

Ventilator-Associated Lung Disease in an Emergency Intensive Care Unit: Epidemiological, Clinical and Bacteriological Characteristics and Antibiotic Resistance Status: Study of 202 Cases

I. Karrati^{1*}, L. Ait Said¹, M. Diakité¹, A. Hilmi¹, M. Khallouki², K. Zahlane¹¹Microbiology Laboratory, Ibn Tofail Hospital, CHU Mohamed 6 Marrakech, FMPM, Rue Abdelouahab Derrag, Marrakech 40000, Morocco²Resuscitation Service, Ibn Tofail Hospital, CHU Mohamed 6 Marrakech, FMPM, Rue Abdelouahab Derrag, Marrakech 40000, MoroccoDOI: [10.36347/sjams.2022.v010i01.010](https://doi.org/10.36347/sjams.2022.v010i01.010)

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*Corresponding author: I. Karrati

Abstract

Original Research Article

Nosocomial pneumonia is the second most common cause of nosocomial infection in the intensive care unit. They pose serious diagnostic, therapeutic and economic problems and increase the risk of death by increasing the length of stay in the ICU. Our work is a retrospective descriptive study of all patients hospitalized in the ICU who presented with ventilator-associated pneumonia (VAP) over a period of one year in the intensive care unit of Ibn Tofail Hospital in Marrakech. In our study, gram-negative bacilli were the most frequently isolated germs, with *Acinetobacter baumannii* predominating. Gram-positive cocci came in second place, represented by *Staphylococcus aureus*. In 69% of cases, the infection was polymicrobial. The resistance rate of the isolated strains was high; 95.7% of *Acinetobacter baumannii* were resistant to imipenem. Isolated strains of Enterobacteriaceae were resistant to the combination of amoxicillin and clavulanic acid in 53.3% of cases, to C3G in 30.7% of cases, to imipenem in 2.7% of cases, to amikacin in 1.4% of cases and to cotrimoxazole in 41.7% of cases. *Staphylococcus aureus* resistance was 4% to penicillin M and decreased compared to other antibiotics. The emergence of resistance to antibiotics of last resort in therapy defines multi-resistant bacteria. These were isolated in 38% of cases. *Acinetobacter baumannii* was the most isolated multidrug-resistant pathogen. In the light of this study, it appears that good management of antibiotic prescriptions, strict application of hygiene and asepsis measures as well as resistance monitoring within each ICU are necessary for the reduction of nosocomial pneumopathies with multi-resistant germs.

Keywords: Ventilator-associated pneumonia- Epidemiology- Antibiotic resistance - Intensive care unit (ICU).

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INTRODUCTION

Nosocomial infections are recognised as major public health problems in almost all countries, due to their frequency, severity and the cost of hospital care for patients. Ventilator-associated lung disease (VALD) is classically defined as occurring more than 48-72 hours after invasive mechanical ventilation via endotracheal intubation. The diagnosis is based on clinical, biological, radiological and bacteriological criteria.

The microorganisms involved are most often environmental bacteria that have acquired multiple resistances in the hospital environment, making their treatment difficult, despite the discovery of new anti-infective molecules. Therefore, we conducted a descriptive study on bronchial samples of patients

hospitalized in the ICU of Ibn Tofail Hospital with the aim of establishing the epidemiological and bacteriological profile of nosocomial pneumopathies encountered, while determining the antibiotic resistance of the most frequently isolated germs.

MATERIAL AND METHODS

This is a retrospective study conducted at the microbiology laboratory in collaboration with the ICU department of Ibn Tofail Hospital in Marrakech over a period of one year from 1 January to 31 December 2019.

Bacteriological samples are taken in case of infection established on a set of clinical, biological and radiological arguments. They are accompanied by the necessary clinical information. The different samples

received in the laboratory are: Endo-tracheal aspiration (ETA), protected distal sampling (PDS), bronchoalveolar lavage (BAL). Each sample is examined macroscopically, microscopically in the fresh state and after gram staining, cultured, identified and finally tested for antibiotic sensitivity.

RESULTS

1- Epidemiological data

The average age of our patients was 35 years, with extremes ranging from 16 to 79 years. Traumatic pathology (severe head trauma and polytrauma) was the most common reason for hospitalization in the ICU. The duration of hospitalisation varied between 4 and 52 days with an average duration of 19 days. The average onset of nosocomial pneumonia was 6 days with a minimum of 2 days and a maximum of 25 days. In our study, 26 patients developed nosocomial pneumonia (NP) before 5 days, i.e. a rate of 43% of early NP, against 35 cases of late NP, i.e. a rate of 57%. The presence of an associated infection was 15%. Urinary tract infection was the most common.

All our patients benefited from resuscitation care consisting of: semi-seated position, intubation, ventilation, sedation, urinary and nasogastric probes.

The presence of a central venous catheterisation was found in 74%. The presence of other invasive procedures (tracheotomy, reintubation, thoracic drainage, etc.) was found in 22%.

Clinically and paraclinically, fever was found in 73.77% of cases, hypothermia in 5% of cases, and abundant purulent secretions were noted in 42.62% of cases. Hyperleukocytosis was present in 90.16%. CRP was positive in 95.7% of cases with a value >100 mg/l in 89.2% of cases. A radiological image suggestive of nosocomial pneumonia was found in 75.4% of cases. The evolution was unfavourable in almost 2/3 of the cases.

2- Microbiological data

Of the 202 samples received, 115 were obtained by PDS, 37 by BAL and 50 by TEA. On direct examination, 154 samples were positive and 48 were negative. Gram staining showed the presence of BGN in 178 samples, CGP was present in 73 samples and BGP in 2 samples. For yeasts, we isolated them in 4 samples. Of the 154 direct examination positive samples, 137 were culture positive while 18 were sterile (Figure 1).

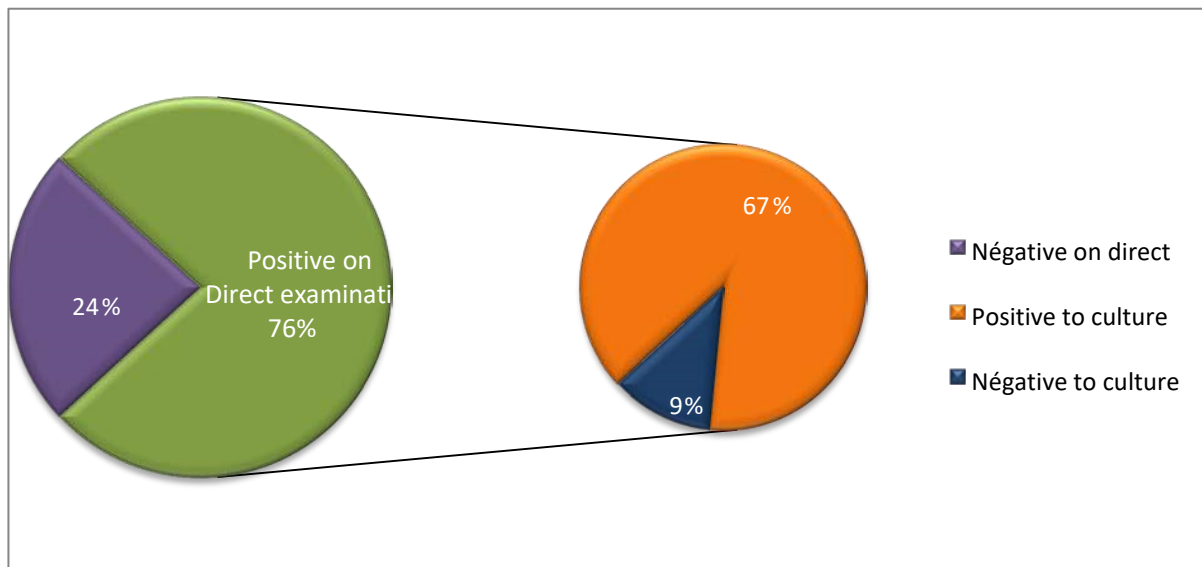


Figure 1: Frequency of positive samples

Of the positive cultures, 43 were single microbial. The number of germs isolated was 233, distributed over 14 different species. 72% of the germs

were BGN, dominated mainly by *Acinetobacter baumannii* (30%) (Table I).

Table I: Distribution of bacteria

Bacteria	Number	Percentage
Gram-negative bacilli (BGN)	168	72%
Entérobactéries	76	32,5%
<i>Klebsiella pneumoniae</i>	27	11,6%
<i>Proteus spp</i>	22	9,5%
<i>E.coli</i>	7	3%
<i>Enterobacter spp</i>	4	1,7%

Bacteria	Number	Percentage
Citrobacter spp	2	0,8%
Serratia marcescens	1	0,4%
Entérobactérie.spp	13	5,5%
BGN non fermentaires	89	38,2%
Acinetobacter baumannii	70	30%
Pseudomonas aeruginosa	19	8,2%
BGN exigeants : Haemophilus influenzae	3	1,3%
Gram- positive cocci (CGP)	65	28%
Staphylocoque	57	24,5%
Staphylococcus aureus	49	21%
Staphylococcus à coagulase négative	8	3,5%
Streptocoque : Streptococcus pneumoniae	7	3%
Entérocoque	1	0,4%

3- Antibiotic resistance profile of the main germs isolated

Acinetobacter Baumannii

Of the 70 strains of Acinetobacter baumannii isolated, the majority showed increased resistance to beta-lactams, aminoglycosides, ciprofloxacin and cotrimoxazole.

The rate of Acinetobacter baumannii resistant to imipenem (ABRI) and ceftazidime was 98.6% and 95.7% respectively.

All Acinetobacter baumannii isolates retained sensitivity to colistin (Figure 2).

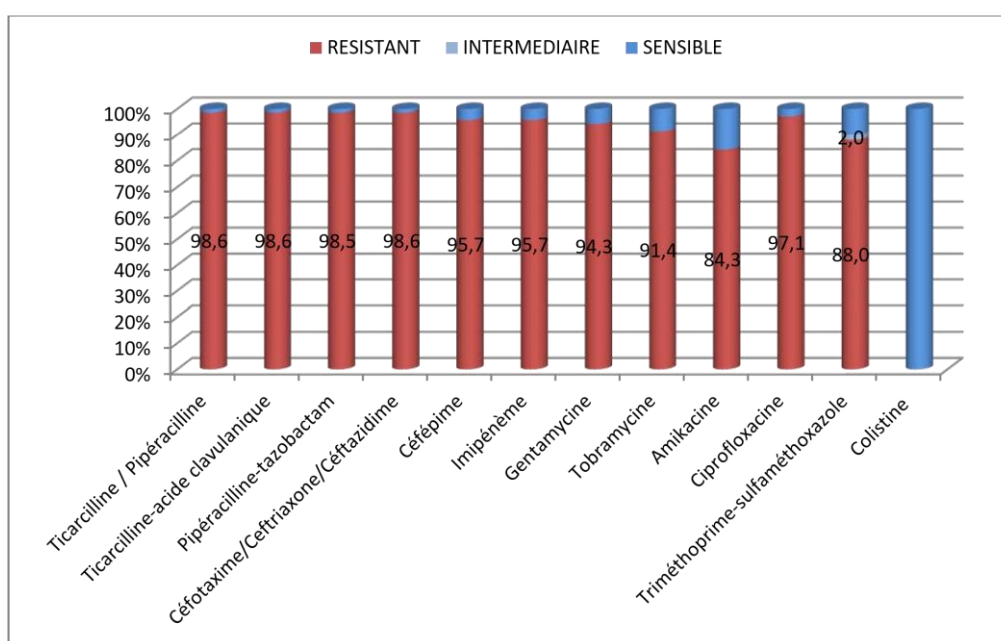


Figure 2: Resistance rates of Acinetobacter baumannii to different antibiotics (%)

Pseudomonas Aeruginosa

The rate of Pseudomonas aeruginosa resistant to imipenem (IRAP), aztreonam and ticarcillin was 5.3% 14.3% and 26.3% respectively. All Pseudomonas

aeruginosa isolates retained susceptibility to piperacillin-tazobactam and to ceftazidime and cefepime (Figure 3).

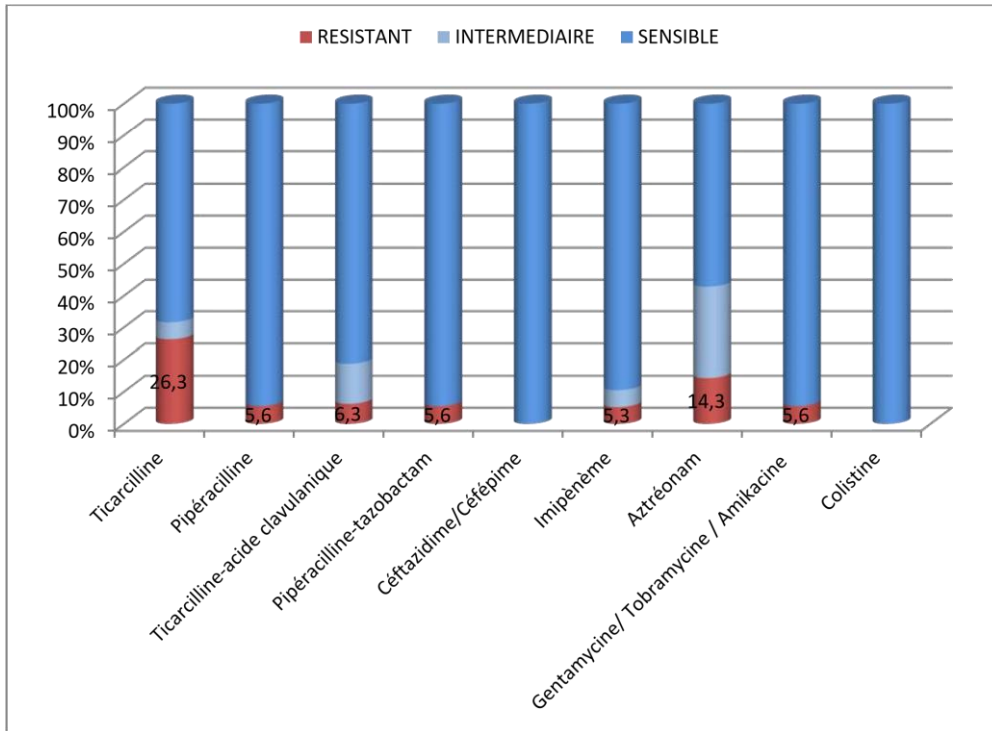


Figure 3: Resistance rates of *Pseudomonas aeruginosa* to different antibiotics (%)

Enterobacteriaceae

The study of resistance to beta-lactam antibiotics revealed a high rate of resistance to amoxicillin, ticarcillin and piperacillin, a moderately high rate of resistance to amoxicillin and clavulanic acid, cephalotin, 3rd generation cephalosporins, etc.

The study of resistance to other antibiotics showed a moderately high rate for gentamycin, tobramycin, ciprofloxacin and cotrimoxazole, cefepime, aztreonam. Our strains, on the other hand, expressed a discrete level of resistance to imipenem and amikacin (Figure 4).

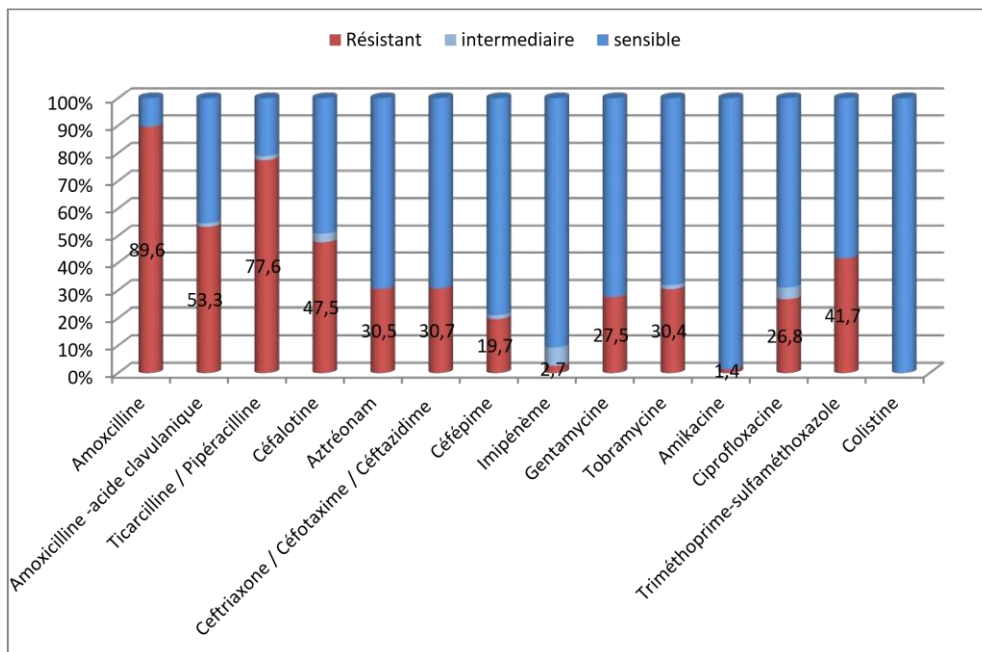


Figure 4: Resistance rates of enterobacteriaceae to different antibiotics (%)

The study of the resistance of the main enterobacteria in our series shows that *Proteus* spp. has a lower rate of resistance to all antibiotics, compared to

Klebsiella pneumoniae and *E.coli*. The latter two bacteria have very similar resistance rates (Figure 5).

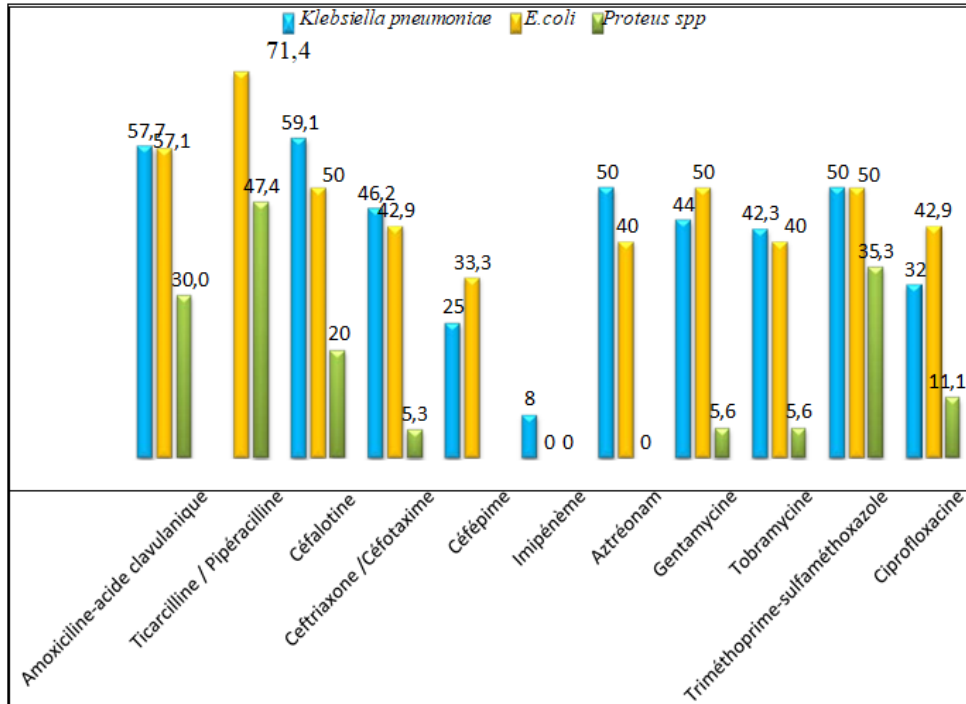


Figure 5: Resistance rates of different enterobacteria to different antibiotics

Staphylococcus Aureus

The resistance rate of *Staphylococcus aureus* was high for penicillin G, amoxicillin, ticarcillin and piperacillin. The combination of amoxicillin and clavulanic acid, methicillin, cefotaxime, imipenem, aminoglycosides, lincomycin and possibly erythromycin and tetracycline showed good activity on strains isolated from *Staphylococcus aureus*.

All *Staphylococcus aureus* isolates were fully susceptible to amikacin, fusidic acid, rifampicin, cotrimoxazole, vancomycin and teicoplanin (Figure 6).

For the streptococcus and enterococcus strains, no acquired resistance was noted.

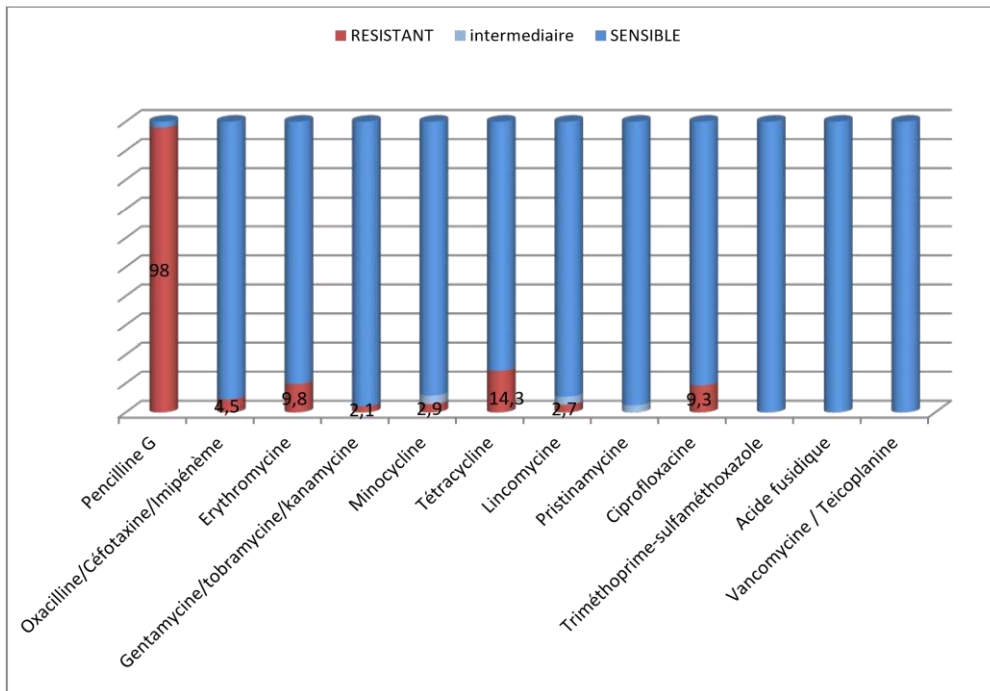


Figure 6: Rate of resistance of Staphylococcus aureus to different antibiotics (%)

DISCUSSION

Epidemiological Data

In our series, we noted a clear predominance of young people and the average age was 35 years, which is in line with French studies (39 years) and Moroccan studies carried out at the university hospitals of Rabat and Casa [2, 3]. A higher average age of up to 64 years was noted in Egypt, Saudi Arabia, India and the United States [4-7].

For sex, there is a notable variability in the sex ratio between studies. However, male predominance is frequently noted. The reason for hospitalisation in our study was dominated by traumatic pathology (72.2%), as in other Moroccan and European studies. Respiratory pathology is also a frequent reason for hospitalisation in several studies [8, 9].

The young age, the predominance of the male sex, the importance of traumatic pathology as the first reason for hospitalization and the low rate of comorbidities could be explained by the plague of public road accidents in the region of Marrakech, which essentially affects young males.

In the literature, the duration of hospitalization varies between 18 and 26 days. Our results are in line with those of the literature with an average duration of 19 days [2, 4, 10] and an average delay of 6 days for the appearance of NP with a slight predominance of the late one. These results are also consistent with those reported in several similar studies [2, 3, 11, 12].

NP associated with another nosocomial infection was found in 15% of cases with a predominance of urinary tract infection; this association could be explained by the fact that 100% of our patients were intubated and sedated with a bladder catheterisation, as in other studies in Morocco, Egypt, Saudi Arabia and France [2, 3, 5, 13, 14]. Regarding other invasive procedures, the use of a central line was observed in 74% of cases. Tracheostomy, chest drainage and reintubation represent minimal percentages compared to other publications [15, 16].

On the clinical-paraclinical level, a retrospective study carried out in the ICU of the Avicenne Military Hospital in Marrakech over a period of 3 years showed the same data as in our population [17] with a mortality rate of 63%, similar to the results found in publications from the Ivory Coast, China and India, however, this rate is still high compared to studies carried out in France, Italy and the United States; this variation could be linked to the degree of severity of the reason for hospitalisation [18-19-20].

Microbiological Data

In our study, 3 sampling methods were applied: PDS, BAL and TEA. The majority of the samples were PDS (57%); other similar studies use the same types of samples, while others also use pleural

samples and blood samples for bacteremia or serum antigens, especially streptococcal [8, 13, 16, 14, 21-23].

A negative culture after 48 hours of incubation was found in 11.7% of cases in our study. This is in line with the literature, such as two American and international studies. This rate remains low compared to studies conducted in the Czech Republic, Serbia and China.

In our study, cultures were polymicrobial in 69% of cases and monomicrobial in 31% of cases. Similar results to the results of our study have been reported by Quartin *et al.* and Mira *et al.* In contrast, studies from Morocco, Iran, Spain, Brazil and Thailand have shown the predominance of monomicrobial cultures [20, 24-26].

Our study showed the predominance of gram-negative bacilli with an isolation rate of 72%. The isolation rate of gram-positive cocci was 28%. The most frequent bacterial family was non-fermentative BGN followed by Enterobacteriaceae which represented 38.2% and 32.5% respectively. The most frequently isolated species were *Acinetobacter baumannii* followed by *Staphylococcus Aureus* which accounted for 30% and 21% respectively. These results are consistent with most studies in the literature reporting that NPs are dominated by BGNs of which non-fermentative BGNs are the most frequently isolated. The prevalence of bacteria in different studies show that *Acinetobacter baumannii* is the leading causative germ of NPs at slightly different rates. *Staphylococcus Aureus* ranks 2nd in most studies. *Pseudomonas aeruginosa* and *klebsiella pneumoniae* share the 3rd position according to the studies [12, 27, 28].

1. Antibiotic resistance profile of *Acinetobacter baumannii*

The results in terms of antibiotic resistance found in our study are alarming. Resistance of *Acinetobacter baumannii* to ceftazidime reached a very high level with piperacillin-tazobactam (98.5%), ceftazidime (98.6%), cefepime (95.7%), gentamycin (94.3%), amikacin (84.3%), ciprofloxacin (97.1%) and cotrimoxazole (88%). The *Acinetobacter baumannii* strains isolated in our study expressed a high rate of resistance to imipenem (95.7%) similar to those reported in studies [29-31].

2. Antibiotic resistance profile of *Pseudomonas aeruginosa*:

Our study showed the lowest rates of resistance of *Pseudomonas aeruginosa* to ceftazidime and imipenem compared to national studies or those conducted in Europe, Asia or the USA. Most other antibiotics remain active on our strains compared to other literature [32-34].

3. Enterobacteriaceae antibiotic resistance profile:

For all species of Enterobacteriaceae, the resistance rates to beta-lactams were in the same ranges described by the studies. However, for aminoglycosides, ciprofloxacin, cotrimoxazole and colistin, our strains were more susceptible than in other studies. For *Klebsiella pneumoniae*, our strains were more sensitive to most antibiotics, especially in comparison with international studies. For *E. coli*, our strains were less resistant to cephalosporins compared to international studies. They did not show resistance to imipenem and colistin. For *Proteus* spp, our strains were more resistant to penicillins and less resistant to the remaining beta-lactams and aminoglycosides compared to the studies consulted [12, 35-37].

4. Antibiotic resistance profile of *Staphylococcus aureus*

In our series, we found low resistance to methicillin, gentamycin, lincozamide, cotrimoxazole, minocycline and erythromycin compared to other studies. 98.2% of our strains were resistant to penicillin G. Vancomycin remained active against all strains of *Staphylococcus aureus*. This has been described in the literature [38, 32, 36].

CONCLUSION

The control of nosocomial pneumonia remains a major concern in intensive care units throughout the world; but mainly, in developing countries.

Our study allowed us to describe the epidemiological and resistance profile of the germs responsible for nosocomial pneumonia during the year 2019, based on the data available in the microbiology laboratory and the intensive care unit of Ibn Tofail Hospital. Therefore, this work constitutes a starting point for a better understanding of nosocomial pneumopathies; it should be supported by a multicentre study including several Moroccan and even Maghrebian intensive care units. Finally, the increased rate of bacterial resistance, and in this case to carbapenems, should reconsider our daily practices in terms of prevention and prescription of antibiotics.

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