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Epidemiological aspects and resistance profile of bacteremia in the region of Marrakech

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Abstract

Introduction: bacteremia in hospitals is a major public health problem that can lead to mortality and morbidity. The aim of our study is to establish the bacteriological profile of bacteremia and the state of antibiotic resistance in order to optimize probabilistic antibiotherapy at the Avicenna military hospital in Marrakech.

Materials and methods: This is a descriptive retrospective study spanning a period of 5 years (January 2019 - December 2023), conducted in the laboratory of bacteriology-virology and molecular biology of the Avicenna Military Hospital in Marrakech, on the all bacteria isolated from blood cultures in hospitalized patients.

Results: During this period, we collected 839 blood cultures, 140 of which resulted to isolate a bacterium. The predominant causative organism was *Staphylococcus aureus* (27%), The resistance profile of the strains was as follows: 3.57% for methicillin for *Staphylococcus aureus* and 50% for staphylococcus coagulase negative. Regarding *Enterobacter*ia; 30.28% were producing ESBL, ciprofloxacin resistance was involved in 41.8% of *Enterobacter*ia while all strains were sensitive to kanamicin. The resistance of *Acinetobacter baumanii* was 100% to ciprofloxacin, and 91% to ticarcillin, ceftazidime, imipenem and amikacin while remaining 100% sensitive to colistin.

Conclusion: surveillance of bacteria's epidemiological characteristics and their antibiotic susceptibility profile should be continuous for appropriate adaptation of initial empirical treatment of bacteraemia.

Keywords: Bacteremia; Antibiotic; Resistance; Infection; Morocco

1. Introduction

Hospital bacteremia is a major global mortality and morbidity problem. Their incidence is on the rise, paradoxically to the progress made in medicine [1-4]. The clinical translation of bacteraemia ranges from signs of sepsis to septic shock, thus worsening the prognosis, and increasing the risk of morbidity if necessary [5,6]. Blood culture remains the routine and reference examination for the detection of bacteremia. The time taken to obtain the results in terms of diagnostic and therapeutic urgency is long (24 hours to a few days depending on the case). Consequently, a probabilistic initial antibiotic treatment must be initiated, relayed according to the results of the blood cultures. However, in the face of continuous changes in the epidemiological characters of bacteria and their resistance to antibiotics, it becomes increasingly difficult to maintain appropriate treatment regimens for initial empirical treatment [7-9]. Up-to-date knowledge of the epidemiology of bacteria and their resistance to antimicrobial agents is necessary to ensure adequate treatment regimens.

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The aim of our study is to establish the bacteriological profile of bacteremia, and to evaluate the rate of resistance of bacteria to antibiotics.

2. Materials and methods

This is a retrospective descriptive study, based on data from the microbiology laboratory of the Avicenna Military Hospital of Marrakech. This study was conducted on all diagnostic samples from inpatients or outpatients received between January 01, 2018 and December 31, 2022. Were included all patients hospitalized in the Avicenna military hospital in Marrakech with one or more positive blood cultures.

In our study, the blood culture bottles used are BacT/ALERT bottles compatible with the bacterial growth identification machine used in the microbiology department of the Avicenna hospital in Marrakech. The samples were taken at the patient's bedside, by direct venipuncture. Blood collection by catheter was carried out only in the context of suspicion of a vascular device infection (VDI), and this in parallel with sampling by direct venipuncture.

The labeling and clinical information of the samples received at the laboratory were verified. Blood culture bottles sent quickly or kept in less than 24 hours away from light at room temperature were incubated in the detection machine for BacT/ALERT positive blood cultures.

Bottles detected positive by the BacT/ALERT are unloaded from the automaton and analyzed. Part of the specimen is spread on different selective or non-selective agar media (blood agar, Chapman agar, chocolate agar) to obtain colonies. A Gram stain was performed. The biochemical identification and the sensitivity of the strains to antibiotics were carried out by the PHOENIX i1000 automaton (Becton Dickinson), supplemented by the method of diffusion discs in enriched agar medium according to the recommendations of EUCAST /CASFM. During our study period, 839 blood cultures were performed in the microbiology laboratory for hospitalized patients. 267 blood cultures were found to be positive, including 140 blood cultures retained as true positive and 127 considered contaminated. 102 patients were retained with bacteremia, after subtracting duplicates.

The data entry of the study was done on an Excel spreadsheet. The statistical analysis consisted of a univariate descriptive method with calculation of percentages and means.

3. Results

Among the 102 patients with bacteremia, 30 cases were women and 72 man, the sex ratio (M/F) was 2.19. In order of frequency, the internal medicine department was in the majority with 52 cases of bacteremia (51%), followed by the resuscitation department with 38 cases (37%).

A total of 105 bacterial strains isolated from blood cultures were found to be responsible for bacteremia in 102 patients, with only 3 patients having poly-microbial bacteremia. We found that 56.6% of bacteremia were due to Gram-negative bacilli (GNB), mainly *Enterobacter*ia (41% of bacteremia), with *Escherichia coli* the most isolated strain (20% of bacteremia). Non-fermenting BGN bacteremia accounted for 16.20% of all bacteremia and were due to *Pseudomonas aeruginosa* and *Acinetobacter baumanii*. Gram-positive cocci bacteria (GPC) accounted for 42.85% of all bacteremia and were mainly due to *Staphylococcus aureus* (27% of all bacteremia). In order of frequency, the main bacteria isolated were *Staphylococcus aureus* (28%), followed by *Escherichia coli* (20%), *Enterobacter* (10%), *Acinetobacter baumanii* (10%), *Klebsiella* (7%), *coagulase-negative staphylococci* (7%) and *Pseudomonas aeruginosa* (6%).

In the medical departments, *Staphylococcus aureus* (n=22), *Escherichia coli* (n=12) and *Enterobacter* (n=6) came first among the bacteria isolated; followed by *Klebsiella* (n=4) and SCN (n=4). In the intensive care unit, *Acinetobacter baumanii* (n=9) occupied the first place in bacteremia, followed respectively by *Escherichia coli* (n=7), *Staphylococcus aureus* (n=6), *Pseudomonas aeruginosa* (n= 5) *Klebsiella* (n=4), *Enterobacter* (n=3) and *Enterococcus* (n=3). The surgery departments had 6 cases of bacteremia and they were due twice to *Streptococci* and *Escherichia coli*, and once to *Enterobacter* and SCN.

The number of cases/year of bacteremia increased over the study period between 2018 and 2022 (table 1).

Table 1 The frequency rates of isolated bacteria according to the study period

Bacterial species	**2018 n (%)**	**2019 n (%)**	**2020 n (%)**	**2021 n (%)**	**2022 n (%)**
S.Aureus	2 (22%)	6 (32%)	4(19%)	10 (50%)	7 (18%)
S.non Aureus	0 (0%)	1 (6%)	2 (9.5%)	0 (0%)	4 (10%)
Streptococcus	1 (11%)	0 (0%)	2 (9.5%)	1 (5%)	1 (2.5%)
Enterococcus	0 (0%)	1 (6%)	0 (0%)	2 (10%)	1 (2.5%)
E.coli	0 (0%)	3 (16%)	6 (28.5%)	5 (25%)	7 (18%)
E.cloacae	2 (22%)	2 (12%)	2 (9.5%)	0 (0%)	5 (12.5%)
K.pneumoniae	2 (22%)	0(0%)	1 (4.25%)	2 (10%)	3 (7.5)
Salmonella	0 (0%)	1 (6%)	0 (0%)	0 (0%)	1 (2.5%)
C.Freundi	0 (0%)	0 (0%)	1 (4.25%)	0 (0%)	0 (0%)
A.baumanii	1 (11%)	1 (6%)	3 (12.75%)	0 (0%)	6 (15%)
P.aeruginosa	1 (11%)	1 (6%)	0 (0%)	0 (0%)	4 (10%)
Total	9	16	21	20	39

Resistance rates for the main bacteria responsible for bacteremia in our study are shown in Table 2.

Table 2 The ATB resistance rates of the different isolates found

	S. aureus	***CNS***	***Enterococcus***	***Streptococcus***	***E. coli***	***Enterobacter***	***Klebsiella***	***Pseudomonas aeruginosa***	***Acinetobacter baumanii***
Penicillin G	96%	100%	-	-	-	-	-	-	-
Amoxicillin	93,4%	86,4%	-	0%	-		-	-	-
Methicillin	3.57%	50%	-	-	-		-	-	-
Ticarcillin			-	-	80.95%	18.18%	-	-	91%
Piperacillin			-	-	-	-	-	16.67%	91%
Amoxicillin-Clavulanic Acid			-	-	71.14%	-	62.50%	-	-
Ticarcillin-Clavulanic Acid			-	-	66.66%	18.18%	62.50%	-	-
Piperacillin-Tazobactam			-	-	23.80%	18.18%	62.50%	16.67%	91%
Cefoxitin	3.57	50%	-	-	14.28%	-	37.50%	-	-
Ceftaroline	-	-	-	-	-	-	-	-	-
Cefexime	-	-	-	-	14.28%	27.27%	62.50%	-	-
Ceftazidime	-	-	-	-	-	-	-	16.67%	91%
Cefepime	-	-	-	-	9.52%	18.18%	62.50%	-	-
Ertapenem	-	-	-	-	-	18.18%	-	-	-
Imipenem	-	-	-	-	-	9.10%	-	-	91%
Colistin	-	-	-	-	-	-	-	-	0%
Vancomycin	-	-	-	-	-	-	-	-	-
Teicoplanin	-	-	-	-	-	-	-	-	-
Fosfomycin	-	50%	-	-	-	-	25%	33.34%	-
Erythromycin	14.28%	83.33	100%	20%	-	-	-	-	-
Clindamycin	-	-	100%	40%	-	-	-	-	-
Pristinamycin	-	-	-	-	-	-	-	-	-
Gentamicin	28.57%	0%	100%	-	-	9.10%	62.50%	-	82%

Amikacin	-	-	-	-	-	-	-	-	91%
Tobramycin	28.57%	33.33%	-	-	-	-	-	-	-
Kanamycin	32.14%	33.33%	-	-	-	-	-	-	-
Doxycycline	-	-	-	-	-	-	-	-	-
Tetracycline	28.57%	66.66%	-	-	-	-	-	-	-
Nalidixic Acid	-	-	-	-		9.10%	62.50%	16.67%	-
Ciprofloxacin	-	-	-	-	47.61%	9.10%	62.50%	16.67%	100%
Norfloxacin	-	-	-	40%	47.61%	-	-	-	-
Levofloxacin	7.14%	50%	0%	40%	-	9.10%	62.50%	16.67%	-
Fusidic Acid	14.28%	-	-	-	-	-	-	-	-
Nitrofurantoin	-	-	-	-	-	-	-	-	-
Co-Trimoxazole	17.85%	33.33%	-	40%	42.85%	18.18%	62.50%	-	100%

4. Discussion

The importance of blood culture in detecting bacteremia is well recognized. Numerous studies have been dedicated to this topic, notably those by Diekema DJ. et al. and Takeshita N. et al. [10,11]. Indeed, according to a study conducted in India in 2016, the blood culture positivity rate was 16.5% [12]. Similarly, in the series by Bhandari P. et al. and Eshetu S. et al., blood cultures were positive in 15.4% and 15.2% of cases respectively [13,14]. These rates are consistent with the findings of our study (17%). However, a Moroccan study conducted in Meknes found a higher rate of bacteremia (34.90%) [15]. Conversely, in other series, these rates are relatively lower, as reported in a study conducted in Senegal [16] and another in Tunisia [17], where the rates were 4.1% and 10% respectively.

These disparities in the literature can be explained by several factors. In fact, it is common practice in some hospitals to perform blood cultures for all patients with a temperature above 38 °C. However, the literature does not support this strategy [18]. Unlike fever, chills are more predictive of bacteremia, especially rigors, which have high positive predictive values for bacteremia (PPV=4.7) [19]. The timing of specimen collection is crucial for detecting bacteria in the blood [18]. The clinical context is also a major factor in predicting bacteremia. Indeed, the source of infection allows for stratification of patients into low, moderate, and high risk of bacteremia. For example, cellulitis is low risk (2%) compared to acute pyelonephritis (19%-25%), acute bacterial meningitis (53%), or septic shock (69%) [18]. However, the issue of subjectivity in interpreting a positive blood culture, particularly for low-pathogenicity organisms, also plays a role in the differences observed in the literature. In our study, commensal organisms (such as *Coagulase-negative staphylococci*) detected in only one positive blood culture were not considered responsible for bacteremia but rather considered contaminants.

The bacteriological profile of bacteremia in our study was marked by the predominance of Gram-negative bacilli (56,6%). *E. coli* was the most isolated Gram-negative bacterium in our study (20%), it ranked second in terms of bacteremia after *S. aureus*, its isolation rate among all the bacteria identified was (28%). *Acinetobacter* and *Enterobacter* were the third most isolated bacteria in our study. Their rate of isolation was 10.37% each. These results are broadly in line with those found in the literature, which are reported in Tables 3 and 4.

Table 3 The levels of Gram-positive bacteria compared to the total bacteria identified according to different studies

Series	**Country**	**Gram(+)**	***S.Aureus***	***CNS***	***Streptococcus***	***Enterococcus***	**Others**
Mom R. [15]	Morocco (Meknes)	67%	21.17%	35.29%	4.70%	2.32%	5%
Gupta S et al [12]	India	41.65%	18.30%	17.40%	1.80%	4.80%	0%
Takeshita N et al [11]	Japan	56.02%	10.75%	27.18%	4.49%	8.15%	6%
Banik A et al [20]	India	62.37%	42.14%	14.55%	2.68%	3%	0%
Lakhe N et al [16]	Senegal	41.8%	10.5%	23.30%	8%	0%	0%
Our series	Morocco (Marrakesh)	43%	27.50%	7.54%	4.62%	2.83%	0%

In our study, we observed that 28% of bacteremia cases were caused by *S. aureus*, among which 96% of the isolated strains were resistant to penicillin G, a rate similar to that found at the Military Hospital of Rabat (86.8%) [21]. This high resistance to penicillin G is attributed to the prevalence of *S. aureus* strains producing penicillinase. Furthermore, 28.57% of isolated strains were resistant to gentamicin, an antibiotic commonly used in hospital practice. Similar figures have been reported in other studies in Morocco and Tunisia [15,17]. A higher rate reaching 61.53% of gentamicin resistance in *S. aureus* was reported in a study conducted in Algeria in 2015 [22]. For fusidic acid, routinely prescribed in outpatient settings, our study revealed a resistance rate of 14.2%, comparable to those found in other hospitals in Morocco [15, 21]. For tetracycline, resistance reached 28.57% of cases, a percentage also noted in studies conducted in Rabat and Tunisia, respectively reporting rates of 29.1%, and 29.3% [21,23]. Methicillin-resistant *S. aureus* (MRSA) accounted for 3.54% of the isolated *S. aureus* in our study. This rate is approximately similar to that found in Rabat (10%) [24]. However, a study conducted at Ibn Tofail Hospital in Marrakech in 2018 reported a global MRSA rate of 17.82%, with a decreasing trend in MRSA prevalence described in this study [25].

In our study, *Enterobacter*iaceae represented 41.78% of the isolates and therefore corresponded to the bacterial family most encountered during bacteremia. Tables 5, 6 and 7 show the resistance of *Enterobacter*iaceae to different antibiotics according to several studies.

Table 4 The levels of Gram-negative bacteria compared to the total of bacteria identified according to different studies

Series	**Country**	**Gram(-)**	***E.coli***	***Klebsiella***	***Enterobacter***	***Acinetobacter***	***P. aeruginosa***	**Others**
Mom R. [15]	Morocco (Meknes)	33%	20.82%	2.35%	2.35%	1.17%	4.70%	1.05%
Gupta S et al [12]	India	58.34%	22.40%	19.70%	0.03%	5.20%	8.40%	2.61%
Takeshita N et al [11]	Japan	43.96%	18.1%	9.9%	2.5%	0.8%	3%	9.66%
Banik A et al [20]	India	37.54%	4.21%	9.96%	0.76%	11.49%	1.53%	9.59%
Lakhe N et al [16]	Senegal	58.1%	8.1%	5.8%	7%	8.1%	15.1%	14%
Our series	Morocco (Marrakesh)	56.60%	19.81%	7.54%	10.37%	10.37%	5.66%	2.85%

Table 5 The resistance of the main *Enterobacter*iaceae to aminopenicillins associated with Ac. clavulanic according to different studies

Series	**Country**	***E.coli***	***Klebsiella***	***Enterobacter***
Lakhe A et al [16]	Senegal	100%	100%	83.3%
Bitew A et al [14]	Ethiopia	100%	89.9%	60%
Gupta S et al [12]	India	88.8%	97.28%	50%
Mom R. [15]	Morocco (Meknes)	76%	-	-
El Mouali A. [27]	Morocco (Rabat)	77.7%	93%	
Our series	Morocco	71.14%	62%	100%

Table 6 The resistance of the main *Enterobacter*iaceae to Fluoroquinolones according to various studies

Series	**Country**	***E.coli***	***Klebsiella***	***Enterobacter***
Lakhe A et al [16]	Senegal	42.8%	40%	16%
Bitew A et al [14]	Ethiopia	25%	27.3%	20%
Gupta S et al [12]	India	25%	27.3%	
Mom R. [15]	Morocco (Meknes)	41%	-	-
El Mouali A. [27]	Morocco (Rabat)	28%	60%	69%
Our series	Morocco	47.1%	62.50%	9.1%

Table 7 Resistance of the main *Enterobacter*iaceae to third-generation cephalosporins according to various studies

Series	Country	*E.coli*	*Klebsiella*	*Enterobacter*
Lakhe A et al [16]	Senegal	71.50%	60%	50%
Bitew A et al [14]	Ethiopia	50%	81.80%	80%
Gupta S et al [12]	India	68.8%	85.46%	50%
Mom R. [15]	Morocco (Meknes)	23.52%	-	-
El Mouali A. [27]	Morocco (Rabat)	15%	64%	
Our series	Morocco	14.28%	62.5%	27.27%

Bacteria resistant to 3rd generation cephalosporins by ESBL production constitute a major concern in the hospital environment due to their epidemic spread and their multi-resistance to antibiotics. In France, data from the EARS-Net network show, contrary to *S.aureus*, a marked increase in resistance of E.coli and *Klebsiella* isolated from blood cultures, since 2005. Resistance to C3G in France increased between 2005 and 2017 from 1.4% to 10.2% for *E. coli* and 4% to 29% for *Klebsiella* [26].

Concerning *P. aeruginosa*, we found a ceftazidime resistance rate of 16.67%, comparable to the rate found in a study carried out at the Mohamed VI University Hospital in Marrakech on a paediatric population, and in a study carried out at the Rabat Military Hospital [28,29]. However, a rate of up to 58% was found in India in 2016 [12]. With regard to aminoglycosides, which are often prescribed in combination with ß-lactam antibiotics in the treatment of serious *P. aeruginosa* infections, a sensitivity rate of 100% has been noted for gentamicin, amikacin and tobramycin in our study. However, analysis of our results compared with other studies must take into account the number of isolates (n=6). As with aminoglycosides, no strains of *P. aeruginosa* were resistant to fluoroquinolones in our study.

Furthermore, *Acinetobacter* baumannii resistance reached 91% for ceftazidime, cefepime, and piperacillin-tazobactam. Comparable resistance rates have been reported in other national studies [32, 33]. Recent studies in other countries have also shown similar rates, particularly in Egypt, Greece, and India [34, 35, 31]. Imipenem, being one of the main therapeutic options for these infections, has seen its effectiveness diminish in some countries due to the emergence of new resistant strains. In our study, results were alarming, showing a 91% resistance rate to imipenem. High resistance rates have been reported nationally in Meknes and Rabat [32, 33]. These carbapenem resistances in *A. baumannii* are mainly due to the expression of OXA-type carbapenemases or metallo-beta-lactamases (MBL), impermeabilities related to mutations altering porins, and the expression of efflux pumps [36]. Colistin is often the only therapeutic alternative for carbapenem-resistant *A. baumannii* strains. In our study, all strains remained 100% sensitive to this molecule. Our results are consistent with most of the literature. However, some studies, such as those in China, Greece, and Iran, have noted colistin resistance with percentages of 1.9%, 3.4%, and 16%, respectively [30, 35, 36].

5. Conclusion

Faced with the emergence and growth of bacterial resistance to antibiotics, up-to-date studies of the epidemiological profile of bacteria and the evaluation of their sensitivity profiles are necessary for the rationalization of initial antibiotic therapy in bacteremia. These results should encourage us to pursue more efforts to strengthen hygiene measures in hospitals in order to be able to reduce bacteremia caused by multi-resistant germs. Furthermore, the rate of contamination of blood cultures requires reminders of good practices to reduce contamination of blood cultures.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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