Bacterial Multidrug Resistant Patterns Associated with Intensive Care Unit Infections in Akum, Cameroon

Asakizi Augustine Nji¹* and Forcham Emmanuel Duna²*

¹Ministry of Higher Education, Department of Biological Sciences, University of Bamenda, North West, Cameroon.
²Department of Medical Microbiology & Parasitology, University of Buea, Higher Institute of Business and Management Science, Department of Medical Laboratory Sciences, School of Medical Biological Science, Cameroon.

Authors’ contributions

This work was carried out in collaboration between both authors. Author AAN designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author FED managed the analyses of the study. Authors AAN and FED managed the literature searches. Both authors read and approved the final manuscript.

ABSTRACT

Background: Patients admitted into the intensive care unit (ICU) usually have impaired immunity and are therefore at high risk of acquiring hospital associated infections. Infections caused by multidrug resistant bacteria now constitute a major problem, limiting the choice of antimicrobial therapy.

Objectives: This study was aimed at determining the antimicrobial resistance pattern of pathogens causing ICU infections at the Catholic Holy Family Hospital Akum-Bamenda. The etiological agents, prevalence and types ICU infections were also determined.

Methods: Thirteen months hospital associated infections surveillance was conducted in the hospital for patients admitted into ICU. Blood, urine, tracheal aspirate and wound biopsies

*Corresponding author: E-mail: asji2000@yahoo.com, forchampe@yahoo.com;
specimens were collected under strict asepsis and sent to the Medical Microbiology laboratory of the same institution for immediate processing. All pathogens were isolated and identified by standard microbiological methods. Disk diffusion antibiotic susceptibility testing was performed and interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

**Results:** The overall prevalence of ICU infections was 30.9% out of which 12.9% were bloodstream infections, 31.5% urinary tract infections, 38.9% pneumonia, and 16.7% skin and soft tissue infections. *Klebsiella* species and *Escherichia coli* were the predominant pathogens. Multidrug resistant organisms constituted 59.3% of the pathogens, MDR *Klebsiella* spp and MDR *E. coli* were 70.8% and 71.4% respectively. Resistance to Cefuroxime was the highest (92.9%) while Meropenem had the least resistance (21.4%).

**Conclusion:** There is a high prevalence of multidrug resistant bacteria causing ICU infections. With the advent of covid-19, infection control procedures and institution of functional antimicrobial stewardship are needed to be put in place in order to cover come this herculean task.

**Keywords:** Multidrug; resistant; bacterial; infections.

1. INTRODUCTION

Infections by multidrug resistant bacteria (MDR) occur frequently in patients admitted to intensive care unit (ICU) with incidence up to 40% in many world regions and are usually associated to high mortality [1]. In ICU patients, numerous independent risk factors for infections by MDR bacteria have been identified whose careful management associated to an appropriate use of antibiotics are fundamental. Nosocomial infection is defined as an infection that is acquired in hospital by a patient who was admitted for a reason other than that infection and in whom the pathogen was not incubating at the time of admission [2]. Risk factors for developing a nosocomial infection include: age >70 years, immunosuppression, admission to intensive care, history of trauma, antibiotic use, and use of an indwelling catheter [3]. Nosocomial infections are infections that are a result of treatment in a hospital or a healthcare unit. These infections are identified at least forty-eight to seventy-two hours following admission, so infections incubating, but not clinically apparent, at admission are excluded. It may also be within 30 days after discharge. With recent changes in health care delivery, the concept of nosocomial infections has sometimes been expanded to include other health care associated infections. These infections are also called hospital-acquired infection.

Nosocomial infections are commonly transmitted as a result of negligence of hygiene by some hospital personnel. Medical officials move from one patient to another. Thus, in a situation where they do not maintain high hygiene standards, the officials themselves serve as means for spreading dangerous pathogens. Moreover, body's natural protective barriers of the patients are bypassed by some medical procedures such as surgeries and injections. Hence with such hygienic negligence in our hospitals and other healthcare units, nosocomial infections become the order of the day and my cause severe cases of pneumonia and infections of the urinary tract, bloodstream or other parts of the body.

Despite robust infection control efforts, hospital-acquired (herein described as nosocomial) infections have been reported [4,5,6]. Heightened anxiety among the general public has resulted in individuals' reluctance to attend hospital for diagnostic tests or treatments. This may account for the significant reduction in acute hospital attendances and possibly contributed to the high excess mortality toll [7]. Prior to the current COVID-19 pandemic, nosocomial infections (most commonly from respiratory and urinary tracts and surgical wounds) already posed significant healthcare and economic burdens in both developed and resource-poor countries, with an average estimated prevalence of 8.7% worldwide [8].

Patient risk factors for development of nosocomial infection were similar and included older age, higher illness severity score, longer intensive care unit (ICU) length of stay (LOS), and respiratory insufficiency. ICU-specific exposures such as central venous catheterization and endotracheal intubation also increased risk [9]. Multidrug-resistant (MDR) gram-negative bacterial infections are recognized as one of the major threats to global health. They are leading causes of nosocomial infections in the world. The hospital environment contains a large number of immuno-
compromised individual’s and patients with diverse bacterial pathogens and normal microbiota. Nosocomial infections (NI) accounted 7–10% prevalence in the world. According to 2014 World Health Organization (WHO) report, 15% of all the hospitalized patients suffered from NIs [10]. Critically ill patients without sepsis had similarly high rates of nosocomial infection suggesting that ICU exposure, rather than sepsis itself, contributes largely to the development of nosocomial infections. Intensive care units (ICUs) are confronted with increasing number of patients with marked co-morbidities, severe acute pathology or immune suppression, and intrinsic infectious risk factors. Additionally, given the pathogenicity changes of potentially hospital-acquired pathogens, most healthcare-associated infections (HCAIs) are caused by multidrug-resistant organisms (MDR) [11]. However, infections in patients with sepsis were more commonly due to opportunistic pathogens (enterococci, *Pseudomonas aeruginosa* and viruses) implying there still may be a link to sepsis-related immunosuppression. Both exposures and host susceptibility play a role in development of nosocomial infection. As such, differences among studies in nosocomial infection and mortality rates are likely due to differences in patient selection, ICU type, primary type of sepsis, infectious diagnostics/definitions, infection prevention practices, and geographical location. Nosocomial infections with MDR organisms are major global health issues. They are very difficult for treatment and main causes of poor clinical outcome, morbidity, mortality, prolonged hospitalization and high health care costs. The situation is true and urgent in Cameroon [10]. Multidrug resistant (MDR) is defined as acquired nonsusceptibility to at least one agent in three or more antimicrobial categories or as insensitivity or resistance of a microorganism to the administered antimicrobial medicines (which are structurally unrelated and have different molecular targets) despite earlier sensitivity to it [12,13]. ICUs are often considered the epicentre of development, amplification and dissemination of drug-resistant microorganisms. Critically ill patients are particularly prone to infections because of exposure to multiple invasive procedures compromising the anatomical barriers’ defences, impairment of protective mechanisms such as cough reflex or acid gastric ambient by sedative drugs or stress-ulcer prophylaxis and the frequent impairment of the immune response induced by trauma, surgery and sepsis. Furthermore, the use of broad-spectrum antibiotics, that is closely related to development and spread of drug-resistant microorganisms, is really frequent in ICU clinical practice, with studies reporting a 30% to 60% rate of inappropriate or incorrect antibiotic prescriptions. For these reasons nosocomial infections, often caused by multidrug resistant bacteria (MDR) micro-organisms, are more common in ICUs than in other departments [1]. This study was conducted to determine the resistance pattern of ICU pathogens to antibiotics. We also determined the prevalence of ICU infections, types and pathogens associated with such infections.

2. MATERIALS AND METHODS

All patients admitted into the ICU of the Catholic Holy Family Hospital Akum -Bamenda-, from July 1st 2019 to July 31st, 2020 were included in the study. The Holy family Hospital is run by the missionary sisters of Our Lady of the Holy Rosary. It is located at Akum, Santa sub division, Mezam division of the North West region of Cameroon, in West Africa. It has a capacity of 56 beds and ongoing expanding of its bed capacity.it is a functional hospital with high standards of patient care, visiting and resident doctors, specialist doctors, dedicated and qualified staff and sisters for various fields of services. They offer PHC (primary health care (health education, disease prevention, immunization, hygiene and sanitation), outpatient department, and surgical ward, pharmacy/dispensary, medical laboratory, radiology/x-ray, Echography/ultrasound, ANC, embalmment mortuary etc. It receives patients from Akum, and neighboring villages, Diocese of Bafoussam and francophone zones of the Archdiocese of Bamenda. Socio- demographic and clinical data related to these patients were retrieved from the infection control surveillance records using a structured proforma. Ethical approval was obtained from the services of the Regional Delegation of Public Health for the North West Region.

All patients who developed infections after at least 48 hours of hospitalization were considered to have ICU acquired infections which consequently was considered as nosocomial infections. Appropriate specimens were collected under strict asepsis and sent to the Medical Microbiology laboratory of Catholic Holy Family Hospital for immediate processing. The specimens included blood, urine, wound swabs, biopsies and tracheal aspires. All pathogens were isolated and identified by standard
microbiological methods for aerobic bacteria. [14]. Antibiotic susceptibility testing was performed using the disk diffusion technique with antibiotics discs containing Augmentin 20+10 µg, Cefuroxime 30 µg, Ceftazidime 30 µg, Ceftriaxone 30 µg, Gentamycin 30 µg, Amikacin 30 µg, Ciprofloxacin 5 µg, Pefloxacin 5 µg, Levofloxacin 5 µg and Meropenem 10 µg. It was interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines [15].

Data analysis was done using the Statistical Package for the Social Sciences (SPSS), version 22 software. Data was categorized into appropriate groups and summarized using means, range and proportions and then presented using frequency tables. Differences in proportions were compared using the one sample t-test. Level of significance was set at p<0.05.

3. RESULTS

3.1 Prevalence of ICU Infections

A total of 302 patients were admitted into the ICU during the study period. Of these, 68 developed infections giving a prevalence rate of 22.51%. Three of these patients had more than one infection therefore there was a total of 71 infections.

3.2 Demographic Characteristics of Patients with Infections

The age range of patients was 4 - 80 years with a mean age of 42 (±19) years. Table 1 shows the distribution by age group. The highest number of patients was in the 60-69 age group followed by 40-49 years age group. There was no significant difference in the proportion.

Among the 71 patients with ICU infections, there were more males than females (63.38%) as opposed to 36.61% of females compared. In addition, the adult population were mostly found in the ICU units than the adolescents.

3.3 Types of ICU Infections

Table 2 shows the distribution of the types of infections acquired in the ICU. The most common site was the lungs, accounting for about 44% of infections, followed by the urinary tract (32%). Blood stream infections had the lowest prevalence of 9%.

| Characteristic | Frequency | Percentage |
|---------------|-----------|------------|
| Sex           |           |            |
| Male          | 45        | 63.38      |
| Female        | 26        | 36.61      |
| Age group1    |           |            |
| (years)       |           |            |
| 0-9           | 1         | 1.41       |
| 10-19         | 3         | 4.23       |
| 20-29         | 08        | 11.27      |
| 30-39         | 10        | 14.08      |
| 40-49         | 15        | 21.13      |
| 50-59         | 07        | 9.86       |
| 60-69         | 18        | 25.35      |
| >70           | 09        | 12.68      |
| Age group2    |           |            |
| (years)       |           |            |
| <40           | 22        | 30.99      | 0.3 |
| ≥40           | 49        | 69.01      |     |
3.4 Organisms Isolated and Prevalence of Multidrug Resistant Pathogens

The distribution of isolates is as shown in Table 3. The frequency of Gram-negative organisms was significantly higher than that of Gram-positive (79.7% vs 20.3%, \( p=0.001 \)). There were 29 isolates of *Klebsiella* spp (*Klebsiella pneumoniae*-21, *Klebsiella oxytoca*-3 and *Klebsiella aerogenes*-5) which was the predominant Gram-negative organism while *Staphylococcus aureus* was the only Gram-positive pathogen isolated. The overall prevalence of MDR organisms was 69.01%. MDR *Klebsiella* spp, *E. coli* and *Proteus* spp constituted 86.21, 75.00 and 20% of the pathogens respectively.

### 3.5 Antibiotic Resistance Profile of Pathogens Isolated

Table 4 shows the resistance pattern of the Gram-negative isolates to the tested antibiotics. Antibiotics classes tested included Penicillins (Augmentin 20+10 µg), Cephalosporins (Cefuroxime 30 µg, Ceftazidime 30 µg and Ceftriaxone 30 µg), Aminoglycosides (Gentamycin 30 µg and Amikacin 30 µg), Fluoroquinolones (Ciprofloxacin 5 µg, Pefloxacin 5 µg and Levofloxacin 5 µg) and Carbapenem (Meropenem 10 µg). There was high level of resistance to most of the antibiotics especially the Cephalosporins. Resistance to Amikacin and Meropenem was low except among *Pseudomonas* and *Enterobacter* isolates.

## 4. DISCUSSION

We found a prevalence of 22.51% of ICU-acquired infections. This is a high rate signifying that at least one out of every three patients developed infections during the study period. This value is even though a bit lower than those of Makanjuola et al., [13] reported by a study done a few years earlier in a similar setting though different geopolitical setting, implying an increasing rate of infection. Generally, urinary tract infections, pneumonia and blood stream infections appear to be the most common ICU infections which corroborates the findings of similar authors [16].

| Site of infection          | Frequency (n=71) | Percentage (%) |
|----------------------------|-----------------|---------------|
| Blood stream infections    | 6               | 8.45          |
| Skin and Soft tissue infection | 11           | 15.49         |
| Pneumonia                  | 31              | 43.66         |
| Urinary tract infection    | 23              | 32.39         |

Table 2. Types of ICU-acquired infections

| Organism isolated       | MDR (%) | Non-MDR (%) |
|-------------------------|---------|-------------|
| *Klebsiella* spp        | 25 (86.21) | 4 (13.79) |
| *Escherichia coli*      | 3 (75.00) | 1 (25.00)   |
| *Pseudomonas aeruginosa*| 9 (56.25) | 7 (43.75)   |
| *Hafnia alvei*          | 0 (0)    | 1 (100)     |
| *Proteus* spp           | 2 (20.00) | 4 (80.00)   |
| *Acinetobacter baumannii* | 1 (100) | 0 (0)       |
| *Staphylococcus aureus* | 7 (77.78) | 2 (22.22)   |
| *Enterobacter cloacae*  | 2 (40.00) | 3 (60.00)   |
| Total                   | 49 (69.01) | 22 (30.99)  |

*MDR* - Multidrug resistant organisms
### Table 4. Antibiotic resistance profile of isolated organisms

| Organisms                  | Augmentin (20+10 µg) | Cefuroxime | Ceftazidime (30 µg) | Ceftriaxone | Ciprofloxacin | Pefloxacin | Levofloxacin (5 µg) | Gentamycin | Amikacin | Meropenem |
|----------------------------|----------------------|------------|---------------------|-------------|---------------|------------|---------------------|------------|----------|-----------|
| **Klebsiella spp**         | 72.7                 | 100        | 66.7                | 92.3        | 69.2          | 71.4       | 0.0                 | 83.3       | 38.5     | 16.3      |
| **Escherichia coli**       | 80.0                 | 100        | 83.3                | 80.0        | 75.0          | 75.0       | NT                  | 100        | 0.0      | 0.0       |
| **Enterobacter spp**       | 50.0                 | 100        | 100                 | NT          | 100           | 100        | 50                  | 100        | 0.0      | 100       |
| **Hafnia alvei**           | 100                  | 0.0        | 0.0                 | NT          | 100           | NT         | NT                  | NT         | NT       | NT        |
| **Acinetobacter baumannii**| 100                  | 0.0        | 0.0                 | NT          | 100           | NT         | NT                  | NT         | NT       | NT        |
| **Proteus spp**            | 25.0                 | 80.0       | 50.0                | 0.0         | 33.3          | 100        | NT                  | 33.3       | 0.0      | 0.0       |
| **Pseudomonas aeruginosa** | NT                   | 100        | 100                 | 66.7        | 100           | 0.0        | 100                 | 50.0       | 25.0     | 50.0      |
| **Overall resistance to antibiotic (%)** | 66.7 | 92.9 | 67.7 | 81.8 | 68.0 | 70.0 | 50.0 | 71.4 | 28.6 | 21.4 |

* NT- Antibiotic was not tested
From the results obtained, it is very clear that multi drug resistant bacteria is still causing havoc and the potential of it subsiding is far from being over. This because similar works [17,13] have all indicated how severe this situation is added to the recent emergence of covi-19. Appropriate and timely antibiotic therapy using combination strategies or novel molecules is the cornerstone for treatment of complex infections. Multi resistance to clinically relevant antibiotics has been studied in Cameroon, and multidrug resistance has been identified not only in strains of Klebsiella spp, Staphylococcus aureus but Pseudomonas spp. [18]. However, even in case of appropriate antibiotic strategies, the mortality rate of patients with infections by MDR agents remains higher [1]. It has become clear that persistent immune dysfunction, a frequent occurrence in critically ill patients, plays a pivotal role in acquisition of secondary/breakthrough infections and, thus, special attention ought to be dedicated, together with the best antibiotic strategy and standard of care, to identification and management of this dysfunction in ICU patients with difficult infections. prolonged hospitalization, MDR-infections patients may have the economic impact due to increase in financial burden which was highlighted by [19]. MDR provokes obstruction in disease control by intensifying the possibility of spreading of resistant pathogens, thus, declining efficacy of treatment and, hence, resulting in prolonged time of infection in patient. The cost of treatment is also increased due to MDR as the pathogens have become resistant to commercially available drugs, which has triggered the use of more expensive therapies. Resistance to commonly prescribed antibiotics in Cameroon is high [20]. The rate of success of present-day medical applications like organ transplantation and cancer chemotherapy has contributed immensely towards development of MDR. Differences in the resistance profiles of bacterial and fungal pathogens as well as the quality of public hygiene also have a considerable impact on the effectiveness of antimicrobial agents. Expansion of global trade and tourism lead to increased potential of MDR to spread all over the world and decrease in export and import of various products affecting the economy of developing countries. Antimicrobial resistance is associated with high mortality rates and high medical costs and has a significant impact on the effectiveness of antimicrobial agents [21]. Consequently, it is important that monitoring for the evolution of multidrug resistant bacteria in Cameroon, to improve treatment guidelines and management be highlighted which is in line with Karyom Djim-Adjim-Ngana et al. [22], and to highlight the need for the implementation of screening methods rapidly.

5. CONCLUSION AND RECOMMENDATION

Despite all the measures taken bacterial multi drug resistant infections are still recurrent. This highlights the need of a continuous collaboration between ICU care specialists, medical microbiologists and the infection control team in the care of these patients compounded with covid-19 infections which has come to stay. At the same time, medical institutions can reduce the impact through triage, and setting up separate fever clinic and isolation wards. Awareness of the critical situation needs to be improved among medical staff, so that they can protect themselves adequately and help in control programmes within hospitals.

6. LIMITATIONS OF THE STUDY

The study was limited by small sample size which resulted from the short duration of data collection which conceded with covid-19 epidemic. A larger sample size spanning several years and other health facilities in adjoining town would be more robust for more statistical conclusions to be made.

7. FUNDING STATEMENT

The authors received no specific funding for this work.

DATA AVAILABILITY

All data underlying the findings described in this manuscript are fully available without restriction and have been presented in the manuscript.

CONSENT AND ETHICS APPROVAL

Ethics approval and consent to participate. Written informed consent was sought from each participant prior to inclusion in the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.
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