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# Multi-drug resistant bacteria carriage on admission in a surgery reanimation of Antananarivo

**Zakasoa Mbololona Ravaoarisaina**[1*], Lalaina Vonintsoa Rahajamanana[2], Saïda Rasoanandrasana[2], Mihaja Raberahona[3], Dera Styvio Wilson Andriantahina[2], Dauphin Santatriniaina Randriarimanana[1], Mala Rakoto-Andrianarivelo[1], Tovohery Rajaonera[4], Andry Rasamindrakotroka[2] and Zelyarivelo Randriamanantany[2]

[1]*Centre of infectiology Charles Mérieux (CICM), Ankatso, Antananarivo (Madagascar)*
[2]*Department of Biology, Faculty of Medicine, University of Antananarivo (Madagascar)*
[3]*Department of Infectiology, Faculty of Medicine, University of Antananarivo (Madagascar)*
[4] *Surgery reanimation of University Hospital Centre Joseph Ravoahangy Andrianavalona, Antananarivo (Madagascar)*

## Abstract

Nosocomial infections (NCIs) are a major problem when they are caused by multi-drug resistant (MDR) bacteria. Surgery reanimations are a site frequently concerned by the emergence and spread of these germs but we found limited data of MDR bacteria in patients hospitalized in surgery reanimation. This is a first prospective, observational at the Hospital, in the surgical reanimation, from August to October 2017. The aims of this study are to screen the carriage of MDR bacteria on patient admitted in the surgical reanimation of the University Hospital Center Joseph Ravoahangy Andrianavalona (UHC-JRA), to determine the risk factors associated with the antimicrobial resistance. Nasal carriage of Methicillin resistant *Staphylococcus aureus* (MRSA) and fecal carriage of extended-spectrum β-lactamase producing (ESBL) Enterobacteria, Imipenem-resistant *Acinetobacter baumannii*, multi-resistant *Pseudomonas aeruginosa (*MDR *P. aeruginosa)* and Carbapenem resistant Enterobacteria (CRE) were assessed among patients within 24 hours of surgery reanimation admissions. Among 99 newly admitted patients, 80.80 % (80/99) were colonized with at least one MDR. The colonization prevalence with MRSA was 66.66 % (60/99) with PLP2a in 90 % (45/50). The colonization prevalence with ESBL was 44.44 % (44/99). ESBL-producing *Escherichia coli* were the most common bacteria isolated from 34 patients (34.34 %) followed by ESBL-producing *Klebsiella pneumoniae* and ESBL-producing *Enterobacter cloacae*. Indeed, the surgery reanimation patients have a high rate of colonization by MDR bacteria. The risk of infection, transmission and dissemination of resistant germs are important and requires adequate hygiene measures.

**Keywords:** Bacteria, Multi-drug resistant, Nosocomial infection, Surgery reanimation.

***Correspondence Info:**
Dr. Zakasoa Mbololona Ravaoarisaina
VK 2 TER AA Andrangaranga- Morarano
(Antananarivo, Madagascar)
Tel : +261 34 13 270 38

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## 1. Introduction

Multidrug-resistant bacteria (MDR) are currently a common cause of nosocomial infections (NSIs). NSI is a major public health concern in hospitals and health care facilities at global levels. NSI are very difficult to cure when they are caused by MDR. These infections lead in additional costs due to the length of stay, the cost of antibiotics, and care load. In addition, specific hygiene measures must be taken in addition to a greater number of analysis. They are causing an increase in mortality and morbidity.

The spectrum of antibiotic resistance is ranging from mild resistance to a broad-spectrum antibiotic. This latter

was firstly described by the World Health Organization's (WHO) on global antimicrobial susceptibility antibiotics surveillance (GLASS) published in 2014. Studies on the gastrointestinal carriage of Extended-Spectrum Beta-Lactamase-producing enterobacteria (ESBL-producing enterobacteria) conducted in Africa show results ranging from 10 to 100 %. The rate of Methicillin resistance *Staphylococcus aureus* (MRSA) varies from one country to another. The global level of MRSA is high worldwide, including in southern countries, such as Colombia where the resistance rate is 39 % [1-3].

This study aimed to assess the rate of some MDR bacteria on admission in surgery reanimation service of the UHC-JRA. The screening was including MRSA, ESBL-producing enterobacteria, Imipenem-resistant *A. baumanii* and MDR*P. aeruginosa*. After some findings about an increase of the use of carbapenems in hospitals, we wanted to determine the presence of carbapenems resistant enterobacteria (CRE) because existence in intensive care unit (ICU) in the previous studies [4-6] in Antananarivo didn't deal with the carriage of MDR bacteria, at the admission in surgical or medical reanimation.

## 2. Material and Methodology

### 2.1 Study framework and type of study

This is a monocentric, prospective observational study performed in surgery reanimation service of UHC-JRA in Antananarivo.

### 2.2 Study population and procedure

Newly admitted patients were screened at admission during August and October 2017. Nasal and rectal swabs were collected within 24 hours of surgery reanimation for screening carriage of MRSA, ESBL-producing enterobacteria, CRE, imipenem-resistant *A. baumannii* and MDR *Pseudomonas aeruginosa*.

### 2.3 Microbiological methods

One nasal swab and one rectal swab were taken at admission for each patient. The samples were transported in sterile tubes without transport medium and were processed immediately upon arrival at the laboratory.

Nasal swabs soaked with saline water 9%o were cultured directly on Chrom ID MRSA (BioMérieux, Marcy l'Etoile, France). Then microbiologist selected probable Staphylococcal colonies from the agar that are colored in green or blue green.

Rectal swabs soaked with saline water 9% were cultured on ChromID ESBL (BioMérieux, Marcy l'Etoile, France) and ChromID CARBA/OXA (BioMérieux, Marcy l'Etoile, France) for Gram negative bacteria (GNB). The identification was confirmed by API 20E or 20NE systems (BioMérieux, Marcy L'Etoile, France), depending on the reactivity with the oxidase test which was performed with OXIDASE© (OXOID). When the strains were oxidase negative, the API 20E system where used for the identification of enterobacteria and when it was positive, the API 20NE system was used for the identification of fermentative GNB.

The antibiotic sensitivity of all isolated strains tested by the disk diffusion method on Mueller-Hinton (MH) medium according to the CLSI (Clinical and Laboratory Standard Institute) and interpreted using the recommendation of CA-SFM/EUCAST 2017 [7].

We tested antimicrobial susceptibility of *Staphylococcus* strains with 14 antibiotics manufactured by OXOID as shown in **Table 1.** All suspicious *Staphylococcus aureus* strains were checked for methicillin resistance by using Cefoxitin disc diffusion where the critical diameter should be less than 22 mm as recommended by the CA-SFM/EUCAST (2017).

Antimicrobial susceptibility test for GNB strains was realized with 21 antibiotics that are seen in **Table 2**. The isolates were then screened for ESBL production using both the resistance phenotype and the double-disk synergy test by the use of conventional combination [5]. The double disc diffusion test has been done by using amoxicillin + clavulanic acid (AMC30) discs, $C_3G$ and $C_4G$ discs including Cefepime (FEP30), Cefotaxime (CTX30), Ceftazidime (CAZ10) and Aztreonam (ATM30) discs with a distance of 3 mm from center to center. When high level cephalosporinase is produced by enterobacteria, seeding on medium with cloxacilline 250µg/ml of MH was carried out.

Before using all culture media, two references strains manufactured by ATCC were used. *S. aureus* ATCC 29213 and *E. coli* ATCC 25922 were seeded on MH agar and respectively on the prefabricated ChromID MRSA and ChromID ESBL agar plates as part of an internal quality control (IQC). An agar sterility test was performed (incubation for 48 h) at each production batch for MH agar plates and at the beginning of the study for MRSA and ChromID ESBL.

**Table 1: List of antibiotics tested for *S. aureus* strains**

| Antibiotics | Charge | Abbreviations | Diameter of inhibition by CASFM/EUCAST 2017 (mm) | |
|---|---|---|---|---|
| | | | S ≥ | R < |
| Penicillin G | 1 unité | P1U | 26 | 26 |
| Cefoxitin | 30 µg | FOX30 | 22 | 22 |
| Kanamycin | 30 µg | K30 | 18 | 18 |
| Tobramycin | 10 µg | TOB10 | 18 | 18 |
| Gentamicin | 10 µg | CN10 | 18 | 18 |
| Ciprofloxacin | 5 µg | CIP5 | 21 | 21 |
| Norfloxacin | 10 µg | NOR10 | 17 | 17 |
| Erythromycin | 15 µg | E15 | 21 | 18 |
| Clindamycin | 2 µg | DA2 | 22 | 19 |
| Pristinamycin | 15 µg | PT15 | - | - |
| Fusidicacid | 10 µg | FA10 | 24 | 24 |
| Rifampicin | 5 µg | RD5 | 26 | 23 |
| Chloramphenicol | 30 µg | C30 | 18 | 18 |
| Sulfamethoxazole-trimethoprim | 25 µg | SXT25 | 17 | 14 |

**Table 3: List of antibiotics tested for gram negative bacilli**

| Nom | Charge(µg) | Abbreviations | Diameter of inhibition by CASFM/EUCAST 2017 (mm) | |
|---|---|---|---|---|
| | | | S ≥ | R < |
| Amoxicillin | 20 | AMX20 | 19 | 19 |
| Amoxicillin-clavulanic | 30 | AMC30 | 19 | 19 |
| Ticarcillin | 75 | TIC75 | 23 | 23 |
| Ticarcillin-clavulanic acid | 85 | TIM85 | 23 | 23 |
| Piperacillin | 30 | PIP30 | 20 | 17 |
| Piperacillin-tazobactam | 36 | TZP36 | 20 | 17 |
| Cefoxitin | 30 | FOX30 | 19 | 19 |
| Cefotaxim | 30 | CTX30 | 20 | 17 |
| Ceftazidim | 10 | CTZ10 | 22 | 19 |
| Cefepim | 30 | FEP30 | 27 | 21 |
| Imipenem | 10 | IMI10 | 22 | 16 |
| Ertapenem | 10 | ERT10 | 25 | 25 |
| Aztréonam | 30 | AZT30 | 26 | 21 |
| Ciprofloxacin | 5 | CIP5 | 26 | 24 |
| Ofloxacin | 5 | OFX5 | 24 | 22 |
| Nalidixicacid | 30 | NA30 | 19 | 14 |
| Amikacin | 30 | AK30 | 16 | 13 |
| Gentamicin | 10 | CN10 | 17 | 14 |
| Tobramycin | 10 | TOB10 | 17 | 14 |
| Sulfamethoxazole-trimethoprim | 25 | SXT25 | 14 | 11 |
| Chloramphénicol | 30 | C30 | 17 | 17 |

### 2.4 Statistical analysis

Data was collected with Excel including patient risk-related (RR) factors as age, gender, profession, prior hospitalization, reason of hospitalization, co-morbidities, prior exposure to antimicrobials (defined as the administration of antibiotics for more than 48 hours within 3 months preceding current hospitalization), hospitalization within the last 6 months, length of stay in ICU, use of antibiotics during hospitalization.

Treatment and analysis of data were done with Excel 2010, Epi INFO version 7 and STAT4. Relative risk (RR) was used to interpret the results with a 95 % confidence interval (CI) and a 5% margin of error α. The Chi2 test and Fisher's exact test are used to study the proportions. P value < 0.05 was considered to indicate a statistically significant difference.

### 2.5 Ethical considerations

The study was reviewed and approved by the Ethics Committee of the Ministry of public health of Antananarivo. Written informed consent was obtained from all the participants or their representatives when the patient was unconscious.

## 3. Results

During the period, 99 of 144 (68.75 %) patients admitted in the surgical reanimation of the hospital met the inclusion criteria and were included in the study. The global result is shown by the **figure** 1. Out of the total 99 patients enrolled for the study, colonization by MDR bacteria were found in 80 patients (80.80%). The mean age was 35 years old, ranging from 1 to 74 years old and the sex-ratio was 1.7.

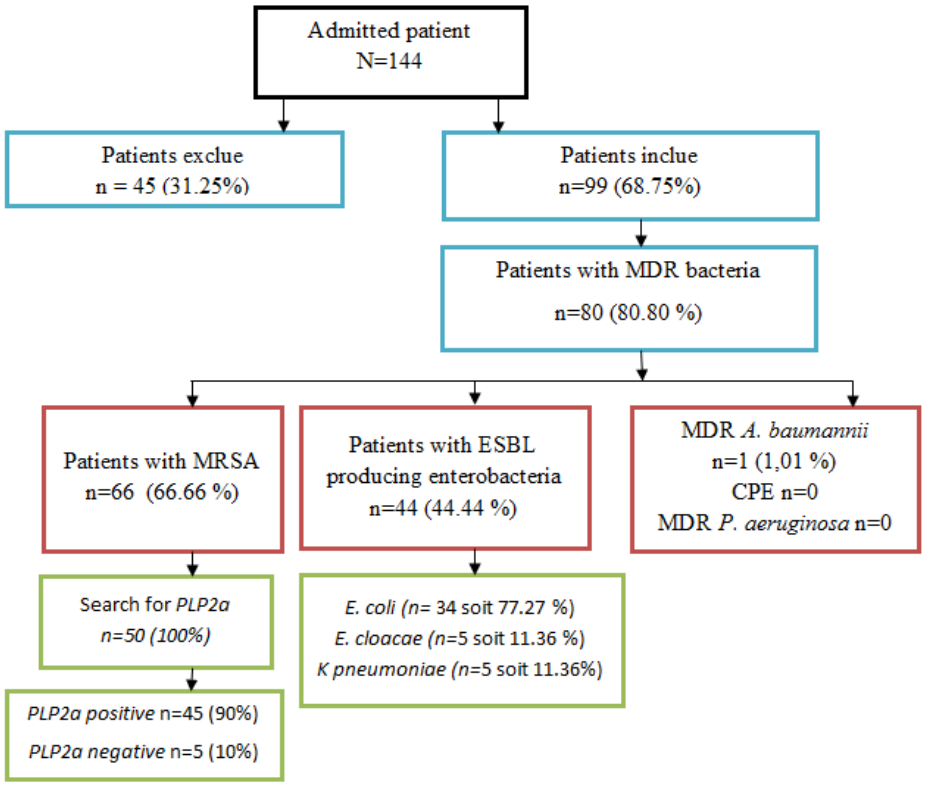


**Figure 1: Flow chart**

The demographic characteristic of MRSA is shown in **Table 3.** The rate of nasal MRSA colonization among admitted patients was 66.66% (n=66). The rate of the colonization from the emergency service was significantly higher than those admitted from other services (46.97% vs 43.93% from surgical, 9.09 % from medicine with p value = 0.05). The risk factors of carriage were studied but none of these results were statistically significant (**Table 4**). The majority (66.67%, n = 44) of MRSA carriers were transferred to other services.

**Table 3: Demographic characteristic of MRSA carriage**

| Characteristics | | MRSA n = 66 (100 %) | MSSA n = 33 (100 %) | *RR* | *CI95%* | *P value* |
|---|---|---|---|---|---|---|
| **Age** | [0-9] | 10 (15.15%) | 10 (30.30 %) | 0.87 | 0.40-1.90 | 0.74 |
| | ] 9-19] | 7 (10.61%) | 3 (9.09 %) | 1.22 | 0.57-2.61 | 0.58 |
| | ] 19-29] | 8 (12.12 %) | 5 (15.15 %) | 1.07 | 0.49-2.33 | 0.84 |
| | ] 29-39] | 9 (13.64 %) | 4 (12.12 %) | 1.21 | 0.57-2.53 | 0.58 |
| | ] 39-49] | 12 (18.18 %) | 1 (3.03 %) | 1.61 | 0.83-3.12 | 0.06 |
| | ] 49-59] | 9 (13.64 %) | 5 (15.15 %) | 1.12 | 0.53-2.38 | 0.7 |
| | ] 59-69] | 7 (10.61 %) | 2 (6.06 %) | 1.36 | 0.65-2.82 | 0.37 |
| | >69 | 4 (6.06 %) | 3 (9.09 %) | *Ref* | | |
| **Gender** | Female | 21 (31.82 %) | 14 (42.42 %) | *Ref* | | |
| | Male | 45 (68.18 %) | 19 (57.58 %) | 1.17 | 0.85-1.60 | 0.37 |
| **Professional sector** | | | | | | |
| | Primary | 8 (12.31 %) | 1 (3.03 %) | *Ref* | | |
| | Secondary | 7 (10.77 %) | 5 (15.15 %) | 0.65 | 0.38-1.11 | 0.12 |
| | Tertiary | 22 (33.85 %) | 11 (33.33 %) | 0.75 | 0.53-1.04 | 0.19 |
| | Others | 28 (43.08 %) | 16 (48.48 %) | 0.71 | 0.51-0.98 | 0.13 |

MRSA: Methicillin resistant *Staphylococcus aureus*, MSSA: Methicillin sensitive *Staphylococcus aureus CI: confidence interval*

**Table 4: Risks factors of carriage of MRSA**

| Risks factors | MRSA n = 66 (100 %) | MSSA n = 33 (100 %) | RR | CI95% | p value |
|---|---|---|---|---|---|
| **Services origin** | | | | | |
| Medicine | 6 (9.09 %) | 5 (15.15 %) | Ref | | |
| Emergency | 31 (46.97 %) | 22 (66.67 %) | 1.07 | 0.59-1.92 | 0.80 |
| Surgery | 29 (43.93 %) | 6 (18.18 %) | 1.51 | 0.86-2.66 | 0.05 |
| **Reason of hospitalisation** | | | | | |
| Pre-intervention | 11 (16.67 %) | 9 (27.27 %) | Ref | | |
| Others | 12 (18.18 %) | 8 (24.24 %) | 1.09 | 0.63-1.86 | 0.13 |
| Post-intervention | 43 (65.15 %) | 16 (48.48 %) | 1.32 | 0.86-2.02 | 0.74 |
| **Use of antibiotics** | | | | | |
| NO | 36 (54.55 %) | 20 (35.71 %) | Ref | | |
| YES | 30 (45.45 %) | 13 (30.39 %) | 1.08 | 0.82-1.43 | 0.5 |

MRSA: Methicillin resistant *Staphylococcus aureus*, MSSA: Methicillin sensitive *Staphylococcus aureus CI: confidence interval*

About the result of antimicrobial susceptibility of *S. aureus* strains, for the beta-lactamins family, Penicillin and Cefoxitin resistance were observed in 66.66% (n=66). For the quinolones, 77.27% (n=55) of *S. aureus* isolated strains were resistant to ciprofloxacin and 80.30% (n=53) to Norfloxacin and 60.6% (n=40) were resistant to all aminoglycosides. For the macrolids, we found a high level of resistance to Erythromycin in 83.33% of them (n = 55) among them 28.78% (n = 19) were resistant to Erythromycin and Clindamycin (constitutive MLSB phenotype) and 13.68% (n = 9) resistant to Erythromycin and sensitive to Clindamycin associated with an antagonism (inducible MLSB phenotype). We found some modification of PLP2 to PLP2a in 90% (45/50) of MRSA isolates.

About Enterobacteria, we found colonization in 44.44% (44/99) among included patients. The highest prevalence of gastrointestinal carriage of ESBL-producing enterobacteria was found between 0 and 9 years of age (25%, n=11/44). There was male gender predominance (70.45%). The most affected sector of activity was the tertiary sector with 25.58% (n=11/44) (**Table 5**).

Among these 44 patients, we isolated 50 enterobacteriacea among them *E. coli* is the most frequent (n=34) followed by *Klebsiella pneumonaie* (n=5), *Enterobacter cloacae* (n=5). The colonization by *Enterobacteraiceae* occurred mainly after a surgical intervention (63.15%) as shown in **table 6**.

**Table 5: Demographic characteristic of ESBL-E carriage**

| **Characteristics** | | **ESBL-E** n = 44 (100 %) | **Not ESBL-E** n = 55 (100 %) | **RR** | **CI95%** | ***P value*** |
|---|---|---|---|---|---|---|
| **Age** | [0-9] | 11 (25 %) | 9 (16.36 %) | 8.76 | 0.58-131.19 | **0.005*** |
| | ] 9-19] | 3 (6.82 %) | 7 (12.73 %) | 5.01 | 0.30-85.37 | 0.08 |
| | ] 19-29] | 6 (13.64 %) | 7 (12.73 %) | 7.42 | 0.47-115.3 | **0.04*** |
| | ] 29-39] | 4 (9.09 %) | 9 (16.36 %) | 5.14 | 0.31-83.69 | 0.07 |
| | ] 39-49] | 7 (15.91 %) | 6 (10.91 %) | 8.57 | 0.56-131.1 | **0.009*** |
| | ] 49-59] | 9 (20.45 %) | 5 (9.09 %) | 10.1 | 0.67-152.5 | **0.002*** |
| | ] 59-69] | 4 (9.09 %) | 5 (9.09 %) | 7.2 | 0.45-114.9 | **0.02*** |
| | >69 | 0 (0 %) | 7 (12.73 %) | *Ref* | | |
| **Gender** | Female | 13 (29.55 %) | 22 (40 %) | *Ref* | | |
| | Male | 31 (70.45 %) | 33 (60 %) | 1.3 | 0.79-2.14 | 0.28 |
| **Professional sector** | | | | | | |
| | Primary | 5 (11.63 %) | 4 (7.27 %) | *Ref* | | |
| | Secondary | 4 (9.3 %) | 8 (14.55 %) | 0.6 | 0.22-1.61 | 0.35 |
| | Tertiary | 11 (25.58 %) | 22 (40 %) | 0.6 | 0.28-1.28 | 0.25 |
| | Others | 23 (53.49 %) | 21 (38.18 %) | 0.9 | 0.49-1.8 | 0.87 |

**Table 6: Risks factors of carriage of ESBL-E**

| **Characteristics** | **ESBL-E n = 44 (100 %)** | **Not ESBL-E n = 55 (100 %)** | **RR** | **CI95%** | **p value** |
|---|---|---|---|---|---|
| **Service origin** | | | | | |
| Medicine | 4 (9.09 %) | 7 (12.73 %) | Ref | | |
| Emergency | 20 (45.45 %) | 33 (60 %) | 1.03 | 0.44-2.44 | 0.22 |
| Surgery | 20 (45.45 %) | 15 (27.27 %) | 1.57 | 0.68-3.61 | 0.94 |
| **Reason of hospitalization** | | | | | |
| Pre-operative | 7 (15.91 %) | 13 (23.64 %) | Ref | | |
| Post-operative | 29 (65.91 %) | 30 (54.55 %) | 1.40 | 0.73-2.69 | 0.27 |
| Others | 8 (18.18 %) | 12 (21.82 %) | 1.14 | 0.51-2.55 | 0.74 |
| **Use of antibiotics** | | | | | |
| NO | 18 (32.14 %) | 38 (67.86 %) | Ref | | |
| YES | 26 (60.47 %) | 17 (39.53 %) | 1.14 | 0 .51-2.55 | **0.004*** |

Antibiotic resistance of ESBL-producing enterobacteria has been reported in the **Table 7.** For the beta-lactamins family, the level of bacterial resistance rates to amoxicillin, ticarcillin and ticarcillin-clavulanic acid were all 100%. ESBL-producing enterobacteria have 27.35% resistance to piperacillin-tazobactam combination. For cephalosporins, resistance to $C_3G$ and $C_4G$ (Cefotaxim, Ceftazidim, Cefepim) was noted in approximately 80% of strains. For aminoglycosides, lower resistance was observed with 24.94% to Amikacin, 31.13% to Tobramycin and 32.25% to Gentamicin. For fluoroquinolones, high resistance was found with 76.65% to Ciprofloxacin, 79.11% to Ofloxacin and 72.24% to Nalidixic Acid respectively. The Sulfamethoxazole-trimethoprim resistance rate was 57.88%. A low rate of resistance was observed at Chloramphenicol was 11.38%.

About other germs, one carriage of Imipenem resistant *A. baumannii* was detected during this study but none CRE carriage and nor MDR *P. aeruginosa* strains was isolated.

**Table 7: Antimicrobial susceptibility of ESBL-producing enterobacteria strains**

| | *E. coli n=34(%)* | *K. pneumoniae n = 5 (%)* | *K. oxytoca n = 1 (%)* | *Raoultellaterrigena n = 5 (%)* | *E. cloacae n = 5 (%)* | *E. sakazakii n = 2 (%)* | *Pantoae n = 1 (%)* | *p value* |
|---|---|---|---|---|---|---|---|---|
| AMX | 34 (100) | 5 (100) | 1 (100) | 2 (100) | 5 (100*) | 2 (100) | 1 (100) | *1* |
| AMC | 20 (58.8) | 3 (66.66) | 0 | 1 (50) | 5 (100*) | 2 (100) | 1 (100) | *0.14* |
| TIC | 34 (100) | 5 (100) | 1 (100) | 2 (100) | 5 (100) | 2 (100) | 1 (100) | *1* |
| TCC | 34 (100) | 5 (100) | 1 (100) | 2 (100) | 5 (100) | 2 (100) | 1 (100) | *1* |
| PIP | 33 (97.05) | 4 (83.33) | 1 (100) | 2 (100) | 5 (100) | 2 (100) | 1 (100) | *0.4* |
| TZP | 6 (17.65) | 1 (16.66) | 0 | 0 | 3 (57.14) | 2 (100) | 0 | *0.06* |
| FOX | 4 (11.77) | 0 | 0 | 0 | 4 (85.71) | 2 (100) | 0 | ***0.0003**** |
| CTX | 34 (100) | 5 (100) | 1 (100) | 2 (100) | 5 (100) | 2 (100) | 0 | *0* |
| CAZ | 33 (97.06) | 5 (100) | 1 (100) | 2 (100) | 5 (100) | 2 (100) | 0 | *0.7* |
| FEP | 32 (94.11) | 5 (100) | 1 (100) | 2 (100) | 4 (85.71) | 2 (100) | 0 | *0.12* |
| IMI | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ***0.03**** |
| ETP | 0 | 0 | 0 | 0 | 0 | 0 | 0 | *0.3* |
| ATM | 27 (79.42) | 4 (83.33) | 1 (100) | 2 (100) | 5 (100) | 2 (100) | 0 | *0* |
| AK | 10 (29.41) | 1 (16.66) | 0 | 2 (100) | 1 (28.57) | 0 | 0 | *0.2* |
| TOB | 15 (44.12) | 1 (16.66) | 0 | 2 (100) | 3 (57.14) | 0 | 0 | *0.1* |
| CN | 12 (35.29) | 2 (33.33) | 0 | 2 (100) | 3 (57.14) | 0 | 0 | *0.07* |
| CIP | 27 (79.42) | 5 (100) | 1 (100) | 2 (100) | 3 (57.14) | 2 (100) | 0 | *0.07* |
| OFX | 28 (82.35) | 5 (100) | 1 (100) | 2 (100) | 4 (71.42) | 2 (100) | 0 | ***0.02**** |
| NA | 23 (67.64) | 3 (66.66) | 1 (100) | 2 (100) | 4 (71.42) | 2 (100) | 0 | *0.15* |
| C | 2 (5.88) | 1 (16.66) | 0 | 0 | 3 (57.14) | 0 | 0 | ***0.0003**** |
| SXT | 22 (64.70) | 4 (83.33) | 1 (100) | 1 (50) | 0 | 2 (100) | 0 | *0.07* |

Natural and acquired resistances were combined in the result.

## 4. Discussion

Since a few years, Madagascar physicians are more aware of antibiotic resistance, especially in hospital services. Then, some programs dealing with fight against NSIs exists. The surgical reanimation service was chosen as a site of MDR bacteria in this study. The antibiotic selection pressure is higher in this sector due of the massive use of antibiotics with a very broad spectrum on admission large broad range of treatments. The severity of the pathology leading to resuscitation exposes the patient to the risk of infection following the secondary immunodrepression state.

The reanimation service is a place of acquiring and disseminating MDR bacteria, especially MRSA and ESBL-producing enterobacteria. They are commensal bacteria, hand-held germs, naturally present on the skin and could be transmitted by care.

In this series, the prevalence of MDR bacteria carriage on admission was 80.80% (80/99). This prevalence is very high compared to that found in Vietnam [9], Europe [10], China [11], the USA [12], Morocco [13], and Algeria [14]. The lack of hygiene may explain this result. Recommendations dealing with hygiene measures exist in order to reduce the cross-transmission of MDR bacteria outside epidemic situations [15]. Some measures can be implemented in the surgical reanimation department of the UHC-JRA, despite the lack of resources and infrastructures. Hand hygiene is not common. There is no hydro-alcoholic solution anywhere in the ward. Hand washing at the entrance of the service is not carried out by the health staff. The lack of staff forces nurses to move from one patient to another one without any possibility of taking into account the preventive measures of cross-transmission of hospital germs. The knowledge of MDR bacteria transmission factors specific to reanimation service is the key elements in the fight against the spread.

The prevalence of MRSA colonization on admission in our study is very high (66.66%) compared with similar studies in Africa [16]. Thus, this result could be a reflection of a high proportion of permanent MRSA carriage in the general population of Antananarivo or a high proportion of intermittent carriage of MRSA following the passage through the various hospital services as the emergency, the operating room or during transport to the hospital before arrivals in emergency service. There is a disparity in the

proportion of MRSA between hospital's services: it reaches 72% in long stays, 35% in ICU and 32% in short stays.

The rate of carriage on admission depends on the multiple factors such as epidemiological situation at the country or hospital level, individual risk factor of carriage including age of patient, history of prolonged hospitalization, and chronic diseases or in areas at risk (resuscitation, long-term care). The admission carriage prevalence is different between the surgical reanimation services (10.3%) and the medical reanimation services (6.1%) [17].

The male gender predominance could be explained by the inclusion of male patients admitted in hospital [18]. However, there is no correlation between gender and nasal carriage of *S. aureus*. Some risk factors are well known, such as age superior than 60 years. Compared with literature data, there was no decrease in carriage with age [19] because in our finding, there is an increased prevalence; the high prevalence was noted in the age group 39-49 years followed by children under 9 years of age. There's also a lack of correlation between nasal carriage and profession [20] in our series.

The carriage of hospital or community acquired-MRSA has no clinical definition in this study, any carrier of nasal MRSA from the Emergency was considered suspect of carriage of community-acquired MRSA because of lack of genotyping. The lack of early sampling is a limitation to define hospital or community acquired-MRSA.

Depending on the reason for hospitalization in surgical reanimation, postoperative management was found in 65.91% (n = 43/66) of the cases. The most common reason for surgical intervention is the evacuation of cerebral hemorrhages. The risk of surgical site infection with MRSA in these patients is high. Screening for pre-operative carriage for all types of surgery, particularly in thoracic surgery, neurosurgery, urology, orthopedics and traumatology, is essential to contribute to surgical site infection prevention.

In the literature, a parallelism between antibiotic consumption and the incidence of resistant bacterial infections was demonstrated [21]. The emergence of antibiotic-resistant bacteria can be promoted by the appropriate or inappropriate use of antibiotic molecules. In this study, this hypothesis was not demonstrated. Most patients with MRSA carriage, reported in this study, had not taken antibiotics.

The absence of risk factor in patients with MRSA confirms the suspicion of carriage community-acquired MRSA spread. These last are generally less multi-resistant than hospital strains and often express Panton Valentine Leucocidin (PVL) [22] which causes serious skin infections. These so-called community-acquired MRSA remained sensitive to most conventional antistaphylococcal antibiotics, except beta-lactam antibiotics.

In this study, all *S. aureus* isolated were resistant to Penicillin, which was found in other study. Cefoxitin resistance confirmed by the presence of a modification of PLP2 [23] defines resistance to oxacillin and methicillin. Isolated MRSA strains exhibited high resistance to usual antistaphylococci. These elevations of resistance to frequently used molecules confirm the misuse of antibiotics in hospital and community settings.

Nasal carriage of MRSA has no impact on the length of stay, but the length of stay in surgical resuscitation patients could promote the transmission and dissemination of MRSA. An extended stay in the service is a source of dissemination of germs in the service itself. The risk of cross-transmission from one patient to another one during care is increased both in a short stay and long stay in the service.

About ESBL-producing enterobacteria carriage, the prevalence of gastrointestinal carriage on admission to surgical reanimation is 44.44% (n = 44/99) vs 66% in Saudi Arabia [24]. The frequency of admission of the male gender to the surgical reanimation during the study caused a high proportion of male carriage, but other studies found female gender predominance [25].

The highest prevalence of ESBL-producing enterobacteria carriage was found in children. In this study, a community lifestyle and a concept of child dependency from 0 to 9 months is an acquisition risk factor. Also, the high prevalence of carriage of the tertiary sector population shows that community living is the main factor in the acquisition of these MDR.

Community (45.45%) or hospital (45.45%) acquired ESBL-producing enterobacteria patients led to the conclusion that the acquisition risk is the same in both community and hospital settings. Some departments of Surgery, where the use of invasive devices such as urinary catheters and mechanical ventilation have been more concerned with carriage such as thoracic surgery services and urology. Others studies have shown other services that are more concerned with the rectal carriage of ESBL-producing enterobacteria such as orthopedic and reanimation services, which accounted 30% and 27% of carrier cases respectively, followed by medicine woman with a rate of 20% [26].

The enterobacteria strains most frequently isolated in this study were ESBL-producing *E.coli* followed by ESBL-producing *K. pneumoniae*. In contrast, other studies were found a high rate of ESBL-producing *K. pneumoniae* (45% to 51%) followed by ESBL-producing *E.coli* (8.5% to 18%) [27]. Various factors related to antibiotic therapy, place of origin, pathology, invasive devices used, gender and age

were frequently associated with the acquisition of an ESBL-producing strain. During hospitalization, the most common acquisition factors for ESBL-producing enterobacteria were age> 65 years old and broad-spectrum antibiotic therapy [28, 29].

About antibiotic susceptibility of enterobacteria strains, all strains were resistant to β-lactams except against Piperacillin-tazobactam and Imipenem. Piperacillin-tazobactam and Sulfamethoxazole-trimethoprim could be used to treat infection by ESBL-producing enterobacteria or other MDR bacteria before using Carbapenems. So, a susceptibility test of antibiotic resistance is essential before any treatment of an infection despite the strong presumption of MDR bacteria even in epidemic period and not rush to use Carbapenems.

For detection, the recommended screening of MDR bacteria carriage is to have an early, weekly and then exit sampling that could increase the number of isolated enterobacteria [30], but the most cost-effective screening strategy would be two swabs: the first at the admission to avoid risk of transmitting in hospital and the second at the exit to avoid risk of transmitting in the community.

About the carriage of CRE, no carrier was detected while this study. When suspected MDR bacteria infection was suspected, the primary preventive measure is to test antimicrobial susceptibility of the strains. Faced the resistance of enterobacteriaceae against Carbapenems, alternative antibiotics are recommended [31] including penicillin-β-lactamase inhibitor combinations; Cephamycin (Cefoxitin), Fosfomycin and furans (lower urinary tract infections), Cotrimoxazole (urinary tract infections).

One carriage of Imipenem resistant *A. baumannii* was detected during this study. This was a 5-month-old child who was hospitalized for one month in the Reanimation Department of Tamatave University Hospital for a probable bronchogenic cyst. In the surgical reanimation department, there's no patient carrier of *A. baumannii* at admission. According this finding, this situation could be in favor of a hospital origin of the germ. In the literature, several acquisition risk factor of MDR *A. baumannii* may be due to contaminated surfaces that could concern ventilation equipment, invasive device, vacuum equipment to blankets and mattresses [32].

No MDR *P. aeruginosa* was found in this study. It is an environmental bacteria but it can be commensal of the digestive tract. These bacteria are rarely isolated in colonization in healthy subjects, and are common among hospitalized patients, particularly in the ICU [33].

## 5.Conclusion

Reanimation services are a starting point for the spread of multidrug-resistant bacteria that cause nosocomial infections or surgical site infection due to the multiplicity of treatments, invasive procedures and flow of patients. Our findings about MDR carriage in UHC-JRA surgical resuscitation have raised a major public health problem. The high prevalence of multi-resistant bacteria carriage on admission in surgical reanimation confirms that the service could act both as a reservoir and a source of dissemination of these germs. In addition, the germs isolated have a high resistance to the usual antibiotics. Recommendations on the hygiene and the organization of the care, specific to the reanimation service, are to be provided in order to protect the patients; the health staff. Community acquired multidrug-resistant bacteria carriage and infection with these germs must be prevented. A multidrug-resistant bacteria screening policy in surgical reanimation is essential to avoid nosocomial infections. Detection of multidrug-resistant bacteria carriage within 24 hours of admission was used as a referral to search a probable bacterial origin outside reanimation service.

**Conflict of interest:** The authors declare no competing interest.

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