RAPID RISK ASSESSMENT

Outbreak of VIM-producing carbapenem-resistant *Pseudomonas aeruginosa* linked to medical tourism to Mexico

11 March 2019

Main conclusions

This outbreak of Verona integron-encoded metallo-beta-lactamase-producing carbapenem-resistant *Pseudomonas aeruginosa* (VIM-CRPA) surgical site infections, related to invasive procedures performed in healthcare facilities in Tijuana, Baja California, Mexico, highlights the risks associated with medical tourism for patients and healthcare systems in the countries of origin. Only a few European Union (EU)/European Economic Area (EEA) citizens are likely to have travelled to and undergone surgical procedures in the healthcare facilities associated with the outbreak, mainly the Grand View Hospital, in Tijuana, Mexico. Therefore, the risk of introduction and further spread of VIM-CRPA from this specific outbreak to healthcare facilities in the EU/EEA is low. However, there is an ongoing high risk of multidrug-resistant organisms (MDROs) being imported into hospitals and other healthcare settings in the EU/EEA from patients hospitalised abroad for planned medical procedures and unexpected medical events. This applies to patients who travel and are hospitalised within the EU/EEA as well as outside the EU/EEA.

Options for response

Information to healthcare providers and patients

National authorities should consider raising awareness among the public and healthcare providers concerning the risk of acquiring healthcare-associated infections and multidrug-resistant bacteria during medical procedures and hospitalisations abroad, especially in healthcare facilities with poor infection prevention and control standards. Travellers could be provided with this information through sources such as healthcare- and travel-related websites, travel clinics, or their healthcare provider. Sharing information on ongoing outbreaks, such as the current VIM-CRPA outbreak, with healthcare providers could facilitate the timely detection of potential cases and control of further spread. Healthcare providers should be encouraged to remain vigilant at patient admission for the possible introduction of multidrug-resistant bacteria from patients who have been transferred from, or had recent contact with healthcare settings in other countries, and ask about recent travel history and potential exposure to healthcare while abroad.

Prevention of spread of VIM-CRPA in healthcare facilities

Implementation of enhanced surveillance, screening and pre-emptive isolation in healthcare facilities for patients who have been transferred from, or had recent contact with hospitals and other healthcare settings in countries with a high prevalence of multidrug-resistant bacteria, including CRPA, is recommended to reduce their transmission in healthcare facilities and prevent further spread. Documentation of known infection with, or carriage of CRPA at the time of cross-border patient transfer would optimise the early and effective implementation of measures to prevent its spread. According to WHO guidelines, measures to prevent transmission of CRPA in healthcare facilities should at least include the following components: hand hygiene (appropriate use of alcohol-based hand rub), contact precautions, patient isolation (single room or cohorting), environmental cleaning and surveillance [1].

Testing of exposed patients for blood-borne pathogens

Due to the breach of standards in the sterilisation of medical devices and instruments at Grand View Hospital, Tijuana, patients who were subjected to invasive procedures in this facility should be tested for hepatitis B, hepatitis C and HIV as a precaution [2]. Follow-up of the exposed patients by national authorities is important to ensure that testing is undertaken and adequate support given.

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Public health issue

Risk assessment question: What is the risk of acquisition of VIM-CRPA by EU/EEA citizens and the introduction and spread of VIM-CRPA in EU/EEA healthcare facilities due to the outbreak at Grand View Hospital Tijuana, Mexico?

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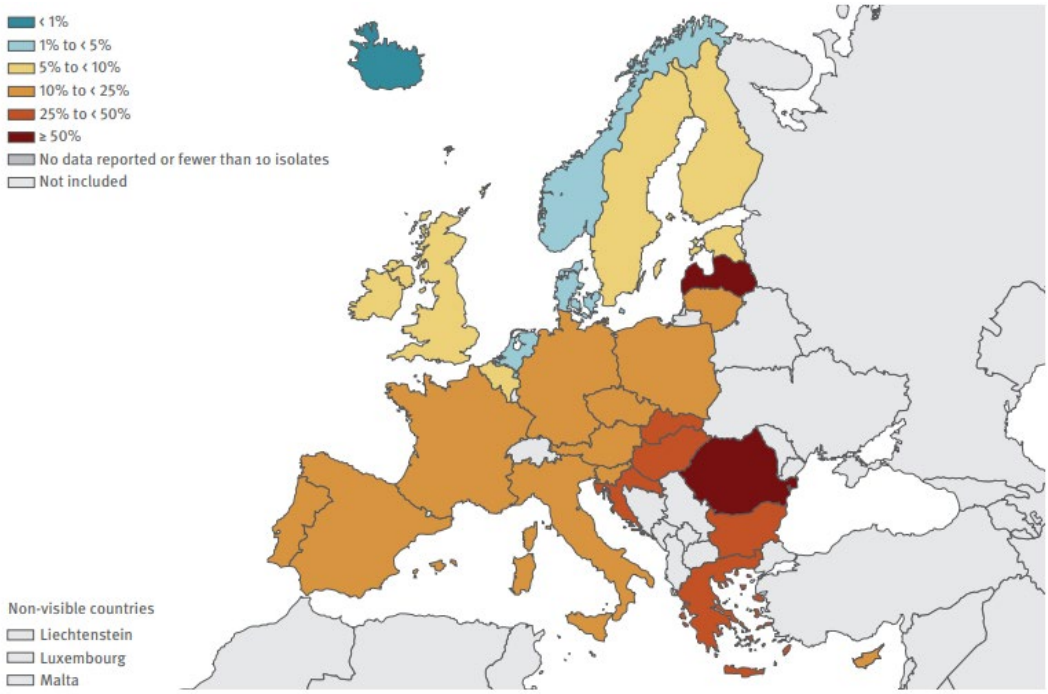
Experts from WHO reviewed the risk assessment, but the views expressed in this document do not necessarily represent the views of WHO.

Disease background information

Carbapenem-resistant *P. aeruginosa* (CRPA)

Pseudomonas aeruginosa harbours multiple mechanisms of intrinsic and acquired resistance and frequently displays high resistance rates to multiple antimicrobial classes. In 2017, the European Antimicrobial Resistance Surveillance Network (EARS-Net) reported an EU/EEA population-weighted mean for carbapenem resistance in *P. aeruginosa* invasive isolates of 17.4%, with a statistically significant decreasing trend from 2014 to 2017 [3]. However, carbapenem resistance proportions showed large variation between countries, from 0% in Iceland to 63.4% in Romania (Figure 1) [3]. Infections with carbapenem-resistant *P. aeruginosa* (CRPA) are difficult to treat as there are often no treatment options available that are both effective and safe. Moreover, these infections have been assessed as having a higher mortality than infections with carbapenem-susceptible *P. aeruginosa* [4].

Figure 1. ***Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2017 [3]**



VIM-producing carbapenem-resistant *P. aeruginosa*

Resistance to carbapenems is commonly linked with down-regulation of the carbapenem-specific porin Opr-D, often in combination with overexpression of efflux pumps [5]. Metallo-beta-lactamases (MBLs), such as VIM, can also be responsible for carbapenem resistance and are often carried on mobile genetic elements, such as integrons. VIM is widely disseminated in Europe [6]. Numerous healthcare-associated outbreaks of VIM-CRPA have been reported in European countries: Belgium [7], France [8], Germany [9], Greece [10], Hungary [11], Italy [12], the Netherlands [13] and Spain [14]. Some of these outbreaks could be attributed to invasive medical procedures [9,13]. In addition, high-risk clones have been described for *P. aeruginosa*, characterised by their worldwide dissemination in hospitals and their ability to readily acquire additional antibiotic resistance genes [15,16].

Control of *P. aeruginosa* in healthcare facilities

Due to its ubiquitous presence in the environment, and especially in water, and its ability to form biofilms, controlling the spread of *P. aeruginosa* is a challenge for hospitals and other healthcare settings. *P. aeruginosa* commonly contaminates water sources, sink surfaces and drains and can spread through aerosols to the hands of healthcare staff [17,18]. Patients may acquire *P. aeruginosa* through contact with the contaminated hands of healthcare providers or with the environment. A wide range of medical devices and equipment and non-medical products including bronchoscopes [19], oral intubation equipment [20], disinfectant-soap dispensers [21], mouth swabs [22] and commercially available bottled mineral water [23] have also been identified as outbreak sources in hospitals and other healthcare settings.

Healthcare-associated infections due to *P. aeruginosa* in the EU/EEA

P. aeruginosa is one of the major causes of healthcare-associated infection in Europe. In the Healthcare-Associated Infections Surveillance Network (HAI-Net) surgical site infection (SSI) surveillance, which collected data on seven common surgical procedures from 16 EU/EEA countries between 2014 and 2017, *P. aeruginosa* was the sixth most commonly reported microorganism, reported in a total of 1 022 SSIs. For intensive care unit (ICU)-acquired pneumonia from the HAI-Net ICU surveillance, *P. aeruginosa* was the most frequently isolated microorganism (28%) of 16 869 microorganisms associated with 9 569 ICU-acquired pneumonia cases in 2016 [24]. In ECDC's point prevalence survey of healthcare-associated infections at acute care hospitals in 28 EU/EEA countries during the period 2016–2017, *P. aeruginosa* was the fourth most common microorganism (8.0% of all reported microorganisms) associated with healthcare-associated infections, and the EU/EEA proportion of carbapenem resistance for all reported *P. aeruginosa* healthcare-associated infections with antimicrobial susceptibility results was 32.2% [25].

Event background information

Outbreak of VIM-CRPA in Tijuana, Mexico

On 12 February 2019, the Pan American Health Organization/World Health Organization received a report regarding surgical site infections caused by VIM-CRPA traced to a healthcare facility in Tijuana, Mexico [26]. As of 11 February 2019, 20 cases had been identified in nine states of the United States, including 16 confirmed cases (defined as VIM-CRPA isolated from a patient who had an invasive procedure in Mexico in the month prior to collection of the VIM-CRPA positive specimen according to the CDC case definition) and four suspected cases (defined as CRPA unavailable for or pending resistance mechanism testing from a patient who had an invasive procedure in Mexico in the month prior to collection of the specimen) [26].

The cases had dates of specimen collection between September 2018 and January 2019, except for two cases from 2015 and 2017 that were retrospectively identified [26]. All cases were travellers who received medical care from healthcare facilities in Tijuana, Mexico. Fifteen of the reported cases had surgery, primarily for weight loss, at Grand View Hospital in Tijuana, while the remainder reported attending four other healthcare facilities in Tijuana. Most patients presented with a surgical site infection and 13 cases were hospitalised in the US for complications of the procedures in Mexico. One case with underlying comorbidities and a bloodstream infection died [26]. The outbreak has received considerable media attention in the US [27,28]. The source of the outbreak at Grand View Hospital has not been identified.

Half of the cases used the same medical tourism agency based in the US to coordinate their surgery in Mexico. Although most referred patients were from the US and Canada, the same medical tourism agency has also reportedly referred patients from other countries to Grand View Hospital since 1 August 2018, including two European citizens. A sanitary inspection conducted at Grand View Hospital by Mexico's Directorate of Protection Against Sanitary Risks for Baja California's Secretary of Health, has identified reusable equipment that was not being appropriately processed, thereby representing a potential risk for the transmission of blood-borne infections. As a result of these findings, the CDC and the Public Health Agency of Canada have issued blood-borne pathogen notifications, recommending that patients who had received treatment at this hospital get tested for hepatitis B virus, hepatitis C virus and HIV as a precaution [2,29].The Directorate of Protection Against Sanitary Risks for Baja California's Secretary of Health in Mexico has ordered the closure of the operating rooms at the hospital. The National Epidemiological Surveillance System in Mexico is on alert for detecting cases linked to this outbreak.

Medical tourism

Medical tourism has grown in popularity in recent years, leading to the establishment of several health care brokers and medical tourism companies across the world. Some of the main medical tourism destinations are Costa Rica, India, Malaysia, Mexico, Singapore, South Korea, Taiwan, Thailand, Turkey and the US [30]. Medical tourism most frequently relates to dental treatment, cosmetic surgery, cardiac surgery, in vitro fertilisation, weight loss surgery, liver and kidney transplantation and spinal surgery [30].

An estimated 50 million people worldwide travel abroad each year seeking medical care services [31]. Shorter waiting times and lower costs in the country of destination are some of main drivers for this phenomenon. In the EU/EEA, about 49% of citizens would be willing to travel abroad for medical care, according to a recent European Commission survey [32].

ECDC threat assessment for the EU

Healthcare-associated infections caused by VIM-CRPA can be severe and lead to death. Due to carbapenem resistance, antimicrobial treatment options for patients with such infections are very limited. The few remaining treatment options for VIM-CRPA infections are often less effective and have more adverse effects than the carbapenems, thereby potentially resulting in prolonged clinical courses and poor outcomes. Furthermore, admission of patients returning from Mexico with VIM-CRPA after invasive procedures might pose a risk of further VIM-CRPA transmission in the healthcare system of the country of origin (i.e. the country to which the patient returns).

So far, cases of VIM-CRPA infection associated with the hospital outbreak in Tijuana, Mexico have only been reported in the US, with an unconfirmed case also identified in Canada. Patients from several countries were referred to Grand View Hospital by the same medical tourism agency, therefore the potential may exist for further cases among patients from other countries who had surgery at the same centre. At least two European citizens were among those referred to Grand View Hospital by the medical tourism agency. Due to the time interval between surgery and notification, and the continued performance of surgical procedures at Grand View Hospital, additional cases may still present to healthcare providers. While most cases occurred after surgical procedures at Grand View Hospital, other healthcare facilities in Tijuana have also had VIM-CRPA cases. In addition, there is a large network of multiple travel agencies and multiple bariatric surgery hospitals in Tijuana offering care services to international patients.

Any transfer of patients hospitalised abroad carries a risk of multidrug-resistant bacteria being introduced into the receiving hospital [33,34]. There are also other examples of multidrug-resistant bacteria and healthcare-associated infections related to medical tourism, such as the import of New Delhi Metallo-beta-lactamase (NDM)-producing Enterobacteriaceae [35], or the development of surgical site infections with non-tuberculous mycobacteria associated with plastic surgery [36]. Two studies, in France and Sweden, showed that only a few travellers who consulted travel clinics prior to departure had sufficient knowledge concerning the risk of acquiring multidrug-resistant bacteria during international travel [37,38]. This limited awareness probably also applies to citizens of other European countries and patients travelling for medical procedures.

During the investigation of the VIM-CRPA surgical site infection outbreak, Mexican health authorities identified reusable equipment that was not being appropriately processed for sterilisation at Grand View Hospital, therefore representing a potential risk for the transmission of blood-borne infections. Patients subjected to invasive procedures at Grand View Hospital should therefore be identified and tested for hepatitis B virus, hepatitis C virus and HIV as a precaution.

The risk of introduction and further spread of VIM-CRPA from this specific outbreak to healthcare facilities in the EU/EEA is low. However, there is an ongoing high risk of multidrug-resistant organisms (MDROs) being imported into hospitals and other healthcare settings in the EU/EEA from patients hospitalised abroad for planned medical procedures and unexpected medical events. This applies to patients who travel and are hospitalised within the EU/EEA as well as outside the EU/EEA.

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