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**Current Bacteriological Profile of Nosocomial Pneumonia in Adults and State of Resistance to Antibiotics**

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**Abstract**

Background: Nosocomial pneumonia is the leading cause of infection in intensive care. It is responsible for significant morbidity and mortality. The main objective of our study was to identify the bacteria involved in nosocomial pneumonia and to determine their antibiotic resistance profile, in order to improve their management and reduce the associated morbidity and mortality.

Methods: This is a retrospective and descriptive study, conducted from April 2015 to March 2018. Only pulmonary infections occurring beyond 48 hours of admission to the intensive care unit have been included.

**Results:** The incidence of the nosocomial pneumonia was 77%. Gram-negative bacilli were found in 76% of cases, dominated by *Acinetobacter baumannii* (44%), followed by enterobacteria (24%), most of which was represented by *klebsiella pneumoniae* (10%). Gram-positive Cocci (13%) were dominated by *Staphylococcus aureus* (11%). The study of antibiotic resistance, shows a multi-resistance especially for Gram-negative bacilli, which must be taken into consideration by setting up an active prevention strategy.

**Conclusion:** This alarming finding of virulence and multidrug resistance should lead practitioners to prescribe antibiotics rationally based, preferably, on the data of an antibiogram; this will reduce the selection pressure exerted by a broad spectrum antibiotic, sometimes abusive and inappropriate.

**Keywords:** Adult; Nosocomial pneumonia; Bacteriological profile; Resistance; Antibiotics.

### **Introduction**

Nosocomial Pneumonia (NP) are acquired by definition in a hospital setting and occur 48 hours or more after admission and not during its incubation phase. NP generally result from the penetration and development of microorganisms in the lower airways which, after a colonization phase, will lead to infection of the lung parenchyma by passing the mechanical, cellular and/or humoral defenses of the host. Conventionally recognized sources of contamination are related to the technical nature of the care, the environment and the cross-transmission between the patient and the caregiver or other patients. NP can cover different clinical situations, namely pneumonia acquired through mechanical ventilation and pneumonitis related to care[1].

They represent the first cause of nosocomial infection in intensive care and they are at the origin of an extension of the hospital stay and a significant extra cost. NP cause specific problems in the intensive care environment and especially when they occur for a ventilated patient. They are then difficult to diagnose, the agents responsible are often resistant and their prognosis is serious[2].

The microbiological data of NP require regular epidemiological surveillance to determine the bacterial ecology and resistance profile of each unit. The aim of this work is to determine the current bacteriological profile of NP and to study the antibiotic resistance of the bacteria responsible.

### **Patients and methods**

#### **1. Study design and setting**

This is a descriptive retrospective study spanning four years from April 2015 to March 2018, conducted at the microbiology laboratory of the Avicenna Hospital in Marrakech.

#### **2. Study participants**

We collected a total of 219 protected distal samples taken from intubated and ventilated patients (endotracheal intubation), hospitalized in the intensive care/anesthesia department of the same hospital and suspected of nosocomial pneumonia. We only considered adult patients (age  $\geq 18$

years), hospitalized 48 hours or more. Only samples taken 2 days or more after admission of the patient to the service are taken into account.

### 3. Methods

The identification of bacterial strains was based on the study of their morphological, cultural and biochemical characters. The study of antibiotic sensitivity was performed by automated method on PHOENIX 100 (Becton Dickinson). The reading and interpretation criteria are taken from the antibiogram committee of the French Society for Microbiology (CASFM / EUCAST) (European Committee on Antimicrobial Susceptibility Testing).

Third generation cephalosporin resistant strains by production of extended spectrum betalactamases were systematically identified on the antibiogram by the synergy test between a central amoxicillin + clavulanic acid disc and beta-lactam disks (cefotaxime, ceftazidime, cefepime and aztreonam). The presence of ESBL was noted in front of a "champagne cork" appearance.

The detection of enterobacteria producing carbapenemases has been done at the laboratory level by simple phenotypic tests. Any strain which has shown a decrease in susceptibility to eropenem with a minimum inhibitory concentration (MIC) > 0.5 mg/l or an inhibition diameter (disk loaded at 10µg/ml) < 25 mm by the agar diffusion test, has been subjected to the screening algorithm for carbapenemase-producing strains recommended by EUCAST-CASFM. The minimum inhibitory concentrations at imipenem were achieved in these isolates (considered sensitive for imipenem MIC ≤ 2 mg/l).

### 4. Statistical analysis

Data mining was performed using Excel © software and statistical analysis was performed using SPSS Software (version 10) for Windows. The descriptive analysis consisted of frequency calculations for the qualitative variables. For the comparison of percentages in bi-varied analysis, the Pearson Chi-square statistical test was used when needed. The threshold of significance was retained for a  $p < 0.05$ .

## Results

Out of the 219 protected distal samples taken, 170 were positive (77.6%). Isolated microorganisms were predominantly Gram-negative bacilli (76%), with *Acinetobacter baumannii* (44%) at the top, followed by enterobacteria (24%), most of which was represented by *Klebsiella pneumoniae* (10%) and then *Pseudomonas aeruginosa* (10%). Gram-positive Cocci (13%) were dominated by *Staphylococcus aureus* (11%), while yeasts were isolated in 18 cases or 11% (Fig.1). The poly-microbial character was found in 19% of cases.

Regarding the antimicrobial resistance profile of nosocomial pneumonia, isolates of *Acinetobacter baumannii* showed high resistance to the majority of antibiotics tested. The resistance rate of *Acinetobacter baumannii* to imipenem and ceftazidime was 95.6% and 82.6%, respectively. Isolated strains maintained good sensitivity to colistin (97.1%) (Fig 2).

*Pseudomonas aeruginosa* was particularly sensitive to amikacin 81.3% and imipenem 69%, with a rate of *Pseudomonas aeruginosa* resistant to ceftazidime to 35.7% (Fig 3).

The antibiotic resistance pattern of enterobacteria in all species is shown in Figure 4. Third-generation cephalosporin resistance was observed in 38% of enterobacteria isolates and approximately one in two was resistant to co-trimoxazole and fluoroquinolones. The production of extended spectrum betalactamases accounted for 29% of the isolates. Strains of carbapenem-impaired sensitivity accounted for 21% of cases. (Fig 4).

The overall prevalence of *methicillin*-resistant *Staphylococcus aureus* was 27.8% and no strain of decreased susceptibility to glycopeptides was found among our *Staphylococcus aureus* isolates.

## Discussion

NP are defined as pneumonia acquired during a hospital stay, beyond the 48<sup>th</sup> hour of hospitalization and who were not present in incubation at the time of admission of the patient. Nosocomial pneumonia is at 2<sup>nd</sup> nosocomial infections in France (20%), after urinary infections, and touches 0.5 to 1% of hospitalized patients[3].

There are risk factors for acquisition of nosocomial pneumonia, related to the field (age and comorbidities, immunosuppressant), to the use of artificial ventilation, to the patient's initial severity level and to his pathology (state of shock, intervention recent surgical procedure)[3].

Pneumonia of nosocomial origin usually complicates prolonged assisted ventilation. They are observed mainly with invasive ventilation but have also been reported with non-invasive ventilation by nasal cannula or mask. Nosocomial Pneumonia are responsible for prolonging the duration of ventilation and hospitalization; their mortality is 14% [4]. They cause significant diagnostic, therapeutic and economic problems.

In addition to the radio-clinical diagnosis, it is recommended to carry out a microbiological diagnosis, which relies on blood cultures (systematic), a search for soluble antigen and a lower airway sampling before initiating probabilistic antibiotherapy (endotracheal aspiration, bronchial brushing, bronchoalveolar lavage) [ 2].

Several studies have identified the germs responsible. Whatever the samples used, gram-negative bacilli are at the top of the list, accounting for more than 60% of nosocomial pneumonia [5-7].

In the most recent studies, *Acinetobacter baumannii* is the most frequently isolated organism [8-12]. In our study, gram-negative bacilli are incriminated in 76% of cases and are dominated by *Acinetobacter baumannii*. The main germs found in the literature are shown in Table I.

Polymicrobial pneumonia are not exceptional. A study conducted by Combes et al on 124 patients with nosocomial pneumonia found 48% of poly-microbial infections, with no difference in epidemiology or progression compared with patients suffering monomicrobial pneumonia

[15]. In our study, 2 to 3 germs were isolated in 19% of cases. *Acinetobacter baumannii* (44% of cases), followed by enterobacteria (*Klebsiella pneumoniae* and *Escherichia coli*) (24% of cases), are the most commonly found germs, contrary to the usual literature data where *Staphylococcus aureus* comes first followed by *Pseudomonas aeruginosa* and enterobacteria [16,17].

The major resistance problem arises with *Acinetobacter baumannii*, which is naturally resistant to many antibiotics and which acquires new resistance every day. High levels of resistance to imipenem and ceftazidime were found.

For enterobacteria, the resistance is mainly due to the secretion of a broad spectrum  $\beta$ -lactamase. Strains of carbapenem-impaired sensitivity accounted for 21% of cases.

*Staphylococcus aureus* was isolated in 11% of cases and it was resistant to methicillin in five patients (27.8%). The incidence of nosocomial methicillin-resistant *Staphylococcus aureus* infections ranged from 0.2 to 2.6% in the Larue et al series [18].

### Conclusion

Nosocomial pneumonia has a very high mortality. It is associated with an increase in the duration of mechanical ventilation, the length of stay in intensive care, the use of antibiotics and the cost of hospital stay [19]. Thus it is very important to establish an effective preventive strategy adapted to our needs and our means, and to which all the nursing staff must adhere. The judicious application of these preventive measures can only be conceived within a framework of a prevention program which concerns all hospital services.

Continuous and systematic monitoring of resistance of strains to antibiotics is essential. It should be based on prospective epidemiological studies that require ongoing cooperation between clinicians and microbiologists for a dual purpose: therapeutic and prophylactic.

### Highlights

- Nosocomial pneumonia cause significant diagnostic, therapeutic and economic problems.
- The bacteriological profile of nosocomial pneumonia is dominated by gram-negative bacilli, with *Acinetobacter baumannii* as the leading species.
- The study of antibiotic resistance shows a multi-resistance especially for Gram-negative bacilli, which must be taken into account by implementing an active preventive strategy.
- Continuous and systematic monitoring of resistance of strains to antibiotics is essential.

**Conflict of Interest:** The authors declare no potential conflicts of interest, financial or otherwise.

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**Tables and figures**

*Table I: Main germs responsible for nosocomial pneumonia in the literature*

	J Elhjouji Morocco (Rabat)[9]	Shimi A Morocco (Fès)[12]	Medell Cuba [8]	Marget Europe [13]	Our study
<i>Acinetobacter baumannii</i>	37 %	15,2 %	68,8 %	13,94 %	44 %
<i>Pseudomonas aeruginos</i>	23,2 %	25,77 %	44,2 %	16,97 %	10 %
<i>Staphylococcus aureus</i>	–	21,2 %	14,3 %	27,67 %	11 %

<i>Klebsiella pneumonia</i>	13,6 %	10,7 %	15,6 %	7,47 %	10 %
<i>Escherichia coli</i>	2,27 %	1,5 %	15,6 %	9,50 %	7 %

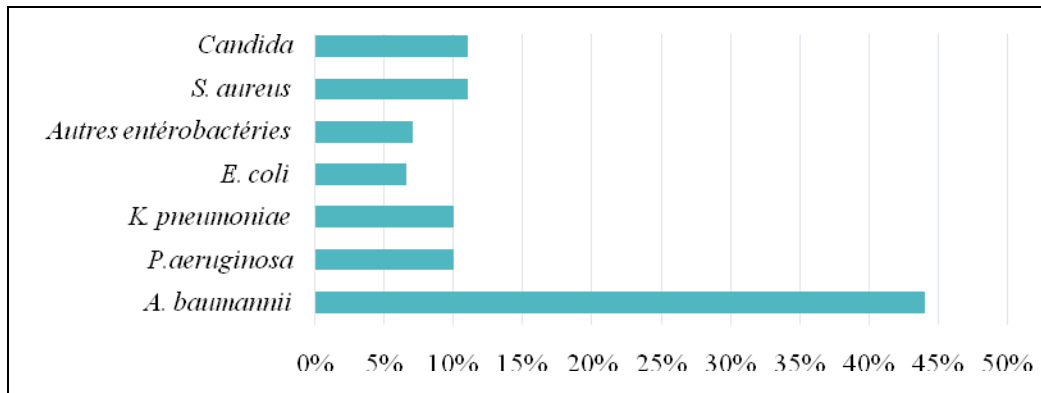


Figure 1: Main germs responsible for nosocomial pneumonia

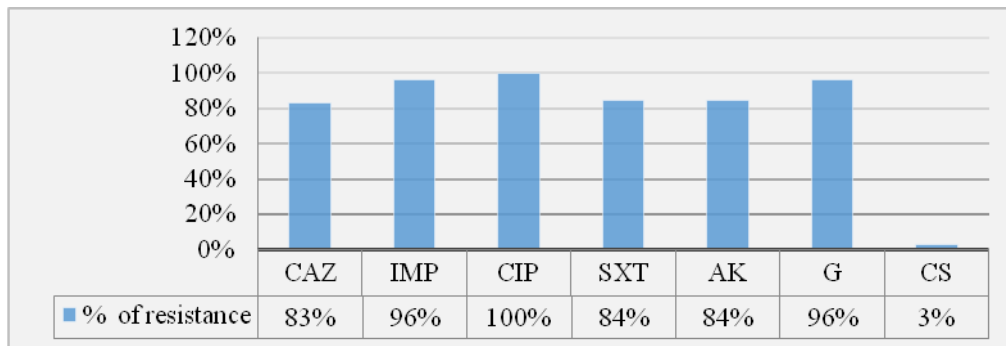
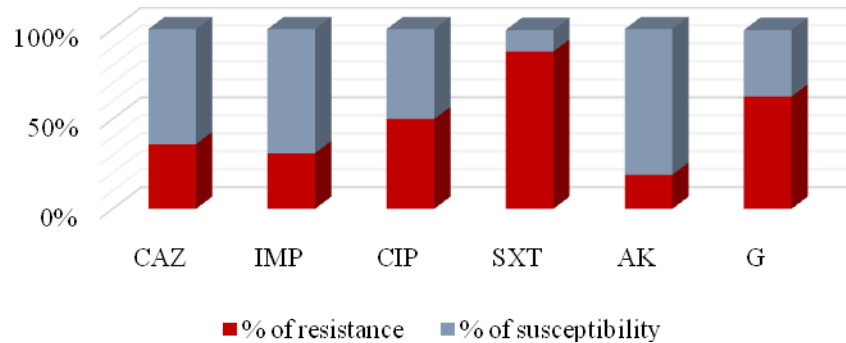


Figure 2: Percentages of antibiotic resistance of isolated Acinetobacter baumannii strains

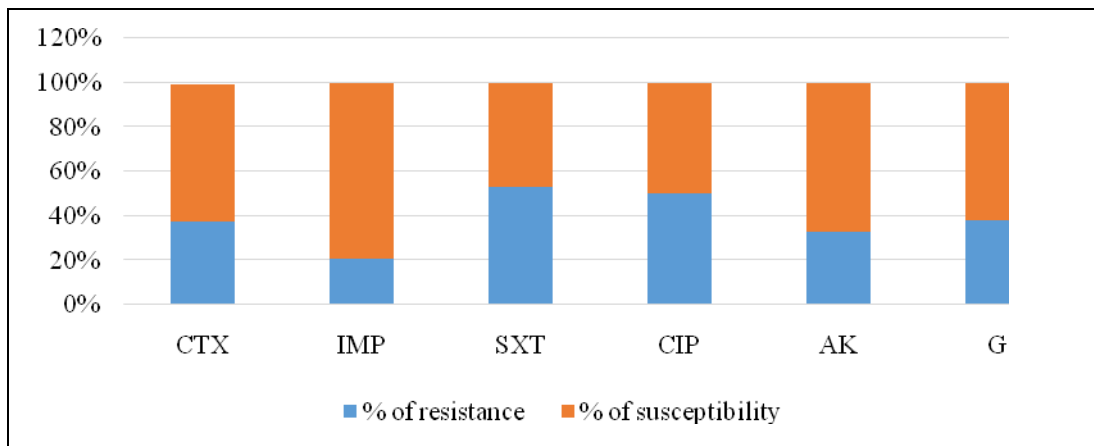
[CAZ: Ceftazidime/IMP: Imipinem/CIP: Ciprofloxacin/SXT: Trimethoprim-sulphametoazole/AK: Amikacin/G: Gentamicin/CS: Colistin]





*Figure 3: Antibiotic susceptibility profile of isolated Pseudomonas aeruginosa strains*

[CAZ: Ceftazidime/IMP: Imipinem/CIP: Ciprofloxacin/SXT: Trimethoprim-sulphametoazol/AK: Amikacin/G: Gentamicin]



*Figure 4: Antimicrobial resistance profile of enterobacteria isolates*

[CTX: Cefotaxime/IMP: Imipinem/CIP: Ciprofloxacin/SXT: Trimethoprim-sulfametoazole/AK: Amikacin/G: Gentamicin]