Open Access Library Journal
2026, Volume 13, e13454
ISSN Online: 2333-9721
ISSN Print: 2333-9705

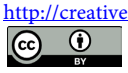
Risk Factors for Acquiring Multidrug Resistant Microorganisms (MDROs) in Hospital Settings: A Retrospective Study in a Reference Center

Volatiana Andriananja[1], Eldinaud Botofotsy[2], Vatsiarizandry Mandrosovololona[3], Laza Randremasinjara[1], Mamy Jean De Dieu Randria[1], Rado Lazasoa Andrianasolo[2]

[1]Department of Infectious Disease, University Hospital of Befelatanana, Antananarivo, Madagascar
[2]Department of Endocrine and Metabolic Disease, University Hospital of Befelatanana, Antananarivo, Madagascar
[3]Infection Prevention and Control, Health Emergency, World Health Organization Country Office, Antananarivo, Madagascar
Email: volatiana.andriananja@gmail.com

How to cite this paper: Andriananja, V., Botofotsy, E., Mandrosovololona, V., Randremasinjara, L., Randria, M.J.D. and Andrianasolo, R.L. (2026) Risk Factors for Acquiring Multidrug Resistant Microorganisms (MDROs) in Hospital Settings: A Retrospective Study in a Reference Center. *Open Access Library Journal*, **13**: e13454.
https://doi.org/10.4236/oalib.1113454

Received: April 17, 2025
Accepted: January 24, 2026
Published: January 27, 2026



Abstract

Multidrug-resistant microrganisms (MDROs) infections are a major challenge in hospitals. MDROs affect developed and developing countries and even intensive care and non-intensive care units. In this context, we conducted a study which aims to identify the factors leading to the acquisition of MDROs in a non-intensive care unit. Our study was a retrospective and analytical study. The frequency of diabetes was 64%. The factors leading to the acquisition of MDROs were: invasive medical care ($P < 0.001$); the presence of MDROs of a urinary catheter and nosocomial infections increased the risk of MDROs infection by six and nine times, respectively (OR 6.2 [95% CI: 2.1 - 17.9] and $P < 0.001$; OR 9.1 [95% CI: 3.2 - 25.2] and $P < 0.001$). MDROs are still common in patients with diabetes; infection prevention and control measures and antimicrobial stewardship programmes need to be implemented to better address the problem.

Subject Areas

Infectious Diseases

Keywords

Multidrug Resistant Microorganisms, Diabetes, Madagascar

1. Introduction

Multidrug resistant microrganism (MDROs) are defined as acquired non-susceptibility to an agent belonging to at least three categories of antimicrobial [1]. The

emergence of antibiotic-resistant bacteria is a major public health concern. The World Health Organisation (WHO) has identified antibiotic resistance as one of the three most important threats to public health in the 21st century [2]. In Western sub-Saharan Africa, mortality linked to antimicrobial resistance is 27.3 deaths per 100,000 people. If no action is taken, this figure could rise to 10 million a year by 2050, exceeding the number of cancer-related deaths [3]. In Madagascar, in the intensive care and surgical wards of two hospitals in the city, Randrianirina *et al.* found ESBL strains in more than 30% of the bacteria isolated from various bacteriological samples taken from the patients included [4]. In the community, Herindrainy *et al.* reported faecal carriage of Gram-negative bacilli-ESBL in 10% of non-hospitalized patients (hospitalized, please change hospitalised in hospitalized, and hospitalisation in hospitalization) [5]. National data were limited on MDROs because the country had restricted surveillance capabilities, several local studies and public health initiatives show that multidrug-resistant microorganisms are actively circulating in various clinical and community settings.

It is in this context that our study will be carried out in a non-intensive care patient ward to better define the extent of the problem. The main objective is to identify the risk factors for the acquisition of multidrug resistant microrganism (MDROs) in a hospital environment in a non-intensive care patient ward.

2. Method

This study was carried out in the Endocrinology and Metabolism Department of the University Hospital in the city of Madagascar. The department specialises in the treatment of endocrine, metabolic and infectious diseases. The Endocrinology and Metabolism Department has 34 beds divided into 08 rooms, including isolation rooms. Our study was spread over a period of 4 years, from 01 January 2020 to 31 December 2023. All patients hospitalized in the Department of Metabolic and Endocrine Diseases from 2020 to 2023 with a documented microbiological diagnosis. Exclusion criteria were patients with microbiological documentation of: a fungal infection or a result suggesting contamination of the sample (e.g. mixed flora). Mycobacteria and other bacteria most commonly associated with community-acquired infections such as *Streptococcus pneumoniae*, *Salmonella spp*, *Shigella spp* and *Neisseria gonorrhoeae* were excluded.

We defined variables such as:

Sociodemographic parameters were sex (male or female), age group (in years), occupation, smoking, alcoholism, history of hospitalisation in the last 6 months.

Clinical parameters were reason for admission, comorbidities: diabetes (random blood glucose ≥ 2 g/dl) and/or hypertension (BP > 140/90 mmHg), chronic respiratory disease, chronic kidney disease, recent antibiotic use (within 3 months prior to hospitalisation), presence of invasive devices (urinary catheter, central venous catheter, mechanical ventilation), complications secondary to MDR infections (severe sepsis or septic shock), site of infection: urinary tract infection, bacteraemia, skin and soft tissue infection, catheter-associated bacteraemia, length of

hospital stay.

Multidrug resistant microorganisms (MDROs): pathogenic strains that are resistant to ≥1 molecule of three or more TYPES of commonly susceptible antimicrobials drugs used in clinical practice at the same time [6].

Biological parameters during infection: CBC, CRP, ESR, serum creatinine, urea-microbiological parameters were type of bacteriological sample, microbiological results, antibiotic resistance profile. According to the literature, we define multi-resistant bacteria as Gram-positive and Gram-negative bacteria "resistant to at least three classes of antimicrobial agents".

Microbiological procedures for identification included microscopic analysis, culture on selective media, and antibiogram according to French recommendations.

Microbiological methods:

Clinical specimens (urine, blood, pus, and other relevant samples) were processed according to standard microbiological procedures. Urine samples were cultured on Cystine-Lactose-Electrolyte-Deficient (CLED) agar and MacConkey agar, while pus and other non-sterile samples were cultured on Blood agar and MacConkey agar. Blood samples were inoculated into blood culture bottles and incubated using standard automated/manual blood culture systems; positive bottles were subcultured on Blood agar and MacConkey agar.

Bacterial identification was performed using conventional biochemical tests, and when available, automated identification systems. Antibiotic susceptibility testing was carried out using disk diffusion method, and results were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Multidrug-resistant organisms (MDROs) were defined as isolates resistant to at least one agent in three or more antimicrobial classes.

- **Data collection**: Data were collected on an individual record, recorded and analysed using Epi Info 7.5.2 software.

- Statistical analysis: Risk factors for acquiring MDROs infection were investigated by univariate analysis using the following statistical tests: odds ratio (OR) and 95% confidence interval (CI), chi-squared, Fisher's exact test and Student's t-test. Variables with a P-value ≤ 0.05 were considered significant.

3. Results

During the study period from 1 January 2020 to 31 December 2023, we recorded 65 cases of MDROs infection from a total of 101 positive specimens, giving a prevalence of 64.4%. The median age was 60 years (IQR: 50 - 67 years). Half of the patients (50.6%) were older than 60 years, the majority of whom were women (38) (59%) and men (27) (41%) (Table 1). Hypertension (37) (56.9%) and diabetes (62) (95.4%) were the most common comorbidities (Table 1). 23 (35.4%) patients had received antibiotics in the previous three months (Table 1). The use of medical devices was observed in 35 (53.8%) patients (Table 1). The site of infection was mainly urinary 30 (50%), Enterobacteriaceae 46 (70.8%) were the most common

BMR (Table 1). The median length of hospital stay was 14 days, with an inter-quartile range (IQR) of 10 to 21 days. Of the patients, 31 (47.7%) have a hospital stay longer than 14 days.

Table 1. Patients' characteristics.

Patient characteristics	n (%)
Comorbidities	
• Strokes	6 (9.2%)
• Diabetes	62 (95.4%)
• Chronic Alcoholism	11 (16.9%)
• HIV	1 (1.5%)
• High blood pressure	37 (56.9%)
• Chronic kidney Diseases	8 (12.3%)
• Chronic respiratory diseases	5 (7.7%)
• Smoking	12 (18.5%)
Admission	
• Change in general condition	10 (15.4%)
• Seizure	4 (6.1%)
• Dyspnea	7 (10.8%)
• Fever	11 (16.9%)
• Wound	17 (26.2%)
• Impaired of consciousness	9 (13.8%)
• Others	5 (7.7%)
History of hospitalization in the last six months	
• Yes	28 (43.1%)
• No	37 (56.9%)
Use of antibiotics in the last 3 months	
• Yes	23 (35.4%)
• No	42 (64.6%)
Use of medical devices	
• Yes	35 (53.8%)
• No	30 (46.2%)
Medical devices	
• Parenteral nutrition	7 (20%)
• Central nervous catheter	3 (8.6%)
• Chest drain	1 (2.9%)
• Nasogastrique Tube	7 (20%)
• Urinary catheter	33 (94.3%)

Continued	
Site of infection	
• Blood stream infection	10 (6%)
• Skin and soft tissues osteitis	22 (36.7%)
• Surgical site infection	3 (3.3%)
• Urinary tract infection	30 (50%)
Type of infection	
• Acquired in community	27 (41.5%)
• Acquired in hospital	38 (58.5%)
Complications	
• Non complicated	18 (28.1%)
• Severe respiratory syndrome	26 (40.6%)
• Septic shock	20 (31.3%)
Biological results (médiane, IQR)	
• ESR, G/L	3.99 (3.42 - 4.59)
• Haemoglobin, g/dl	11.2 (9.6 - 12.5)
• Hematocrit, %	31.9 (27.6 - 35.7)
• WBC, G/L	14.47 (10.4 - 22.2)
• PNN, G/L	11.3 (8.1 - 19.7)
• Lymphocyte, G/L	1.7 (1.2 - 2.67)
• Plaquette, G/L	318 (227 - 442)
• CRP, mg/dl	75.7 (47 - 106)
• Creatininemia, µmol/L	152 (103 - 221)
• Urea, mmol/l	11.7 (7.2 - 18.9)
• HbA1C, %	9.7 (7.6 - 12)
• ASAT, UI	30 (23 - 45)
• ALAT, UI	23 (17 - 43)
• Na2+, mmol/l	136 (130 - 140)
• K2+, mmol/l	4 (3.2 - 4.7)
• Cl–, mmol/l	98.5 (94 - 105)
Type of samples	
• Urine culture	31 (47.7%)
• Pus	28 (43.1%)
• Blood culture	6 (9.2%)
Isolated Microorganisms	
• *Enterobacteria spp*	46 (70.8%)
• *Enterococcus spp*	3 (4.6%)
• *Pseudomonas spp*	5 (7.7%)
• *Staphylococcus spp*	11 (16.9%)

Continued	
***Enterobacteria spp* isolated**	
• *Acinetobacter spp*	2 (4.4%)
• *E. coli*	25 (54.4%)
• *Enterobacter spp*	2 (4.4%)
• *Citrobacter spp*	1 (2.2%)
• *Klebsiella spp*	10 (21.7%)
• *Serratia spp*	1 (2.2%)
• *Shigella spp*	1 (2.2%)
• *Proteus spp*	3 (6.5%)
Antibiotics used	
• AMOXICILLIN-acide clavulanique	3 (3.8%)
• Ceftriaxone	5 (6.3%)
• Imipenem	33 (41.8%)
• Meropenem	1 (1.3%)
• AMIKACIN	25 (31.6%)
• GENTAMICIN	1 (1.3%)
• CIPROFLOXACIN	4 (5.1%)
• Levofloxacin	1 (1.3%)
• Vancomycin	13 (16.5%)
• CLINDAMYCIN	1 (1.3%)
• Chloramphenicol	1 (1.3%)
Availability of prescribed antibiotics	
• Administered	36 (55.3%)
• Non administered	29 (44.7%)
Duration of hospital stay (médiane, IQR)	14 (10 - 21)
Outcome of patients	
• Alive	51 (78.5%)
• Deaths	14 (21.5%)

Here is the profile of resistant Enterobacteriaceae, 37 (80.4%) were ESBL resistant to Third cephalosporin generation, 39 (84%) resistant to CIPROFLOXACIN and 5 (10%) showed resistance to IMIPENEM (Table 2).

In univariate analysis, a significant association was found between the presence of invasive medical care and an increased risk of developing an MDR infection ($P < 0.001$). The presence of a urinary catheter and nosocomial infections increased the risk of MDR infection by a factor of six and nine, respectively (OR 6.2 [95% CI: 2.1 - 17.9] and $P < 0.001$; OR 9.1 [95% CI: 3.2 - 25.2] and $P < 0.001$) (Table 3).

Table 2. Resistance profile according to antibiotics tested.

Antibiotics	Effective	Résistance n (%)
Amoxiciline	44	95.7%
Amoxicilline acide clavulanique	40	87.0%
Ceftriaxone	37	80.4%
Cefixime	37	80.4%
Ceftazidime	37	80.4%
Imipenem	5	10.9%
Gentamicine	38	83.0%
Amikacine	2	4.4%
Acide nalidixique	27	58.7%
Ofloxacine	29	63%
Ciprofloxacine	39	84.7%
Chloramphenicol	11	25.6%
Cotrimoxazole	42	91.3%

Table 3. Risk factors for acquiring MDR infections in univariate analysis.

Risk factors	Non MDR	MDR	OR	IC 95%	P
Gender:					
- Man	12	27	1.36	0.5 - 3.2	0.6
- Women	23	38			
Age:					
- <60 years	21	32	1.4	0.6 - 3.2	0.3
- ≥60 years	14	33			
Comorbidities:					
- Yes	35	62	1.5	1.3 - 1.8	0.2
- No	0	3			
Diabetes:					
- Yes	Not defined	Not defined	-	-	-
- No					
Chronic Kidney disease:					
- Yes	4	8	1.08	0.3 - 3.9	0.8
- No	37	57			
Chronic respiratory disease:					
- Oui	3	5	0.8	0.2 - 3.9	0.8
- Non	32	60			

Continued

Previous hospitalization:					
- Oui	9	28	2.1	0.8 - 5.3	0.08
- Non	26	37			
Previous antibiotic use:					
- Yes	5	23	3.3	1.1 - 9.6	0.02
- No	30	42			
Medical devices:					
- Yes	5	35	6.7	2.3 - 19.7	<0.005
- No	28	29			
Urinary catheter:					
- Yes	5	33	6.2	2.1 - 17.9	<0.005
- No	30	32			
Nasogastrique tube:					
- Yes	0	7	-	-	-
- No	35	58			
Central venous catheter:					
- Yes	0	3	-	-	-
- No	35	62			
Parenteral nutrition:					
- Yes	1	3	1.6	0.1 - 16.4	0.5
- No	34	62			
Hospital acquired infection:					
- Yes	6	43	9.12	3.2 - 25.2	<0.005
- No	28	22			
Length of stay > 7 days:					
- Yes	34	60	2.8	0.3 - 25.1	0.3
- No	1	5			

4. Discussion

This study revealed a high frequency of 64.4% of multidrug resistant microorganisms (MDROs) infections in a non-intensive care unit, particularly in endocrinology. According to the literature, the high percentage of MDROs is mainly found in intensive care units, estimated at 66% [7]. The fact that our study was carried out in diabetic patients explains the high frequency of MDROs. This result is consistent with a study carried out in an African infectious diseases department, which showed that among the 111 MDROs infections hospitalized, the prevalence of diabetics was 59.4% (n = 66, CI95%: 0.50 - 0.68), with an average age of 64.3 years and a sex ratio of 0.44 [8]. In contrast, developed countries have much lower

prevalences, between 20% and 30% [9] [10]. This disparity could be explained by the lack of access to drinking water and WASH services, as well as by the over-consumption of antibiotics in developing countries. Our study population is also characterized by an over-representation of elderly people (≥60 years) and 95% diabetic patients (diabetes, hypertension), who are two groups at increased risk of colonization and infection by BMR due to immunosenescence, metabolic comorbidities and repeated hospitalizations and antibiotic use. In the face of these comorbidities, the use of invasive devices (central venous catheters, urinary catheters, mechanical ventilation, etc.) is necessary. All conditions necessary for the acquisition of MDROs were fully met.

After an analytical study, we identified the risk factors for MDROs acquisition: invasive medical care OR = 6.7 ($P < 0.005$), the presence of a urinary catheter presents an even higher risk, with an OR = 17.9 ($P < 0.005$), nosocomial or healthcare-associated infections appear to be a major risk factor for BMR acquisition, with an OR = 9.12 ($P < 0.005$), demonstrating a highly significant association. These results have been confirmed by previous studies [11] [12]. Invasive medical devices create a direct point of entry for pathogens, bypassing natural defences such as skin or mucous membranes and the biofilm that forms [11].

Among the multidrug-resistant organisms (MDROs), Enterobacteriaceae accounted for 80.4% of isolates in our study, a proportion markedly higher than that reported in some European studies (14%). A comparable prevalence has been reported in studies conducted in Cameroon, where Enterobacteriaceae were identified in nearly 100% of cases [13]-[15]. This high prevalence observed in our setting, compared with developed countries, may be explained by the extensive use of third-generation cephalosporins, which promotes the selection of β-lactamase-producing strains. Resistance to IMIPENEM (10.9%) is particularly concerning, as this antibiotic is often considered a last-resort treatment. Extended-spectrum β-lactamase (ESBL)-producing organisms were the predominant pathogens in both intensive care and non-intensive care units. Furthermore, this study reflects the reality in low- and middle-income countries, which is not directly comparable to the European context. However, it highlights the disproportionate burden of multidrug-resistant organisms (MDROs) in Africa and underscores the suboptimal implementation of antimicrobial stewardship programs in these settings, as well as the urgent need to strengthen infection prevention and control strategies and rational antibiotic use.

This study has several limitations, including its single center nature, methodological constraints and a relatively small sample size, which did not allow for multivariate analysis. In addition, the identified risk factors did not take prior antibiotic consumption into account. Despite of its limitations, it highlights the substantial burden of multidrug-resistant organisms (MDROs), which represent a significant public health threat in Madagascar. This issue affects both intensive care and non-intensive care units. Mortality remains substantial (21.5%) despite very limited medical resources. Consequently, infection prevention and control

(IPC) measures particularly patient isolation, environmental cleaning, and hand hygiene must be strengthened to control infections and prevent their spread. Regular training of healthcare workers is essential to ensure appropriate patient care. In addition, the implementation of a rational antibiotic use program, supported by national guidelines and aligned with the WHO AWaRe classification, is crucial to prevent antibiotic misuse.

5. Conclusion

Diabetic patients are at particularly high risk of infection with multidrug-resistant organisms (MDROs), due to immune dysfunction, frequent healthcare exposure and medical devices use. Strengthening infection prevention and control (IPC) measures, including strict hand hygiene, appropriate patient isolation, and environmental cleaning, is essential to reduce transmission within healthcare settings. In parallel, robust antimicrobial stewardship programs are crucial to optimize antibiotic prescribing, limit unnecessary exposure to broad-spectrum agents, and ultimately improve patient outcomes by preventing the emergence and spread of MDROs.

Conflicts of Interest

The authors declare no conflicts of interest.

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