Profile of multidrug-resistant clinical bacterial isolates at the National Hospital of Zinder (NHZ), Niger Republic in 2021

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Abstract:

Background: Today, bacterial resistance is a public health challenge throughout the world, and infections caused by resistant bacteria are associated with increased morbidity, mortality and healthcare costs. The objective of this descriptive study is to determine the prevalence and distribution of multi-drug resistant (MDR) clinical bacterial isolates at the National Hospital of Zinder, Niger Republic in 2021.

Methodology: We conducted a descriptive cross-sectional study of in- and out-patients from whose clinical samples' bacteria were isolated at the bacteriology unit of the laboratory. Bacteria were isolated from the clinical samples following standard aerobic cultures and identified using conventional biochemical test schemes. Antibiotic susceptibility testing (AST) was performed by the agar disk diffusion technique, and categorization of the isolates into sensitive, intermediate or resistant was done according to the recommendations of the Antibiogram Committee of the French Society of Microbiology (CA-SFM) 2020 version 1.2. MDR was defined as resistance to at least one antibiotic in three or more categories, while selected MDR bacteria such as ESBL was identified using double disk synergy test, and MRSA by cefoxitin disk diffusion test.

Results: Seventy-seven (6.7%) bacterial species were isolated from 1153 clinical samples processed at the bacteriology unit of the hospital laboratory between June and December 2021, of which 65.0% (50/77) were members of the order Enterobacteriales. Escherichia coli represented 40.3% (40/77) of the isolated bacteria, Staphylococcus aureus 13.0% (10/77) and Pseudomonas aeruginosa 11.7% (9/77). The overall prevalence of MDR was 44.2% (34/77), including 61.8% (21/34) ESBL-producing Enterobacteriales (ESBL-E), 26.5% (9/34) multi-resistant P. aeruginosa and 11.7% (4/34) MRSA, with 67.6% (23/34) of the MDR isolates from out-patients. Resistance rates of the Enterobacteriales to ciprofloxacin, gentamicin, amikacin and imipenem were 62.0%, 52.0%, 38.0% and 8.0% respectively. Resistance rates of P. aeruginosa were 100.0%, 88.9%, 77.8%, 33.3%, 22.2%, and 22.2% respectively to ceftazidime, ticarcillin, imipenem, ciprofloxacin, levofloxacin, and amikacin. Resistance rates of S. aureus were 100.0%, 50.0%, 40.0%, 10.0%, 0% and 0% to penicillin G, erythromycin, cefoxitin, tetracycline, fusidic acid, and chloramphenicol respectively. ESBL-E were 47.6%, 85.7% and 0% resistant to amikacin, ciprofloxacin and imipenem, and MRSA resistance rates were 75.0%, 75.0%, 50.0% and 0% to erythromycin, tetracycline, gentamicin, and chloramphenicol respectively.

Conclusion: This study reports high prevalence of MDR bacteria, mainly ESBL-E, with concerning high resistance to carbapenem. Rational use of antibiotics and implementation of surveillance system for MDR bacteria must be implemented in order to limit the emergence and spread of MDR bacteria in Niger Republic.

Keywords: MDR bacteria; inpatient; outpatient; Zinder; Niger Republic

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Résumé:

Contexte: Aujourd'hui, la résistance bactérienne est un défi de santé publique dans le monde entier, et les infections causées par des bactéries résistantes sont associées à une augmentation de la morbidité, de la mortalité et des coûts des soins de santé. L'objectif de cette étude descriptive est de déterminer la prévalence et la distribution des isolats cliniques de bactéries multirésistantes (MDR) à l'Hôpital National de Zinder, République du Niger en 2021.

Méthodologie: Nous avons mené une étude transversale descriptive des patients hospitalisés et ambulatoires dont les bactéries des échantillons cliniques ont été isolées à l'unité de bactériologie du laboratoire. Les bactéries ont été isolées des échantillons cliniques à la suite de cultures aérobiennes et anaérobies et la catégorisation des isolats en sensibles, intermédiaires ou résistants a été faite selon les recommandations du Comité Anti-biogramme de la Société Française de Microbiologie (CA-SFM) 2020 version 1.2. La MDR a été définie comme la résistance à au moins un antibiotique dans trois catégories ou plus, tandis que certaines bactéries MDR telles que les BLSE ont été identifiées à l'aide d'un test de synergie à double disque et le SARM par le test de diffusion sur disque de céfoxitine.

Résultats: Soixante-dix-sept (6,7%) espèces bactériennes ont été isolées à partir de 1153 échantillons cliniques traités à l'unité de bactériologie du laboratoire hospitalier entre juin et décembre 2021, dont 65,0% (50/77) appartenaient à l'ordre des Enterobacteriales. Escherichia coli représentait 40,3% (40/77) des bactéries isolées, Staphylococcus aureus 13,0% (10/77) et Pseudomonas aeruginosa 11,7% (9/77). La prévalence globale des MDR était de 44,2% (34/77), dont 61,8% (21/34) d'Enterobacteriales productrices de BLSE (BLSE-E), 26,5% (9/34) de P. aeruginosa multirésistantes et 11,7% (4/34) SARMS, avec 67,6% (23/34) des isolats de MDR provenant de patients externes. Les taux de résistance des Enterobacteriales à la ciprofloxacine, à l'amikacine, à l'amoxicilline et à l'imipénème étaient respectivement de 62,0%, 52,0%, 38,0% et 8,0%. Les taux de résistance de P. aeruginosa étaient respectivement de 100,0%, 88,9%, 77,8%, 33,3%, 22,2% et 22,2% à la céftazidime, à la ticarcilline, à l'amoxicilline et à la ciprofloxacine, à la lévofloxacine et à l'amoxicilline. Les taux de résistance de S. aureus étaient respectivement de 100,0%, 50,0%, 40,0%, 10,0%, 0% et 0% à la pénicilline G, à l'érythromycine, à la céfoxitine, à la tétracycline, à l'acide fusicaque et au chloramphénicol. Les BLSE-E étaient de 47,6%, 85,7% et 0% de résistance à l'amoxicilline, à la ciprofloxacine et à l'imipénème, et les taux de résistance au SARM étaient respectivement de 75,0%, 75,0%, 50,0% et 0% à l'érythromycine, la tétracycline, la gentamicine et le chloramphénicol.

Conclusion: Cette étude rapporte une prévalence élevée de bactéries MDR, principalement des BLSE-E, avec une résistance élevée aux carbapénèmes. L'utilisation rationnelle des antibiotiques et la mise en place d'un système de surveillance des bactéries MDR doivent être mises en œuvre afin de limiter l'émergence et la propagation des bactéries MDR en République du Niger.

Mots-clés: Bactérie MDR; patient hospitalisé; ambulatoire; Zinder; République du Niger

Introduction:

The discovery of antibiotic and its development for therapy from 1940s has considerably reduced the mortality associated with infectious diseases. However, the widespread use and misuse have resulted in the adaptation of bacteria, with emergence and dissemination of resistant bacteria that continue to be major cause of mortality and increased health care costs from resistant infections for over 50 years (1,2).

The World Health Organization (WHO) has estimated that infectious disease account for 45% of deaths in Africa and South-East Asia and bacterial infections account for a significant proportion of these in Africa (3). More recent estimates indicate 4.95 million associated deaths and 1.27 million attributable deaths due to AMR infections (4). Also, the WHO describes gaps in surveillance despite the threat presented by AMR pathogens. This lack of quality data is problematic and leads to treatment guidelines that are not adapted to the local context (5). In order to better understand the problems and to effectively tackle these, it is necessary to conduct epidemiological surveillance of bacteria.

In Niger Republic, few studies have been conducted on the epidemiology and antimicrobial susceptibility of bacteria to antibiotics. It is for this reason that we conducted this study to determine the epidemiology and susceptibility profiles of clinical bacteria isolates at the National Hospital of Zinder (NHZ) in Niger Republic.
Materials and method:

Study setting and population
We conducted a descriptive cross-sectional study at the National Hospital of Zinder, Niger Republic, from June to December 2021. National Hospital of Zinder is 740 bed capacity hospital with several clinical service departments and units. The study population was composed of all patients (inpatients and outpatients) from whom clinical samples (urine, pus, stool and others) were collected and submitted to the bacteriology unit of the laboratory for analysis.

Only patients from whom bacteria were isolated from their samples during the period of the study were included. Clinical and laboratory variables of the patients such as age, sex, bacterial species isolated, antibiotic sensitivity profile, and multidrug-resistant (MDR) patterns were collected with a designed data collection form.

Ethical approval
The study was approved by the National Hospital of Zinder ethical committee. Anonymity and confidentiality of the data were guaranteed.

Isolation and identification of bacteria
After macroscopic and microscopic examinations of clinical samples, pus was plated on Chapman (Mannitol salt agar) and fresh blood agar; urine was plated on CLED agar; stool samples were plated on Hektoen enteric medium for Salmonella and Shigella; and on Sorbitol MacConkey agar for Escherichia coli. The inoculated media were incubated aerobically at 37°C for 18-24 hours. The identification of bacterial isolates on culture plates was performed on the basis of their cultural characteristics and conventional biochemical test schemes (6).

Antibiotic susceptibility testing
Antibiotic susceptibility testing (AST) was performed using the agar disk diffusion technique (7) against selected antibiotics including penicillin (penicillin, amoxicillin, amoxicillin-clavulinate, piperacillin, piperacillin-tazobactam, ticarcillin, ticarcillin-clavulanic acid), cephalosporin (cefalotin, cefoxitin, ceftiraxone, cefixime, cefotaxime, ceftazidime), aztreonam, carbapenem (imipenem) amnoglycoside (gentamicin, kanamycin, amikacin, tobramycin), fluoroquinolone (ciprofloxacin, levofloxacin), sulfonamide (cotrimoxazole), macrolide (erythromycin), tetracycline, chloramphenicol and fusidic acid. The categorization of the isolates into sensitive, intermediate or resistant was done according to the recommendations of the Antibiogram Committee of the French Society of Microbiology (CA-SFM) 2020 version 1.2. Multi-drug resistance was defined as resistance to at least one antibiotic in three or more antibiotic categories (8).

Detection of selected multi-resistant bacteria
ESBL phenotype was detected on standard antibiogram according to the double disk synergy technique described by Jarlier et al, (9), which entails demonstrating synergy between clavulanic acid disc and a third-generation cephalosporin (cefotaxime, ceftazidime or ceftriaxone) separated by 30 mm on the agar plate. The presence of ESBL was determined after 18 to 24 hours of incubation by the appearance of ‘champagne cork’ synergistic action between the two antibiotics. The detection of methicillin resistance in S. aureus was performed by measuring the zone of inhibition around a 30µg cefoxitin disk (as surrogate for methicillin resistance) of less than 22 mm on Mueller Hinton agar plate after 24 hours of incubation (7).

Statistical analysis
The data were entered into Microsoft Excel 2013 and statistical analysis was performed using EPI INFO software v 3.5.4.

Results:

Sociodemographic characteristics of patients
A total of 77 patients from whose clinical samples’ bacteria were isolated formed the study participants, with a male to female ratio of 1.5. The mean age of the patients was 34.2±22.85 years, with a range of 5 months to 78 years. The socio-demographic data of the patients are summarized in Table 1.

The bacteria isolates were predominantly recovered from clinical samples of outpatients (62.3%, 48/77), urine was the most common specimens (56.7%, 40/77), and Enterobacteriales constituted majority of the isolates (65%, 50/77).

Distribution of isolated bacteria by species
Of the 77 bacteria isolates, E. coli represents 40.3% (n=31) and thus constitutes the majority of the species isolated, followed by S. aureus and P. aeruginosa representing respectively 13% and 11% of the isolated bacteria (Table 2).
Table 1: Distribution of the study population by age, gender, patient type and sample

| Characteristics          | Frequency | Percentage |
|--------------------------|-----------|------------|
| Gender                   |           |            |
| Male                     | 47        | 61.0       |
| Female                   | 30        | 39.0       |
| Mean age (years)         | 34.2±22.85|            |
| Age range                | 5 months-78 years | |
| Type of patients         |           |            |
| Inpatient                | 29        | 37.7       |
| Outpatient               | 48        | 62.3       |
| Types of samples         |           |            |
| Urine                    | 40        | 56.7       |
| Pus                      | 28        | 36.4       |
| Others                   | 9         | 6.9        |

Table 2: Distribution of isolated bacteria by Taxonomical groups and species

| Isolated bacteria                  | Numbers | Percentage |
|------------------------------------|---------|------------|
| **Order Enterobacterales (n=50)**  |         |            |
| *Escherichia coli*                 | 31      | 40.3       |
| *Klebsiella pneumoniae*            | 6       | 7.8        |
| *Klebsiella oxytoca*               | 2       | 2.6        |
| *Klebsiella spp*                   | 1       | 1.3        |
| *Citrobacter koseri*               | 1       | 1.3        |
| *Morganella morganii*              | 1       | 1.3        |
| *Proteus mirabilis*                | 3       | 39         |
| *Providencia stuartii*             | 1       | 1.3        |
| *Serratia odorifera*               | 2       | 2.6        |
| *Salmonella spp*                   | 2       | 2.6        |
| **Order Pseudomonadales (n=10)**   |         |            |
| *Pseudomonas aeruginosa*           | 9       | 11.7       |
| *Acinetobacter baumannii*          | 1       | 1.3        |
| **Gram positive bacteria (n=17)**  |         |            |
| *Staphylococcus aureus*            | 10      | 13.0       |
| Coagulase negative staphylococci   | 6       | 7.8        |
| *Enterococcus faecalis*            | 1       | 1.3        |
| **Total**                          | 77      | 100.0      |
Antibiotic susceptibility of bacterial isolates

All Enterobacteriales isolates (n=50) were resistant to amoxicillin (Table 3). However, the activity of amoxicillin on them was recovered by the combination with clavulanic acid. High level resistance was expressed by the Enterobacteriales to 3rd generation cephalosporins and other antibiotics, with resistance rates to ceftriaxone, cefixime, ciprofloxacin and gentamicin of 60%, 64%, 62% and 52% respectively. Amikacin was the most active antibiotic on the Enterobacteriales with 62% sensitivity of the isolates.

All the S. aureus (n=10) isolates were resistant to penicillin G, and 40% were resistant to cefoxitin, which was used as surrogate for MRSA detection. Aminoglycosides, fusidic acid and cotrimoxazole had good anti-bacterial activity with sensitivity rates of 75% to gentamicin, 87.5% to fusidic acid and 62.5% to cotrimoxazole. The best activity was obtained with chloramphenicol and clindamycin for which no isolate expressed resistance (100% sensitivity). In contrast, the lowest activity was obtained with levofloxacin with a sensitivity rate of only 28.6%.

Pseudomonas aeruginosa (n=9) isolates exhibited high resistance to carbapenam and ureido-penicillins, aminoglycosides and the carbapenems, with resistance rates of 85.7% to ticarcillin, 100% to piperacillin, 71.4% to tobramycin, and 100% to imipenem and ceftazidime. Nevertheless, levofloxacin and amikacin had high activity, with sensitivity rates of 71.4% for levofloxacin and 85.7% for amikacin (Table 3).

Prevalence of multidrug-resistant bacteria

A total of 34 of the 77 isolates were multi-drug-resistant (MDR) representing a prevalence of 44.2% (Fig 1). They were isolated most often in the male patients (46.8%, 22/47) but this was not significantly different from isolation rate from the female patients (40.0%, 12/30) (OR=1.320, 95%CI= 0.5216-3.341, p=0.7253) as shown in Table 4. The ESBL-E constituted the majority of the isolated MDR bacteria (61.8%, 21/34), followed by multi-resistant P. aeruginosa (resistant to ceftazidime and/or imipenem) (26.5%, 9/34) and MRSA 11.7% (4/34) (Fig 2).

The MDR bacteria were isolated more from samples of outpatients (47.9%, 23/48) than from samples of inpatients (37.9%, 11/29) but the isolation rate was not significantly different (OR=0.6643, 95%CI=0.2953-1.701, p=0.5365). Urine (47.5%, 19/40) was the most frequent specimens from which MDR bacteria were isolated, followed by pus (39.3%, 11/28) and others (22.2%, 2/9), but this isolation rate was also not significantly different ($x^2=0.206, p=0.3630$) (Table 4).

| Antibiotics | Enterobacteriales (%) | E. coli (%) | Klebsiella spp (%) | P. mirabilis (%) | P. aeruginosa (%) | S. aureus (%) |
|-------------|-----------------------|------------|-------------------|-----------------|------------------|--------------|
| PG          | NT                    | NT         | NT                | NT              | NT               | 10 (100.0)   |
| AMX         | 50 (100.0)            | 31 (100.0) | 9 (100.0)         | 3 (100.0)       | NT               | NT           |
| AMC         | 15 (30.0)             | 8 (26.6)   | -                 | 2 (66.6)        | NT               | NT           |
| PIP         | 46 (92.0)             | 30 (96.8)  | 2 (22.2)          | 3 (100.0)       | 9 (100.0)        | NT           |
| TIC         | 46 (92.0)             | 29 (93.5)  | 9 (100.0)         | 3 (100.0)       | 9 (100.0)        | NT           |
| PIT         | 46 (92.0)             | 30 (96.8)  | 9 (100.0)         | 2 (66.7)        | 9 (100.0)        | NT           |
| TCC         | 45 (90.0)             | 29 (93.5)  | 9 (100.0)         | 1 (33.3)        | 8 (88.9)         | NT           |
| KF          | 48 (94.0)             | 30 (96.8)  | 9 (100.0)         | 2 (66.7)        | NT               | NT           |
| CX          | 19 (38.0)             | 12 (38.7)  | 3 (33.3)          | 1 (33.3)        | 4 (40.0)         | NT           |
| CTR         | 30 (60.0)             | 20 (64.5)  | 6 (66.7)          | 1 (33.3)        | NT               | NT           |
| CEFM        | 32 (64.0)             | 21 (67.7)  | 6 (67.7)          | 1 (33.3)        | NT               | NT           |
| CAZ         | 33 (66.0)             | 22 (71.0)  | 6 (66.7)          | 1 (33.3)        | 9 (100.0)        | NT           |
| CTX         | 32 (64.0)             | 21 (67.7)  | 6 (67.7)          | 1 (33.3)        | NT               | NT           |
| IMP         | 4 (8.0)               | 3 (9.7)    | 0                 | 0               | 7 (77.8)         | NT           |
| ATM         | 28 (56.0)             | 20 (64.5)  | 5 (55.6)          | 0               | NT               | NT           |
| K           | NT                    | NT         | NT                | NT              | NT               | 3 (30.0)     |
| AK          | 19 (38.0)             | 14 (45.2)  | 1 (11.1)          | 1 (33.3)        | 2 (22.2)         | NT           |
| CN          | 26 (52.0)             | 16 (51.6)  | 5 (55.6)          | 1 (33.3)        | NT               | 2 (20.0)     |
| TOB         | 26 (52.0)             | 17 (54.8)  | 4 (44.4)          | 1 (33.3)        | 6 (66.7)         | 2 (20.0)     |
| CIP         | 31 (62.0)             | 21 (67.7)  | 5 (55.6)          | 1 (33.3)        | 3 (33.3)         | NT           |
| LEV         | NT                    | NT         | NT                | NT              | 2 (22.2)         | 7 (70.0)     |
| TET         | NT                    | NT         | NT                | NT              | NT               | 10 (100.0)   |
| AF          | NT                    | NT         | NT                | NT              | NT               | 1 (10.0)     |
| CHL         | NT                    | NT         | NT                | NT              | NT               | 0            |
| E           | NT                    | NT         | NT                | NT              | NT               | 4 (40.0)     |
| COT         | NT                    | NT         | NT                | NT              | NT               | 2 (20.0)     |

PG=Penicillin G, AMX=Amoxicillin, AMC=Amoxicillin-clavulanate, PIP=Piperacillin, TIC=Ticarcillin, PIT=Piperacillin-Tazobactam, TCC=Ticarcillin-clavulanic acid, KF=Cefotaxin, CK=Cefoxitin, CTR=Ceftriaxone, CFM=Cefixime, CAZ=Ceftazidime, CTX=Cefotaxime, IMP=Imipenem, ATM=Amikacin, AK=Amikacin, CN=Gentamicin, TOB=Tobramycin, CIP=Ciprofloxacin, LEV=Levofloxacin, TET=Tetracycline, AF=Fusidic acid, CHL=Chloramphenicol, E=Erythromycin, COT=Cotrimoxazole, NT=Not tested; n= number of resistant isolates.
Multi-drug resistant clinical bacteria isolates in Niger Republic

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Table 4: Statistical analysis of some variables with prevalence of MDR bacteria

| Characteristic variables | Number of patients with MDR | $\chi^2$ | OR (95% CI) | $p$ value |
|--------------------------|------------------------------|----------|--------------|-----------|
| Gender                   |                              |          |              |           |
| Male (n=47)              | 22 (46.8)                    | 0.1235   | 1.320 (0.5216-3.341) | 0.7253+  |
| Female (n=30)            | 12 (40.0)                    |          |              |           |
| Total (n=77)             | 34 (44.2)                    |          |              |           |
| Type of patients         |                              |          |              |           |
| Inpatient (n=29)         | 11 (37.9)                    | 0.3822   | 0.6643 (0.2595-1.701) | 0.5365+  |
| Outpatient (n=48)        | 23 (47.9)                    |          |              |           |
| Types of samples         |                              |          |              |           |
| Urine (n=40)             | 19 (47.5)                    | 2.026    | NA           | 0.3630+  |
| Pus (n=28)               | 11 (39.3)                    |          |              |           |
| Others (n=9)             | 2 (22.2)                     |          |              |           |

MDR=multi-drug resistance; $\chi^2$=Chi square; OR=Odds ratio; CI=Confidence interval; NA=Not applicable; + =not statistically significant

Table 5: Resistance rates of MRSA and ESBL-E to selected antibiotics

| Antibiotics       | ESBL-E (%)  | MRSA (%)    |
|-------------------|--------------|-------------|
|                   | (n=21)       | (n=4)       |
| Amikacin          | 10 (47.6)    | NT          |
| Kanamycin         | NT           | 3 (75)      |
| Gentamicin        | 14 (66.7)    | 2 (50)      |
| Tobramycin        | 13 (61.9)    | 2 (50)      |
| Imipenem          | 0            | NT          |
| Ciprofloxacin     | 18 (85.7)    | NT          |
| Cefoxitin         | 11 (52.4)    | 2 (50)      |
| Cotrimoxazole     | NT           | 3 (75)      |
| Erythromycin      | NT           | 3 (75)      |
| Chloramphenicol   | NT           | 0           |
| Fusidic acid      | NT           | 1 (25)      |
| Clindamycin       | NT           | 0           |
| Levofloxacin      | NT           | 4 (100)     |

MRSA=methicillin-resistant Staphylococcus aureus; ESBL-E=Extended spectrum β-lactamase-Enterobacteriales; NT=Not tested

Antibiotic profile of selected MDR bacteria

ESBL-producing Enterobacteriales isolates exhibited high resistance to the antibiotics tested in this study. The resistance rates to ciprofloxacin, gentamicin and tobramycin were 85.7%, 66.7% and 61.9% respectively. Imipenem was the most active among the antibiotics tested against ESBL-E with sensitivity rate of 100%, followed by amikacin with sensitivity rate of 52.4% (Table 5).

Resistance rates of MRSA to kanamycin, gentamicin and cotrimoxazole were 75%, 50% and 75% respectively. The highest antibiotic activities against MRSA isolates were obtained with clindamycin (100% sensitivity), chloramphenicol (100% sensitivity) and fusidic acid (75% sensitivity) (Table 5).
Discussion:

In this study, the majority of bacterial species isolated were *E. coli* (40.3%), which is identical to the results obtained by Nadembega et al., (10) in Burkina Faso with 40.2%. Also, Salou et al., (11) in Togo and Okalla Ebongue et al., (12) in Cameroon reported predominance of *E. coli* among the species of bacteria isolated in clinical settings. Members of the order *Enterobacteriaceae* isolated from this study showed high resistance rates to penicillins with 100% resistance to amoxicillin. Gangoü-Piéboji (13) reported 87% resistance rate of *Enterobacteriaceae* isolates to amoxicillin in Cameroon. Our finding could be explained by the very frequent use of amoxicillin, especially for self-medication. However, the combination with clavulanic acid restored the activity of amoxicillin on the *Enterobacteriaceae* of up to 70% in our study. Imipenem and amikacin were the most active antimicrobial molecules on the *Enterobacteriaceae* with in vitro inhibition of 92% and 62% respectively. These results are in line with those from Okalla Ebongue et al., (12) in Cameroon and Affolabi et al., (14) in Benin Republic.

The resistance rate of *P. aeruginosa* to ceftazidime was 100% and 85.7% to imipenem in this study. A low resistance rate to imipenem was reported by Ettu et al., (15) in Nigeria, but Osundiya et al., (16) in Lagos reported high ceftazidime resistance rate of 79.4%, while ceftazidime resistance rate of 23.5% was reported by Kpoda et al., (17) in Burkina Faso. Our study report resistance rate of *P. aeruginosa* to ciprofloxacin of 33.3% but a higher rate (73.8%) was reported by Manga et al., (18) in Nigeria. Levofloxacin and amikacin had the best activity against *P. aeruginosa* isolates with sensitivity rate of 77.2% for each antibiotic in our study. These results are in agreement with those reported by Sakr et al., (19).

All the *S. aureus* isolates in our study were resistant to penicillin G, which is similar to the results reported by Andrianarivelolo et al., (20) in Madagascar and by Salem et al., (21) in Mauritania. Resistance rates to cefoxitin used as surrogate for MRSA was 40% in our study. A cefoxitin resistance rate of 54% was reported by Olabi et al., (22) and Adegoke et al., (23) reported a similar result in Nigeria. The sensitivity rate of *S. aureus* to cotrimoxazole was 80% in our study, which is similar to the rate reported by Salem et al., (21) in Nouakchott Mauritania, but higher rate of 91.7% was reported by Elhamzaoui et al., (24) in Morocco. Resistance rate of *S. aureus* to gentamicin was 20% in our study but lower rates were reported in different studies conducted in Madagascar with 5.67% (18), Burkina Faso with 0% (25), Uganda with 0% (26) and Morocco with 2.2% (24). The best anti-staphylococcal activities were exhibited by chloramphenicol (100% sensitivity), clindamycin (100% sensitivity) and fusidic acid (90% sensitivity), which was in concordance with results from studies conducted in Burkina Faso (25) and Madagascar (20).

The overall MDR prevalence rate of 44% (34/77) was obtained for the isolates in our study. Lower prevalence rate was reported in Tunisia by Kooli et al., (27) but a higher rate of 68% was reported by Metwally et al., (28). ESBL-producing *Enterobacteriaceae* constituted the majority of the MDR bacteria (61.8%. 21/34), followed by MDR *P. aeruginosa* (26.5%, 9/34) and MRSA (11.7%, 4/34). Saidani et al., (29) had previously reported a predominance of ESBL-producing *Enterobacteriaceae* in their study. In our study, ESBL-E expressed high resistance to aminoglycosides with 66.7% to gentamicin, 61.9% to tobramycin and 47.6% to amikacin. A study carried out in Madagascar reported resistance rates of 78.3% to gentamicin, 26.1% to tobramycin, but absolute sensitivity to amikacin (30). The sensitivity to amikacin seems to be more preserved compared to the other aminoglycosides. Imipenem remained active on all the ESBL-E isolates in our study. These results are consistent with those of Rakotovao in Madagascar (30), and in Burkina Faso by Zong et al., (31). Ciprofloxacin showed low activity on ESBL-E with 85.7% resistance rate. This high level of resistance among *Enterobacteriaceae* to fluoroquinolones is alarming, and is thought to be the result of the selection pressure created by over- and mis-use of fluoroquinolones, especially in the treatment of urinary and digestive infections.

In our study, the resistance rates of MRSA isolates to macrolides and aminoglycosides were 75% for erythromycin and 50% for gentamicin. The study by Ojulong et al., (32) in Uganda reported 58.8% resistance to gentamicin and 88.2% to erythromycin but absolute resistance of MRSA isolates to gentamicin and erythromycin was reported by Onwubiko et al., (33) in a study conducted in Kano, Nigeria. However, due to the low number of MRSA isolates in our study, interpretation of our findings have to be done with caution.

Conclusion:

The phenomenon of antibiotic resistance is a reality in Zinder, Niger Republic. Our study reports high antibiotic resistance expressed by clinical bacteria isolates, with high prevalence of MDR bacteria circulating both in the community and the hospital. Appropriate control measures must be desi-
igned and implemented to reduce the prevalence of MDR bacteria in Republic of Niger.

**Contributions of authors:**

All authors contributed equally to the study design, methodology, manuscript preparation and validation of the original version submitted for publication.

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