGN or 4MRGN according to the phenotypic definition of the German Commission on Hospital Hygiene and Infection Prevention (KRINKO). 3MRGN refers to Enterobacteriaceae resistant to 3 of 4 antibiotic groups (penicillins with piperacillin as a surrogate substance, cephalosporins with cefotaxim and/or ceftazi dime as a surrogate substance, and fluoroquinolones with ciprofloxacin as a surrogate substance) and 4MRGN with additional resistance to carbapenems, with imipenem and/or meropenem as surrogate substances [25]. Microbiological diagnostics were performed in the hospitals’ laboratories using standard laboratory methods and technologies (e.g., Biomérieux VITEK II, Biomérieux VITEK mass spectrometry, Beckman Coulter Microscan WalkAway 96, Cepheid GeneExpert etc.).

**Results**

Thirty-two (9.8%) of the 325 refugees tested for MRSA were MRSA carriers (range 0–14.8% per clinic), and 67 (23.2%) of the 290 patients tested positive for MRGN colonization with any extended-spectrum beta-lactamase (ESBL)-forming bacteria (range 13.5–34.1% per hospital), of which 24 (8.3% of the total, range 0–21.4% per hospital) were resistant to fluoroquinolones as well, i.e. they were 3MRGN. In 6 (2.1% of the persons tested for ESBL/MRGN; range 0–5.9% per hospital) individuals, resistance to carbapenemem was detected, i.e. they were 4MRGN (Table 1).

Table 2 compares the present results of MDRO colonization upon hospital admission with data from other studies in Germany and abroad. The overall prevalence in this study was 8.7% MRSA carriers (range 4.2–13.5% in the various studies), 16.8% ESBL (range 2.0–30.3%), 15.0% 3MRGN (range 5.6–32.5%) and 1.7% 4MRGN (range 0–5.6%), thus confirming our data quite well. In Table 3, the MDRO data of the refugees are compared to current data of “risk groups” for MDRO, especially MRSA colonization, obtained between 2012 and 2015 in the Rhine-Main region, Germany. The refugees’ colonization rates for MRSA and 4MRGN exceed those in hemodialysis patients and in persons requiring nursing care, either in nursing homes or as outpatient home-care.

**Discussion**

The refugee crisis is a great challenge to countries accepting them, not only regarding housing and integration, but also in terms of medical care, including vaccination programs etc. Up to now, large outbreaks of infectious diseases could be prevented, with the exception of one large outbreak of measles in Berlin, 2015, starting in one refugee camp and disseminating into the population, because of insufficiently vaccinated population groups in Germany and thus insufficient herd immunity in the population [26]. Hence, with the refugees arriving, not only are vaccination programs necessary for refugees, but also vaccination rates in the general German population have to be improved. The possibility of refugees importing MDRO and the impact on infection control management, however, has not yet been sufficiently taken into account by the public health sector. MDRO are considered a great threat to the medical system in Europe, and in Germany as well. The prevalence und importance of MRSA has been decreasing in many European countries during the last few years, but the increase of MRGN and especially that of carbapenem resistance is of great concern [1], [27].

In spite of earlier data indicating high prevalences of MDRO in refugees [23], [24] and the call for caution and pre-emptive action [28], [29], it was not until January 2016 that the first study on MDRO in refugees in Germany was published, exhibiting increased rates of MRSA colonization and very high rates of MRGN colonization, includ-
Table 1: MDRO prevalence (MRSA and ESBL/MRGN) in 325 refugees, screened upon admission to 6 hospitals in Germany in winter 2015/2016

| Hospital | MRSA tested | MRSA positive | ESBL/MRGN tested | ESBL/MRGN positive | 3MRGN positive | 4MRGN positive |
|----------|-------------|---------------|------------------|-------------------|----------------|----------------|
| Hospital 1 | N (10.3) | 73 (0.0) | 12 (16.4) | 1 (1.4) |
| Hospital 2 | N (12.2) | 74 (5.6) | 5 (6.8) | 0 (0.0) |
| Hospital 3 | N (0.0) | 14 (0.0) | 3 (21.4) | 0 (0.0) |
| Hospital 4 | N (14.8) | 27 (5.8) | 2 (7.4) | 0 (0.0) |
| Hospital 5 | N (9.4) | 85 (29.4) | 0 (0.0) | 4 (4.7) |
| Hospital 6 | N (9.8) | 325 (12.8) | 24 (8.3) | 6 (2.1) |

*ESBL only, 3MRGN and 4MRGN excluded; 
# 78 children: 8 MRSA, 15 3MRGN, 1 4MRGN; 19 adults: 1 MRSA 
## 49 children: 7 MRSA, 5 ESBL, 3 3MRGN; 25 adults: 2 MRSA, 2 3MRGN

Table 2: MDRO prevalence (MRSA and MRGN) in refugees admitted to hospitals and in asylum centers in Germany and other European countries

| Refugees admitted to the hospital | MRSA tested | MRSA positive | ESBL positive | 3MRGN positive | 4MRGN positive |
|----------------------------------|-------------|---------------|---------------|----------------|----------------|
| **This study** | N (9.8) | 325 (12.8) | 24 (8.3) | 6 (2.1) |
| Hospital admission, various clinics Germany | December 2015 – March 2016 | 325 (9.8) | 290 (12.8) | 24 (8.3) | 6 (2.1) |
| Reinheimer et al. [30] | Hospital admission, university clinic, Frankfurt/Main, Germany | June – December 2015 | 143 (5.6) | 143 (28.0) | 44 (30.8) | 3 (2.1) |
| Reinheimer et al. [31] | Hospital admission, university clinic, Frankfurt/Main, Germany | January – June 2016 | 117 (10.3) | 117 (23.1) | 38 (32.5) | 1 (0.9) |
| Steger et al. [32] | Hospital admission, Ingolstadt, Germany | February – August 2015 | 99 (4.2) | 99 (2.0) | 6 (6.1) | 0 (0.0) |
| Ravensbergen et al. [33] | Hospital admission, university clinic, Groningen, Netherlands | April 2014 – August 2015 | 130 (7.7) | 130 (10.0) | 13 (10.0) | 0 (0.0) |
| Peretz et al. [23] | Hospital admission, children and adults, Israel | Before 2014 | 89 (13.5) | 89 (30.3) | 5 (5.6) | 5 (5.6) |
| **Sum** | 900 (8.7) | 868 (16.8) | 130 (15.0) | 15 (1.7) |

| Refugees living in camps | MRSA tested | MRSA positive | ESBL positive* | 3MRGN positive | 4MRGN positive |
|-------------------------|-------------|---------------|---------------|----------------|----------------|
| Angeletti et al. [35] | 48 Syrian refugees arriving at a refugee camp, Italy | October 2015 | 48 (8.3) | 48 (12.5) | 0 (0.0) | 4 (8.3) |
| Heudorf et al. [34] | 119 unaccompanied refugee minors, Frankfurt/Main, Germany | October – November 2015 | n.a. | 119 (27.7) | 9 (7.6) | 0 (0.0) |
| **Sum** | 48 (8.3) | 167 (23.4) | 9 (5.4) | 4 (2.4) |

*ESBL only, 3MRGN and 4MRGN excluded
Table 3: MDRO prevalence (MRSA and MRGN) in refugees admitted to hospitals (this study) compared to MDRO-point prevalences in risk groups for MDRO (especially MRSA)

|                  | **MRSA** | **ESBL / MRGN** |
|------------------|----------|-----------------|
|                  | **tested** | **N (%)** | **tested** | **N (%)** | **3MRGN** | **4MRGN** |
| **this study**    | refugees upon hospital admission | 325 | 32 (9.8) | 290 | 67 (23.2) | 24 (8.3) | 6 (2.1) |
| Dawson et al. [38] | hemodialysis patients (2012) | 751 | 16 (2.1) | 532 | 40 (7.5) | 20 (3.8) | 0 (0.0) |
| Heudorf et al. [39] | residents of nursing homes for the elderly (2012) | 184 | 17 (9.2) | 150 | 40 (26.8) | 32 (21.4) | 0 (0.0) |
| Hogardt et al. [40] | residents of nursing homes for the elderly (2012 and 2013) | 690 | 45 (6.5) | 455 | 81 (17.8) | 57 (12.5) | 0 (0.0) |
| Neumann et al. [41] | patients with outpatient nursing care (2014/15) | 269 | 10 (3.7) | 132 | 19 (14.4) | 10 (7.6) | 0 (0.0) |

# all ESBL/MRGN, 3MRGN and 4MRGN included

Ravensbergen et al. [33] reported on 130 asylum seekers tested for MDRO upon admission to the University Hospital in Groningen, The Netherlands, from April 2014 through August 2015. Most of them were from Eritrea (36.5%) or Syria (18.6%). Forty (31%) of these asylum seekers were colonized with a total of 52 MDRO. Ten (7.7%) exhibited MRSA, and 26 (20%) were colonized with ESBL-building bacteria (20 E. coli, 4 Klebsiella pneumonia, 1 M. morganii, and 1 E. cloacae). Thirteen of these (i.e., 10% of the total tested) were resistant to fluoroquinolones as well, i.e., 3MRGN according to the KRINKO definition [25]. No carbapenemases were detected in this group of refugees. The authors called for rapid identification of and response to communicable diseases and carriage of MDRO in refugees to optimize treatment and maximize infection control [33].

In 2014, Peretz et al. [23] published screening data of Syrian civilians (29 children and 60 adults) treated in two Israeli hospitals. They found high prevalences of MRSA and CRGN (13.5% and 5.6%), although most of the children had neither been previously ill nor admitted to Syrian hospitals. Regarding the fact that wounded Syrian patients are and have been treated in other countries as well, they concluded: “Due to this alarmingly high carriage rate of MDR isolates we feel that contact isolation of Syrian patients, until carriage of MDR isolates is ruled out, is paramount to prevent further spread of these pathogens” [23].

Outside the hospital setting, two studies screening asylum seekers for MDRO in their refugee camp [34], [35] and two reports on MRSA in refugee camps [36], [37] have been published to date.

Angeletti et al. [35] tested 48 young (median age: 20 years) healthy Syrian migrants in an asylum center in Italy in October 2015, finding that 4 (8.3%) were colonized with MRSA, 6 (12.5%) with ESBL-producing bacteria (4 E. coli, 1 Klebsiella spp, and 1 Shewanella putrefaciens) and 4 (8.3%) with Pseudomonas species with meropenem resistance. Another study performed MRGN
screening in young, healthy, unaccompanied refugee minors (<18 years old) in Frankfurt/Main in October/November 2015 [34]. ESBL was detected in 42 (35.3%) persons, of which 3MRGN were found in 9 (7.6%) of the total persons. No 4MRGN was found. Only 6 (5.0%) of the refugees reported having undergone antimicrobial therapy, and 2 (1.5%) reported hospital admission during the preceding six months.

In Denmark, after negative MRSA screening in 50 Kosovar-Albanian refugees arriving in a refugee camp, 8 Kosovar-Albanian refugees became infected with/colonized by MRSA in the following 14 months in this camp [36]. In the state of Schleswig-Holstein, Germany, a resident of an asylum center was diagnosed with furunculosis caused by a Panton-Valentine leukocidinone (PVL)-positive MRSA: an active case finding was implemented, and two further PVL-positive CA-MRSA cases were identified (0.9%; 2/232) [37].

The refugees’ colonization rates for MRSA and 4MRGN exceed those in patients with special risks for MDRO colonization, such as hemodialysis patients and in persons with need of nursing care, either in nursing homes or in outpatient care [38], [39], [40], [41].

Given this data on MDRO in refugees in various settings, which consequences should be drawn?

With respect to refugee camps, in October 2015, the Robert Koch Institute, Germany, recommended not to screen refugees in asylum centers [42]. Although we agree with that recommendation, we would add a plea for good sanitary facilities as well as hygienic and sufficient laundry facilities with washing machines that reach disinfecting temperatures (>60°C).

With respect to the hospital setting, the German Commission of Hospital Hygiene and Infection Prevention (KRINKO) has published guidelines for prevention and control of MRSA [43] and MRGN [25] encompassing recommendations for screening and specific infection control. The KRINKO recommends admission screening for MRSA for patients with enhanced risk of harboring MRSA, for example, patients with a known history of MRSA colonization, patients from regions/institutions with high MRSA prevalence, hemodialysis patients, patients with a history of hospital treatment in the preceding year, patients with occupational contact with food-producing animals (pigs, cows, poultry), patients with known contact to another person colonized or infected with MRSA, patients who need nursing care and had antibiotic treatment in the preceding 6 months or medical devices (such as urinary catheters, tracheostoma etc.) [43]. With regard to MRGN, screening and pre-emptive isolation is recommended by the KRINKO for patients with an increased risk of colonization and/or infection with 4MRGN, such as those who have had contact with the health-care system in countries with a 4MRGN/CRGN epidemic, patients who had contact with other patient with 4MRGN (e.g., a shared room), and patients with a hospital stay (>3 d) during the preceding 12 months in a region with high 4MRGN prevalence [25]. The KRINKO recommends barrier nursing and isolation for patients colonized or infected with 4MRGN in all hospital wards, and for patients with 3MRGN in wards with special risks (such as intensive care units, neonatal units, burn units etc).

Up to now, the KRINKO has not published a special recommendation for screening and infection control of refugees. The refugees’ MRSA prevalences shown in Table 1 and Table 2 exceed those of the risk groups (Table 3); thus, refugees definitely meet the criteria of a risk group for MRSA and should be screened for MRSA upon hospital admission – even in absence of the criteria for screening for MRSA mentioned in the KRINKO guideline [43].

Systematic data on 3MRGN and 4MRGN in the hospital setting are lacking in Germany. On May 1, 2016, a mandatory reporting system for CRGN was implemented in Germany [44]. In the federal state of Hesse, however, mandatory reporting of CRGN has been in force since December 2011, so that data from a 4-year period are available [45], [46]. In this period, in Frankfurt am Main, CRGN were reported from every hospital, ranging from 0 to >80 specimen/year, and were also reported from the outpatient setting. Only about 30% of the patients colonized or infected with CRGN had a history of living abroad or hospital stay in a foreign country, and thus met the screening criteria of the KRINKO recommendation of 2012 [25]. Therefore, broader screening strategies and infection control measures were demanded [45]. With CRGN prevalences of >1% among refugees in our study, we recommend screening of refugees not only for MRSA but also for CRGN upon hospital admission, followed by intensified supervision and infection control management. Although criticized by Walter et al. [47], Peretz et al. [23] demanded pre-emptive isolation in hospitals, which has been implemented in the Frankfurt am Main University Clinic [30] “as the best medical practice and safety for all patients regardless of their country of origin” [48].

Notes

Competing interests

The authors declare that they have no competing interests.

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