

Ventilator-Associated Pneumonia

**Dr. Amine Schahrakane¹, Dr. Soufiane Hansal², Prof. Dr. Anas Mounir³,
Prof. Dr. Rachid charqab⁴, Prof. Dr. chafik el hamidi el kettani⁵**

^{1, 2, 3, 4, 5}Intensive Care Anaesthetist
P17 surgical resuscitation
CHU Ibn Rochd in Casablanca

Introduction:

Ventilator-associated pneumonia (VAP) is defined as lung infections acquired after at least 48 hours of assisted ventilation and which lead to an increase in oxygen requirements. [1] They represent the most frequent infectious complication related to care (30 to 50%). Added to this is the length of hospitalization of patients, which is increased by 7 days on average, and the high mortality rate attributable to VAP (10 to 30%). [2] The quality of their management in terms of diagnosis, therapy and prevention constitutes a major challenge for intensive care physicians, coupled with a significant economic issue.

From a bacteriological point of view, in addition to the diversity of the germs involved and their multi-resistance to antibiotics, a new concept of growth mode of microorganisms in their natural environment called BIOFILM has taken on particular importance when it has been proven that it is involved in a large number of bacterial infections, including PAVM [3]. This can be explained by the development and adhesion of certain Gram-negative bacilli (*Pseudomonas aeruginosa*, *Escherichia coli*) on the endotracheal tube and the filters of ventilators conducive to the formation of biofilms.

The aim of our work is to determine the epidemiological, clinical, therapeutic and prognostic aspects of healthcare-associated pneumonia, as well as to study the microbiological profile of these types of infections within our department.

Materials and methods:

This is a retrospective study carried out in the surgical intensive care unit P17 of the Ibn Rochd University Hospital of Casablanca over a period of 2 years from January 1, 2023 to December 31, 2024. We collected 510 pulmonary samples including 1 LBA, 19 ASP, 486 PBDP and 3 Sputum from patients hospitalized in this department. We included in our study patients hospitalized in the surgical intensive care unit P17, who had pulmonary samples taken and who received mechanical ventilation.

Results:

Among the 1770 intubated and ventilated patients admitted to the intensive care unit during the period of our study, 238 patients suffered from healthcare-associated pneumonia, an incidence of 13.44%.

The mean age of the patients was 57.04 years, with a range from 16 to 67 years. There was a clear male predominance: 67% of the patients were male.

Among all patients, the most frequent reasons for hospitalization were postoperative care.

Cardiovascular diseases, diabetes, smoking and surgical history constitute the main pathological antecedents encountered in our patients, distributed as follows (Table 1):

Painting1: Distribution of patients according to their history

	Number	Percentage
Cardiovascular disease	87	36.55%
Diabetes	81	34.03%
No ATCs	68	28.57%
Chronic smoking	31	13.03%
Surgical History	29	12.18%
Obesity	15	6.30%
Other	13	5.46%
COPD	12	5.04%
Alcoholism	10	4.20%
Asthma	6	2.52%
IRC	5	2.10%
Psychiatric history	2	0.84%

In our study, antibiotic use before resuscitation was noted in 40 patients, or 16.81%. Amoxicillin-clavulanic acid is the most commonly used.

Purulent secretions were observed in 114 patients, or 47.9% of cases. A very high CRP level (greater than 100 mg/l) was found in 52% of our patients. 42% of these patients presented hyperleukocytosis, 12% leukopenia and 35% thrombocytopenia.

In all the selected samples, 6 main bacteria were found; *Acinetobacter baumannii* is the most frequent representing 28% of all germs, followed by *Pseudomonas aeruginosa* 14%, *Klebsiella pneumoniae ssp pneumoniae* 13%, *Staphylococcus aureus* 8%, *Escherichia coli* 6%, then coagulase-negative *Staphylococcus* 5%. In our study, of the 238 positive cultures, we found 29 polymicrobial cultures versus 209 monomicrobial cultures.

The overall epidemiological profile of germs is shown in Table 2:

Painting2: Overall epidemiological profile of germs

Acinetobacter baumannii	67	28.15%
Pseudomonas aeruginosa	34	14.29%
Klebsiella pneumoniae ssp pneumoniae	33	13.87%

Staphylococcus aureus	18	7.56%
Escherichia coli	15	6.30%
Haemophilus influenzae	12	5.04%
Coagulase negative Staphylococcus	11	4.62%
Proteus mirabilis	9	3.78%
Enterobacter cloacae	8	3.36%
Streptococcus pneumoniae	8	3.36%
Raoultella terrigena	7	2.94%
Stenotrophomonas maltophilia	6	2.52%
Corynebacterium species	6	2.52%
Enterobacter aerogenes	5	2.10%
Serratia marcescens	5	2.10%
Klebsiella oxytoca	4	1.68%
Providencia Spp	4	1.68%
Acinetobacter lwoffii	4	1.68%
Citrobacter koseri	2	0.84%
Moraxella (Branhamella) catarrhalis	2	0.84%
Proteus vulgaris	2	0.84%
Haemophilus influenzae beta-lactamase positive	1	0.42%
Haemophilus influenzae (beta-lactamase negative)	1	0.42%
Klebsiella terrigena	1	0.42%
Pseudomonas alcaligenes	1	0.42%
Shigella	1	0.42%

Reading the antibiograms carried out on the isolated strains of *Acinetobacter baumannii* made it possible to determine the sensitivity and resistance of our isolates to 12 antibiotics (Table 3):

Painting3: Resistance profile of Acinetobacter Baumannii strains

Ceftriaxone	63	94%	4	6%	0	0%	0	0%
Ceftazidime	54	80.60%	5	7.50%	8	11.90%	0	0%
Cefepime	42	62.70%	11	16.40%	3	4.50%	11	16.40%
Imipenem	61	91%	6	9%	0	0%	0	0%
Meropenem	55	82.10%	6	9%	6	9%	0	0%
Cotrimoxazole	55	82.10%	5	7.50%	7	10.40%	0	0%
Ciprofloxacin	61	91%	0	0%	4	6%	2	3%
Levofloxacin	60	89.60%	3	4.50%	2	3%	2	3%
Gentamicin	61	91%	5	7.50%	1	1.50%	0	0%
Tobramycin	56	83.60%	7	10.40%	4	6%	0	0%
Amikacine	58	86.60%	7	10.40%	2	3%	0	0%
Doxycycline	15	22.40%	50	74.60%	2	3%	0	0%

Reading the antibiograms carried out on the isolated Pseudomonas Aeruginosa strains made it possible to determine the sensitivity and resistance of our isolates to 9 antibiotics (table 4):

Painting4: Resistance profile of Pseudomonas Aeruginosa strains

Ceftazidime	27	81.82%	7	21.21%	0	0.00%
Imipenem	29	87.88%	4	12.12%	1	3.03%
Gentamicin	25	75.76%	9	27.27%	9	27.27%
Tobramycin	2	6.06%	3	9.09%	3	9.09%
Aztreonam	2	6.06%	4	12.12%	2	6.06%
Amikacine	27	81.82%	7	21.21%	0	0.00%
Ciprofloxacin	22	66.67%	11	33.33%	0	0.00%
Pipera/tazobactam	21	63.64%	6	18.18%	0	0.00%
Cefepime	19	57.58%	7	21.21%	0	0.00%

Reading the antibiograms carried out on the isolated Staphylococcus Aureus strains made it possible to determine the sensitivity and resistance of our isolates to 13 antibiotics (Table 5):

MRSA (Methicillin-resistant Staphylococcus Aureus) observed in 27.78%

Painting5: Resistance profile of Staphylococcus Aureus strains

Cefoxitin	18	100.00%	0	0.00%	0	0.00%
Gentamicin	18	100.00%	0	0.00%	0	0.00%
Tobramycin	2	11.11%	0	0.00%	16	88.89%
Kanamycin	15	83.33%	3	16.67%	0	0.00%
Norfloxacin	17	94.44%	1	5.56%	0	0.00%
Ciprofloxacin	14	77.78%	0	0.00%	4	22.22%
Cotrimoxazole	7	38.89%	0	0.00%	11	61.11%
Erythromycin	12	66.67%	5	27.78%	1	5.56%
Levofloxacin	0	0.00%	0	0.00%	18	100.00%
Fusidic acid	10	55.56%	4	22.22%	4	22.22%
Rifampicin	17	94.44%	0	0.00%	1	5.56%
Chloramphenicol	11	61.11%	3	16.67%	4	22.22%
Tetracycline	9	50.00%	1	5.56%	8	44.44%

Reading the antibiograms carried out on the isolated Coagulase Negative Staphylococcus strains made it possible to determine the sensitivity and resistance of our isolates to 13 antibiotics (Table 6):

SCNR observed in 0%

Painting6: Resistance profile of coagulase-negative Staphylococcus strains

Cefoxitin	11	100.00%	0	0.00%	0	0.00%
Gentamicin	11	100.00%	0	0.00%	0	0.00%
Tobramycin	0	0.00%	0	0.00%	11	100.00%
Kanamycin	11	100.00%	0	0.00%	0	0.00%

<i>Norfloxacin</i>	11	100.00%	0	0.00%	0	0.00%
<i>Ciprofloxacin</i>	11	100.00%	0	0.00%	0	0.00%
<i>Cotrimoxazole</i>	9	81.82%	1	9.09%	1	9.09%
<i>Erythromycin</i>	11	100.00%	0	0.00%	0	0.00%
<i>Levofloxacin</i>	0	0.00%	0	0.00%	11	100.00%
<i>Fusidic acid</i>	4	36.36%	1	9.09%	6	54.55%
<i>Rifampicin</i>	8	72.73%	3	27.27%	0	0.00%
<i>Chloramphenicol</i>	3	27.27%	8	72.73%	0	0.00%
<i>Tetracycline</i>	5	45.45%	5	45.45%	1	9.09%

Reading the antibiograms carried out on the isolated enterobacteriaceae strains made it possible to determine the sensitivity and resistance of our isolates to 13 antibiotics (table 7):

BLSE positive observed in 57 out of 97 patients

Painting7: Resistance profile of Enterobacteriaceae strains

Ampicillin	93	95.88%	4	4.12%	0	0.00%	0	0.00%
Amox-clav	69	71.13%	28	28.87%	0	0.00%	0	0.00%
Cefoxitin	47	48.45%	50	51.55%	0	0.00%	0	0.00%
Ceftriaxone	42	43.30%	55	56.70%	0	0.00%	0	0.00%
Ceftazidime	42	43.30%	53	54.64%	1	1.03%	1	1.03%
Cefepime	30	30.93%	37	38.14%	29	29.90%	1	1.03%
Gentamicin	32	32.99%	64	65.98%	0	0.00%	1	1.03%
Amikacine	21	21.65%	69	71.13%	1	1.03%	6	6.19%
Ciprofloxacin	36	37.11%	48	49.48%	5	5.15%	8	8.25%
Cotrimoxazole	28	28.87%	45	46.39%	24	24.74%	0	0.00%
Ertapenem	25	25.77%	68	70.10%	4	4.12%	0	0.00%
Imipenem	17	17.53%	57	58.76%	15	15.46%	8	8.25%
Temocillin	17	17.53%	43	44.33%	37	38.14%	0	0.00%

Reading the antibiograms carried out on the isolated strains of *Streptococcus pneumoniae* made it possible to determine the sensitivity and resistance of our isolates to 7 antibiotics (table 8):

Painting8: Resistance profile of *Streptococcus pneumoniae* strains

TICARCILLIN	4	50.00%	2	25.00%	0	0.00%	2	25.00%
PIPERACILLIN	2	25.00%	4	50.00%	0	0.00%	2	25.00%
CEFOXITIN	8	100.00%	0	0.00%	0	0.00%	0	0.00%
CEFTAZIDIME	0	0.00%	8	100.00%	0	0.00%	0	0.00%
CEFEPIME	4	50.00%	2	25.00%	2	25.00%	0	0.00%
IMIPENEME	2	25.00%	6	75.00%	0	0.00%	0	0.00%
GENTAMICIN	2	25.00%	2	25.00%	2	25.00%	2	25.00%

Reading the antibiograms carried out on the isolated *Haemophilus influenzae* strains made it possible to determine the sensitivity and resistance of our isolates to 7 antibiotics (table 9):

Painting9: Resistance profile of *Haemophilus influenzae* strains

Penicillin G	3	25.00%	3	25.00%	6	50.00%	0	0.00%
Amoxicillin	7	58.33%	3	25.00%	2	16.67%	0	0.00%
C3G	10	83.33%	2	16.67%	0	0.00%	0	0.00%
Erythromycin	4	33.33%	2	16.67%	3	25.00%	3	25.00%
Lincomycin	5	41.67%	2	16.67%	4	33.33%	1	8.33%
Gentamicin	4	33.33%	1	8.33%	5	41.67%	2	16.67%
Levofloxacin	6	50.00%	1	8.33%	3	25.00%	2	16.67%

In our study series, 209 patients were given antibiotics, or 87.8%. In general, the average duration of antibiotic treatment was approximately 12.9 days. Polyantibiotic therapy was the usual treatment method representing 85% of cases (179 patients). The most commonly used ATB combination in these patients was imipenem, amikacin, and colistin.

The evolution was assessed on clinical aspects (temperature, hemodynamic and respiratory status, state of consciousness, etc.), biological (NFS, blood gas, CRP, renal function, etc.) and bacteriological. The average duration of hospitalization of patients who presented with care-associated pneumonia was 22 days with extremes ranging from 1 to 102 days. This result was favorable in only 47 of our patients (19.75%) while 191 of our patients (80.25%) died.

Discussion:

Healthcare-associated pneumonia is defined as pneumonia occurring after 48 hours of mechanical ventilation. This definition helps distinguish hospital-acquired VAP from community-acquired infections that were incubating at the time of intubation but were not clinically evident until 1 to 2 days later. Duration of mechanical ventilation is an important risk factor for the development of VAP. [4]

The incidence of VAP varies greatly from one study to another [5]. Pneumonia is the leading cause of infections acquired in intensive care. In a European multicenter study [6] involving 10,000 patients, the prevalence of VAP was 10%, which represents 47% of infections acquired in intensive care. In a study involving 9,080 intensive care patients, mechanically ventilated for more than 24 hours, an incidence of VAP was found to be 9.3% [7].

In another study in the intensive care unit at the Hassan II University Hospital in Fez in 2015 concerning patients who contracted VAP during 2014, the percentage of positive cases was 54% [8]. A large-scale study, carried out in European ICUs (Intensive Care Units), had reported that Mechanical Ventilation was associated with a three times higher risk of developing VAP than that observed for non-ventilated patients. Cross and Roup reported in their analyses of overall VAP rates, a 10 times higher risk of developing VAP for ventilated patients than for people without respiratory assistance [9]. In our study, the incidence rate of VAP is equal to 13.44%. Our rate is comparable to European studies and is very low compared to national studies.

In all national and international literature, it is noted that male gender is a risk factor associated with PAVM.

In our series, *Acinetobacter baumannii* was the leading germ identified as responsible for VAP with a rate of 28.15%. This rate is relatively close to that reported by a study in Marrakech [10] (33.88%). The highest rates are reported by a study carried out in Casablanca in 2019 [11] with a rate of 59.3%, the lowest rate is observed in the study carried out in Brazil 2.2%. In 2013, a systematic review noted the following rates: 4.8% in the United States, 5.6% in Europe and 13.3% in Latin America [12]. This geographical variability in the distribution of *Acinetobacter* within bacterial species isolated between cities and countries is linked to differences in the use of antibiotics, infection control policies but especially to hygiene and disinfection practices.

Pseudomonas aeruginosa is a hardy, ubiquitous, saprophytic Gram-negative bacterium that is naturally resistant to antibiotics (hydrophilic beta-lactams). It can become an opportunistic pathogen, responsible for serious infections when favorable circumstances are met. According to our results, *Pseudomonas aeruginosa* was isolated in only 14.29% of samples during the period of our study. Our result is comparable to that of the literature, which varies from 7% to 23.3%, it represents the 4th most isolated germ in our study. This result is consistent with that reported by most studies: *Pseudomonas* was the 2nd

or 3rd germ incriminated in PAVM in Algeria, Rabat 2020 and Fez 2015 [13, 14], while it was the 4th in a study carried out in Marrakech 2016 [15]. In studies carried out in different North American countries, [16] *Pseudomonas* was found to be ranked first with high rates: Cuba 44.2%, Guatemala 43%, Mexico 38%.

In our study, 4 cases of *Pneumococcus* were found, representing a rate of 3.38%. The majority of national studies agree that the rate of *Streptococcus pneumoniae* is very low. On the other hand, two studies find that *Streptococcus Pneumoniae* is ranked 1st or 2nd among the germs identified: A study carried out in Iraq in 2019 [17] found a rate of *Streptococcus Pneumoniae* equal to 26% Another study carried out in Algeria in 2020 [18] found a rate of *Streptococcus pneumoniae* at 30.50%. In this study, streptococcus was ranked 1st.

In the majority of studies observed, the frequency of *Haemophilus Influenzae* is less than 5%. Our rate is consistent with the results of these studies. At the same time, most studies do not find this germ. For example, the study carried out in Marrakech 2016, in India 2018, in Iraq 2019.... [17, 10,24] The highest rate is observed in the study carried out at the Hassan II University Hospital in Fez 2015[20], with a rate of 7.75. On the other hand, another study carried out in Fez in the period of 2017 [21] does not find this germ.

Enterobacteriaceae were involved in 29.41% of cases, the majority of which was represented by *Klebsiella pneumoniae* (13.87%), which ranks 3rd after *Acinetobacter baumannii* and *Pseudomonas aeruginosa* as the cause of VAP in our study. According to the study by Righi. E et al [22], this result is reversed in ICUs, where the most frequently isolated germs were Enterobacteriaceae (32.9%) followed by *Pseudomonas* spp (30.1%) and *Staphylococcus aureus* (14.1%), Another study conducted in Iraq in 2019 [17] also found that the most frequently isolated Enterobacteriaceae with a rate of 54% are represented by *Klebsiella pneumoniae*. In the USA, the causative germs are mainly represented by aerobic Gram-negative bacilli, *Pseudomonas aeruginosa* and enterobacteria essentially. VAP caused by Gram-positive cocci, in particular methicillin-resistant *Staphylococcus aureus*, is nevertheless increasing in frequency in intensive care units [23]. *Klebsiella pneumoniae* remains the most common germ found in all studies in India (16.1%) [24], Hassan II University Hospital of Fez (10.7%) [17], Marrakech (13.2%) [15], Algeria [18] (16%) and Casablanca [11] (12.1%).

In our study, the polymicrobial character was found in 12.18% of positive samples. This rate remains low compared to that reported in the United States: 50.4% of PAVM had a polymicrobial etiology. [25] The Marrakech 2016 study agrees with the results of our study, they found that the polymicrobial character is in 22.4% of cases. [15]

Conclusion:

Ventilator-associated pneumonia (VAP) is a serious and increasingly common complication in intensive care settings. VAP represents a leading cause of morbidity and mortality, posing significant diagnostic and therapeutic challenges.

Therapeutic management is generally based on dual antibiotic therapy. This can be guided by data from non-invasive samples, such as tracheal aspirations, taken periodically and systematically. The duration of treatment is debated, but the latest data support a relatively short course of antibiotics lasting 8 days.

Finally, the management of VAP depends mainly on prevention. It is clear that the performance of certain simple and accessible actions, such as oropharyngeal decontamination several times a day, the elevated position of the head, and mainly the respect of hygiene rules (wearing gloves, wearing a mask and hand hygiene) is directly related to a reduction in the incidence of nosocomial infections in the intra-hospital environment, hence the importance of training healthcare staff as well as the development of intensive care units. This leads us to the need to establish systems for monitoring and controlling nosocomial infection.

Within our hospital, these systems are made up of the Nosocomial Infection Control Committee (CLIN), which aims to improve the organization of the fight against nosocomial infections and carry out actions adapted to national and local priorities. It is a multidisciplinary structure in which clinicians, hygienists, pharmacists, and bacteriologists, among others, collaborate. Its objectives are not only the surveillance of nosocomial infections, but also their relationship with workload, the type and severity of illnesses, antibiotic consumption, and bacterial resistance.

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