Reunion, a sentinel island for multidrug-resistant bacteria surveillance in South-western Indian ocean: a retrospective survey using hospitalised patients screening, 2015-2017

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Abstract

Background

Since 2015, antimicrobial resistance was identified as a public health priority for the Southwestern Indian ocean (SWIO) (Comoros, Madagascar, Mauritius, Mayotte (France), Reunion (France), and Seychelles). However, multidrug-resistant Bacteria (MRB) colonization rates in human populations from most islands of SWIO were still unknown in 2020 with neither hospital nor community baseline colonization rates estimated.

Methods

Based on exhaustive hospital MRB screening laboratory data, we provided the first estimation of MRB colonization rates in hospitalized patients residing in SWIO (2015-2017). Using Reunion (European Union) MRB colonization rate as a baseline we identified at risk patients according to their territory of residence.

Results

The survey pointed out significantly higher overall MRB colonization rates in patients from Comoros, Madagascar, Mayotte, and Seychelles when compared to Reunion (France) with extended-spectrum betalactamase producing Enterobacteriaceae as a generalized public health issue for these territories. Specific epidemiological dynamics were pointed out in Mayotte and Seychelles patients with significantly higher methicillin-resistant *Staphylococcus aureus* (MRSA) colonization rates; and in Mauritius patients with higher carbapenemase producing Enterobacteriaceae (CPE) colonization rate.

Conclusion

These results could be the first step to set up a regional MRB surveillance in SWIO hospitals.

Background

Since the 90's, an increase of the prevalence of multidrug-resistant bacteria (MRB) was observed in Reunion (France).[1] Epidemiological surveillance at Reunion hospitals pointed similar incidence trends as in main France territory in 2015 (*i.e.* Occitanie region) for extended-spectrum betalactamase producing Enterobacteriaceae (ESBL-E) and lower incidence for methicillin-resistant *Staphylococcus aureus* (MRSA).[2]

Southwestern Indian Ocean (SWIO) is composed of islands (Union of Comoros, Madagascar, Mauritius, Mayotte (France), Reunion (France), and Seychelles). Based on literature, extended-spectrum betalactamase producing Enterobacteriaceae (ESBL-E) and carbapenemase producing Enterobacteriaceae (CPE) were identified as a main public and veterinary health issue for SWIO.[3] Antimicrobial resistance was considered as a main public health priority for the area since 2015. However, the absence of MRB surveillance network in other SWIO territories and scarce publications on the topic prevented from identifying most affected islands and to implement targeted action plans.

Felix-Guyon University hospital, in Reunion, is well suited for medical evacuations and receives most of the evacuated patients from the territories of SWIO. Since 2015, a MRB screening strategy for all patients residing abroad, arriving through medical evacuation, visiting a foreign country within the three preceding months, and/or hospitalized abroad in the past year was implemented. Furthermore, in Felix-Guyon hospital all intensive care admitted patients are screened in order to avoid introduction of MRB in the unit.

Based on exhaustive laboratory data, we estimated the prevalence of MRB colonization in hospitalized patients residing in SWIO (i.e. ESBL-E, CPE, MRSA, vancomycin-resistant enterococci, and both multidrug-resistant *Acinetobacter* sp., and *Pseudomonas* sp.). This study provided the first estimation of the MRB colonization rates in patients from SWIO territories using a comparable design setting.

Methods

Data collection, inclusion criteria, and statistical analyses

We performed a retrospective survey on all patients admitted to the Felix-Guyon University hospital in Reunion from 2015 to 2017 (main hospital). Only SWIO residing patients were included. All these patients were screened for MRB detection (i.e. anal and nasal swabbing) and patients admitted to intensive care unit were used as baseline for odds ratio estimation as all patients from Reunion intensive care were screened.

The MRB included were MRSA, ESBL-E, carbapenemase-producing Enterobacteriaceae (CPE), vancomycin-resistant enterococci (VRE), and both multidrug-resistant *Acinetobacter* sp. (AB), and *Pseudomonas* sp. as defined by Magiorakos et al.[4]

A patient was considered MRB positive if carrier of one, or more than one MRB. MRB colonization rates in patients were compared according to their country of residence using χ^2 test with Fisher correction or Fisher exact test if theoretical frequency were less than 5. Odds ratio were calculated with Reunion patients as reference and threshold was set at p-values <0.05. Confidence intervals were estimated using the Woolf method. The statistical analyses were performed using R software version 3.4.2.

The study was approved by the French national commission on data protection and liberties (reference 2210228 v0, 10th of January 2019).

Bacterial isolates and antibiotic susceptibility testing

Bacterial isolates were routinely obtained at hospital laboratory and species identified for all isolates using MALDI-TOF mass spectrometry (Bruker Daltonics, Breme, Germany). ESBL-E, and CPE were screened using two selective chromogenic agar ChromID-ESBL and ChromID CARBA SMART (bioMérieux, Marcy l'Étoile, France). ESBL-E phenotypes were confirmed using combined disk synergy testing.

Gram-positive bacteria (MRSA and VRE) were detected using respectively Chrom-ID MRSA SMART and Chrom-ID VRE agar (bioMérieux, Marcy l'Étoile, France). Multidrug-resistant *Acinetobacter* sp. (MRA) and *Pseudomonas* sp. (MRP) were identified using additionally Drigalski agar plate with ceftazidime disk. All MRB were checked by antibiogram using disc diffusion method according to the European Committee on Antimicrobial Susceptibility Testing 2015 recommendations.[5] CPE and VRE were all confirmed by PCR using the GenXpert system (Cepheid, Sunnyvale, USA).

Results

From the 1st of January 2015 to the 31th of December 2017, a total of 4,135 hospitalized patients from SWIO territories were included in the survey. Overall 23.7% (978/4,135) of patients were found positive for MRB colonization.

If the number of hospitalized patients according to their territory of residence varied widely (from 13 in Seychelles to 2,184 in Reunion), high MRB colonization rates were observed for patients residing in Seychelles and Madagascar (61.5% and 41.3% respectively) (Figure 1). Among all MRB positive patients, 94,4% (923/978) were ESBL-E carriers. MRB colonization rates varied according to the patient's country of residence.

MRB colonized patients were significantly higher in SWIO (excluding Mauritius patients) when compared to patients from Reunion as a baseline, ESBL-E colonization rates followed the same trend (Table 1). MRSA colonization rates were significantly higher in Seychelles and Mayotte hospitalized patients than in Reunion patients. CPE colonization rates were significantly higher in patients residing in Mauritius when compared to Reunion patients.

Table 1. Comparison of MRB colonization rates according to the patient's territory of residence (2015-2017) using Reunion (France) as reference

		MBR positive patients		ESBL-E		MRSA		CPE	
	Patients (n)	**OR** (95% CI)	**Prevalence** (95% CI)	**OR** (95% CI)	**Prevalence** (95% CI)	**OR** (95% CI)	**Prevalence** (95% CI)	**OR** (95% CI)	**Prevalence** (95% CI)
Seychelles	13	**7.4 [2.4-22.6] ****	61.5% [35.5%-82.3%]	**7.4 [2.4-22.6] ****	61.5% [35.5%-82.3%]	**32.9 [6.6-164.6] ****	15.6% [04.3%-42.23%]	_	_
Madagascar	322	**3.1 [2.4-3.9] ***	41.3% [36.1%-46.8%]	**3.1 [2.4-3.9] ****	40.1% [34.9%-45.5%]	2.3 [0.7-7.1]	01.2% [0.01-0.03]	2.7 [0.9-8.8]	01.2% [0.01-0.03]
Comores	30	**2.3 [1.1-5.0] ***	33.3% [19.2%-51.2%]	**2.3 [1.1-5.0] ***	33.3% [19.2%-51.2%]	_	_	_	_
Mayotte	1,475	**1.7 [1.4-1.9] ****	26.4% [24.3%-28.8%]	**1.5 [1.3-1.8] ****	24.7% [22.6%-26.9%]	**3.6 [1.9-7.1] ****	2.0% [01.4%-02.8%]	2.1 [0.9-4.7]	1.0% [0.6%-1.6%]
Mauritius	111	**1.6 [1.1-2.5] ***	26.1% [18.9%-35.0%]	1.1 [0.7-1.8]	19.8% [13.5%-28.2%]	_	_	**19.2 [7.6-48.2] ****	8.1% [4.3%-14.7%]
Reunion[b]	2,184	1 (ref)	18.7% [17.1%-20.4%]	1 (ref)	17.9% [16.3%-19.5%]	1 (ref)	0.5% [0.3%-1.0%]	1 (ref)	0.4% [0.3%-0.8%]

MRB: multidrug-resistant bacteria; ESBL-E: Extended-Spectrum Betalactamase producing Enterobacteriaceae; MRSA: Methicillin-resistant *Staphylococcus aureus*; CPE: carbapenemases-producing Enterobacteriaceae; **<0.001; *<0.05; ABR, PYO, and VRE were not presented as none of the IOC hospitalized patients were significantly more carriers.

Discussion

This study pointed out significantly higher MRB colonization rates in hospitalized patients from Comoros, Madagascar, Mayotte and Seychelles when compared to patients from Reunion. ESBL-E seems to be a generalized sanitary issue for SWIO whereas specific epidemiological trends were observed for MRSA and CPE. Higher MRSA colonization rates were reported in Mayotte and Seychelles patients and high CPE colonization rate was identified in Mauritius residing patients (p<0.001). These results could be the first step of a regional hospital-based MRB surveillance as expected by the Indian ocean commission since 2015.[6]

Our survey was based on the biggest sample size of SWIO individuals ever reported in the literature. The study design is based on a convenience sample accordingly individuals included in analysis are not randomly selected; this selection bias was used to explore MRB colonization in SWIO hospitals based on the knowledge that i) patient residence country is a known risk factor for MRB infection and carriage[7-10] and that ii) individuals included in the study were probably looking for care on Reunion after treatment in facilities of their home countries. Thus, MRB colonization rates estimated probably approximates the MRB epidemiological situation regarding in local hospitals. However, socio-economic status of patients seeking care on Reunion (probable people with higher incomes than the general local population) should favor access to healthcare, medicine, and hygiene and thus probably underestimate MRB colonization in local health care settings; poverty identified as a risk factor of MRB colonization.[11] Furthermore, use of intensive care unit patient's screening as reference data could over-estimate odds ratio as fewer Reunion patients should have been hospitalized in the preceding months (risk factor for MRB acquisition[12]) when compared to other SWIO patients. Thus, Reunion intensive care unit were a probable estimate of the community-acquired MRB. Finally, the small number of hospitalized patients from Seychelles and Comoros could limit our interpretations.

If ESBL-E occurrence in IOC was already highlighted as a public health issue both in community and hospitals[3], our analysis confirmed it quantitatively. For instance, ESBL-E colonization rate estimated in Madagascar was high (40.1%) which is in accordance with traveler's colonization rates reported in the literature ranging from 33.3% (1/3)[13] to 57.1% (4/7)[14] in 2013-2013 but higher than the ESBL-E colonization of 18.5% reported in community in 2013-2014[15]. High CPE colonization rate of repatriated patients from Mauritius was already reported[16] which could confirm CPE circulation in Mauritius hospitals and/or community. Important fluxes of travelers from India were probably contributing to MRB epidemiological changes in Mauritius as NDM-producing isolates are considered endemic in India[17]. Finally, comparisons of MRB colonization rates for specific MDR (i.e. MRA, MRP) were difficult to provide in other SWIO territories and Mayotte as no data were available.

Conclusion

Our study offered the first cartography of MDR colonization in SWIO. MDR colonization might constitute a risk of introduction in another country healthcare system. Reunion is a medically attractive territory which could provide the first MRB hospital-based surveillance for SWIO. The suitability of this regional MRB surveillance system should be confirmed.

Abbreviations

MDR: multidrug-resistant bacteria;

SWIO: Southwestern Indian ocean

ESBL-E: extended-Spectrum Betalactamase producing Enterobacteriaceae

MRSA: methicillin-resistant *Staphylococcus aureus*

CPE: carbapenemases-producing Enterobacteriaceae

MRA: multidrug-resistant *Acinetobacter* sp.

VRE: vancomycin-resistant enterococci.

MRP: multidrug-resistant *Pseudomonas* sp.

Declarations

Ethics declaration

Ethics approval and consent to participate

The presented work was carried out with the approval of the French Commission for Data Protection (Commission Nationale de l'Informatique et des Libertés) under the reference 2210228 v0, 10th of January 2019. None research ethics committee nor consent by individuals were required for this study as this was routinely collected and anonymized according to the Rectificatif au règlement (UE) 2016/679 du Parlement européen et du Conseil du 27 avril 2016 relatif à la protection des personnes physiques à l'égard du traitement des données à caractère personnel et à la libre circulation de ces données, et abrogeant la directive 95/46/CE (règlement général sur la protection des données) JOUE L127 2 du 23/05/2018.

Consent for publication

Not applicable.

Availability of data and materials

The data were obtained from Felix-Guyon hospital laboratory, Saint Denis, La Réunion. Data were provided for the survey according to the French law (reference 2210228 v0, 10th of January 2019) but are not publicly available.

Competing interest

The authors declare that they have no competing interests.

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Contributions

NG conceived the study. NG, OB and EC defined the study methods. OB, GM, NL provided the database. NG performed the analyses and drafted the manuscript. All authors provided comments and approved the final version of the manuscript.

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Figures

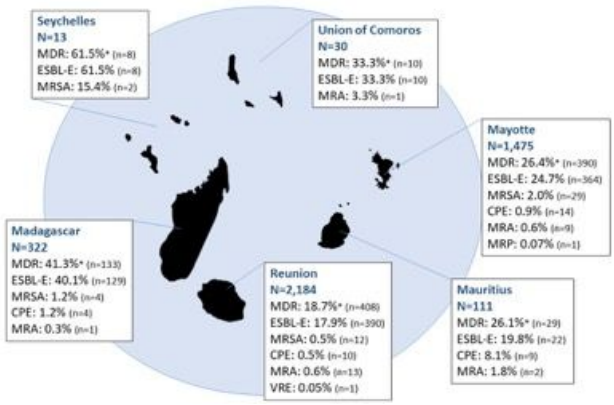

Figure 1

MRB colonization rates according to the patient country of residence in Indian ocean. * A MRB positive patient could be carrier of more than one MRB; MRB: multidrug-resistant bacteria; ESBL-E: extended-Spectrum Betalactamase producing Enterobacteriaceae; MRSA: methicillin-resistant Staphylococcus aureus; CPE: carbapenemases-producing Enterobacteriaceae; MRA: multidrug-resistant Acinetobacter sp.; VRE: vancomycin-resistant enterococci.; MRP: multidrug-resistant Pseudomonas sp.