

Evaluation of bacteremia management practices in a referral service in Dakar, Senegal, (2018 – 2022)

Abstract

Introduction: bacteremia remains a public health problem worldwide. Unfortunately, , none of the studies carried out on this subject in our context has looked at how bacteremia is managed. We therefore undertook this study to assess the management practices of bacteremia at the infectious and Tropical diseases department.

Methods: this was a retrospective and descriptive study based on the analysis of records of patients hospitalized at Infectious and Tropical diseases department of Fann national university hospital in Dakar, Senegal. This study covered a five-year period, extending from January 1st 2018, to December 31 2022.

Results: During our study period, 213 patients were enrolled. The sex ratio was 1.13. The average age was 45.6 ± 17.5 years. Most patients (63.4%) had at least one comorbidity. Thirty-two percent (32%) had a history of recent hospitalization, and 25% had received recent antibiotic therapy. During the study period, 231 bacterial strains were isolated. Gram-positive cocci accounted for 68%, and Gram-negative bacilli for 32%. The main bacteria isolated were *Staphylococcus aureus* (30.3%). Empiric antibiotic therapy had been initiated in 81% of patients. Following antibiotic susceptibility testing, 61% of patients had their antibiotic therapy readjusted. In 61% of cases, the therapeutic protocol was deemed unsuitable, in line with the recommendations of Senegal's national antibiotic guide and international recommendations.

Conclusion: An appropriate therapeutic practice in management of bacteremia can help to limit the increase of AMR.

1 Introduction

In Africa, the prevalence of bacteremia ranged from 4.2% to 38.2% [1]. It is estimated that nearly two million episodes of bacteremia and almost 250,000 deaths are attributable to these infections every year in Europe and North America [2]. This situation is likely to increase considerably over the next ten years, given the rise in life expectancy and the impact of age on the occurrence of bacteremia [3].

In addition, the emergence of antimicrobial resistance (AMR) has become a global challenge, posing a growing threat to public health worldwide.

Bacteremia also poses a problem of therapeutic inadequacy, the prevalence of which varies between 23% and 36% of patients depending on the study [4,5]. This inadequacy prolongs hospital duration and increases risk of complications and death [6,7].

Unfortunately, none of the studies carried out on this subject has looked at how bacteraemia is managed in our context and whether it complies with recommendations. We therefore undertook this study to assess whether the management of bacteremia at the SMIT de Fann complied with national and international standards.

2 Methods

This was a retrospective and descriptive study based on the analysis of records of patients hospitalized at the SMIT of Fann national university hospital in Dakar, Senegal. This study covered a five-year period, extending from January 1st 2018, to December 31 2022.

All patients, hospitalized at the SMIT of Fann, diagnosed with bacteremia confirmed by a positive blood culture with an available antibiogram were included.

To facilitate the retrospective collection of information contained in the files, the following definitions have been adopted:

- **Bacteremia:** presence of viable bacteria in the bloodstream, confirmed by positive blood cultures.
- **Recent antibiotic therapy:** when the patient has received antibiotic therapy in the three months prior to hospitalization.
- **Recent hospitalization:** when the patient has been hospitalized in the six months prior to admission.
- **Adapted treatment:** to assess treatment adaptation, we used the following parameters [11-13] :
 - Duration of treatment: considered appropriate if:
 - A minimum of 14 days for *Staphylococci*.
 - Between 7 and 14 days for coagulase-negative *Staphylococci*, *Streptococci* and *Enterococci*.
 - 7 days for gram-negative bacilli (GNB).
 - 21 days for septic thrombophlebitis.
 - Four to six weeks for cases of associated infective endocarditis.
 - Type of molecule: depending on the germ and its sensitivity, as reported by the antibiogram.
 - Number of antibiotics: dual therapy is considered appropriate for *P. aeruginosa* infections, sepsis (qSOFA ≥ 2), or infections with multi-resistant bacteria. Otherwise, monotherapy is more appropriate.
 - Dosage: based on patient's weight. Dosage may be increased in cases of severe or complicated bacteremia.
 - Route of administration: the intravenous route is generally used, except when the molecule is more bioavailable orally.

Data was entered using Epi Info software version 7.2.5.0 and processed using Microsoft Office 365 Excel version 2021.

3 Results

3.1 Epidemiological and clinical aspects

During our study period, 213 patients had bacteremia diagnosed with a positive blood culture, representing a hospital frequency of 5.9%. The study population was predominantly male (53.1%), with a sex ratio of 1.13. The average age was 45.6 ± 17.5 years. More than half the patients (53%) were from urban regions. Most patients (63.4%) had at least one comorbidity. The main comorbidity was HIV infection (42.7%), hypertension (11.3%) and diabetes (7%).

Thirty-two percent (32%) had a history of recent hospitalization, and 25% had received recent antibiotic therapy. Among patients who had received antibiotic therapy, the most frequently were ceftriaxone (23%), ciprofloxacin (18%) and amoxicillin clavulanic acid (15%). Clinically, the most common signs were fever (73%), altered general condition (64%), cough and pulmonary condensation (38%). The qSOFA score was assessed in 70% of patients and was greater than or equal to 2 in 37%. A primary site was identified in 26% of cases, and a secondary site in 16%. The main routes of entry were cutaneous (47%), urinary (25%) and digestive (14%). The main secondary sites were pulmonary (47%), urinary (37%) and neurological (8%).

3.2 Paraclinical and bacteriological aspects

Hyperleukocytosis (WBC $\geq 12,000/\text{mm}^3$) was present in 26% of patients, and C-Reactive Protein (CRP) was greater than 96 mg/L in 60% of patients. Procalcitonin was measured in 12% of patients, with a mean of $9.3 \pm 24.9 \mu\text{g/L}$.

At least two blood culture sets were performed in 30% of patients. Blood cultures were monomicrobial in 98% of cases. During the study period, 231 bacterial strains were isolated. Gram-positive cocci accounted for 68%, and Gram-negative bacilli for 32%. The main bacteria isolated were *Staphylococcus aureus* (30.3%), *Staphylococcus saprophyticus* (26.0%), *Enterobacter spp.* (7.8%), *Klebsiella pneumoniae* (6.9%), *Staphylococcus epidermidis* (5.6%) and *Escherichia coli* (5.2%). Among Gram-positive cocci, over half (57%) were methicillin-resistant strains, and among Gram-negative bacilli, half (51%) were extended-spectrum betalactamases-secreting (ESBL), methicillin-resistant staphylococci aureus (MRSA) accounted for 62% of bacterial isolates.

3.3 Therapeutic and evolutionary aspects

Empiric antibiotic therapy had been initiated in 81% of patients. Of these, 41.3% had received dual antibiotic therapy. The most frequently prescribed molecule were ceftriaxone (41.6%). Empiric treatment was less than 7 days in 35% of patients, between 7 and 14 days in 56%, and more than 14 days in 9%. Following antibiotic susceptibility testing, 61% of patients had their antibiotic therapy readjusted. Monotherapy was prescribed in 42.3% of patients, while dual therapy was prescribed in 35.4%. The main antibiotic were vancomycin (19.6%). The mean duration of readapted treatment was 9.9 ± 6.4 days. The total duration of antibiotic therapy (probabilistic and readjusted) averaged 13.1 ± 9 days. Most patients (42%) were treated for more than 14 days. In 61% of cases, the therapeutic protocol was deemed unsuitable, in line with the recommendations of Senegal's national antibiotic guide and international recommendations. The unsuitability of the protocol concerned the type of molecules (18.5%), the number of antibiotics administered (9.2%), the dosage (6.2%) and the duration of treatment (41.5). The route of administration was not affected.

The average length of hospital stay was 21.7 ± 14.1 days. During hospitalization, 39% of patients developed sepsis and 8% septic shock. Hospital mortality was 33%.

4 Discussion

The incidence of bacteremia varies according to population, bacterial ecology and infection control practices in the geographical area studied. In our study, an incidence of 5.9% was found. This is higher than the 4.11% found in Senegal four years earlier [8] but lower than the bacteremia rates found elsewhere in the subregion: in Gambia in 2005 (10.7%) [9] and in Côte d'Ivoire in 2014 (22.5%) [10]. We found a male predominance. However, gender does not

appear to be a common factor in the occurrence of [8,11]. As in many studies carried out in Africa [8,12] bacteremia is mainly found in adults, with an average age of 45.6 ± 17.5 years in our study. The main comorbidity found in our patients was HIV infection (42.7%). SMIT is the national referral center for the care of HIV-infected patients, which explains the high rate of PLWHA. Furthermore, immunodepression during HIV infection favors the occurrence of invasive infections [13]. Most of bacteremia were skin-derived. Seydi et al., made the same observation in their study [14]. Secondary sites were mainly pulmonary and urinary. In fact, the type of secondary site varies according to the causative germ. Bacteremia caused by *Staphylococcus aureus* are the biggest source of secondary sites (47 to 87% of cases), which are generally osteoarticular, pulmonary, cutaneous and cardiac, whereas BGN are often responsible for urinary or digestive secondary sites [15].

The main clinical signs in our patients were fever, altered general condition and respiratory signs. These signs are frequently found in HIV-infected patients [16]. Hyperleukocytosis was present in 26% of our patients. Hill et al., reported that patients with hyperleukocytosis were at greater risk of bacteremia, with an odd ratio of 1.81 [9]. Most of our patients (89%) had a positive CRP, while procalcitonin was positive in all patients in whom it was performed. Procalcitonin is more specific than CRP and has a better prognostic value.

In recent years, the bacterial ecology involved in bacteremia has changed, and we are witnessing a decrease in the isolation of Gram-negative bacteria in favor of Gram-positive bacteria [6,17].

Most of patients (81%) had received probabilistic antibiotic therapy, and the most commonly prescribed antibiotics was ceftriaxone as is the case throughout Africa [8,10,18]. Unfortunately, this practice risks increasing AMR and limiting our therapeutic choices. Unlike developed countries, we don't have a wide choice of antibiotics. Sixty-one percent (61%) of the patients in our study had had their antibiotic therapy readjusted following the results of the susceptibility test. Vancomycin was the main antibiotic administered (19.6%). Vancomycin remains the antibiotic of choice for the treatment of MRSA infections [19].

The therapeutic protocol was not adapted in 61% of patients. This was related to the fact that some patients had died or been discharged from hospital before the antibiogram was available. In our countries, antibiotic susceptibility test results can be delayed by several factors (logistical problems, availability of reagents, limited resources, etc.). Thus, antibiotic treatment is often empiric. This practice could contribute to therapeutic failure and the development of bacterial resistance. Studies showed that, antibiotic therapy in hospitals is useless or inappropriate in 30 to 50% of cases [20].

The appropriate protocol in our study, concerned the treatment duration in 41.5%. These results are in line with those of the literature, which has shown that the main explanation for this therapeutic inadequacy lies in the excessive duration of antibiotic therapy [20], despite well-defined standards for treatment duration [21]. The new recommendations, suggest a reduction in the duration of antibiotic therapy whenever possible [20,21,22]. However, in certain cases, reducing the duration of treatment is deleterious: when the probabilistic antibiotic therapy was not readapted, when the portal of entry or secondary site is poorly managed, or when the patient is immunocompromised [22].

The second parameter involved in this therapeutic inadequacy was the type of molecules used. Antibiotics prescribed after the results of the susceptibility test are generally narrow spectrum.

In 9.2% of cases, the number of antibiotics received was inappropriate. The choice of mono- or poly-antibiotic therapy is important, as it is a factor that also contributes to the selection pressure of bacteria leading to antibiotic resistance [22]. Some studies have shown that antibiotic combination therapy does not provide any benefit over monotherapy when the latter is adequate. However, when faced with a complication of bacteremia or septic shock, antibiotic combinations have been shown to be more effective than monotherapies [22]. Furthermore, it is important to de-escalate therapy as soon as the antibiogram results are available, and after re-evaluation of the antibiotic therapy 48 to 72 hours after initiation. This practice has shown good results and limits the use of broad-spectrum antibiotics [22].

The average hospital stay in our study was 21.7 ± 14 days. Previous studies of bacteremia in the same department showed higher mean hospital stays [8]. Shorter hospital stays are beneficial because they reduce the risk of exposure to nosocomial infections and improve patients' emotional and social well-being.

5 Conclusion

Bacteremia remains a major public health problem worldwide. An appropriate therapeutic practice in management of bacteremia could help to limit the increase of AMR. In our context of low-income countries, the best way to reduce AMR remains compliance with the recommendations, particularly the duration of treatment.

Table 1. Therapeutic data

Therapeutic data		Number (n)	Percentage (%)
	Yes	172	81
	Ceftriaxone	148	41.6
	Gentamicin	53	14.9
	Spiramycin	42	11.8
	Metronidazole	24	6.7
Probabilistic treatment and molecules	Amoxicillin clavulanic acid	16	4.5
	Vancomycin	14	3.9
	Ciprofloxacin	11	3.1
	Imipenem	9	2.5
	Levofloxacin	9	2.5
	Azithromycin	8	2.2
	Amikacin	7	2.0
	Cefepime	4	1.1
		Yes	130
Re-adapted treatment and molecules	Vancomycin	46	19.6
	Imipenem	32	13.6
	Ciprofloxacin	24	10.2
	Ceftriaxone	23	9.8
	Gentamicin	20	8.5
	Amikacin	17	7.2
	Levofloxacin	10	4.3
	Metronidazole	9	3.8
	Lincomycin	7	3.0

	Spiramycin	7	3.0
	Fusidic acid	7	3.0
	Cefepime	6	2.6
Total duration of antibiotic therapy	< 7 days	33	17
	[7 - 14 days].	80	41
	> 14 days	82	42
Therapeutic protocol	Adapted	65	31
	Not suitable	130	61
	No treatment	18	8
Raisons of therapeutic inadaptation	Molecule type	24	18.5
	Number of antibiotics	12	9.2
	Dosage	8	6.2
	Duration	54	41.5

REFERENCES

- [1]. Reddy EA, Shaw AV, Crump JA. Community-acquired bloodstream infections in Africa: a systematic review and meta-analysis. *Lancet Infect Dis.* 2010;10(6):417-32.
- [2]. Goto M, Al-Hasan MN. Overall burden of bloodstream infection and nosocomial bloodstream infection in North America and Europe. *Clin Microbiol Infect.* 2013;19(6):501-9.
- [3]. Miniño AM, Murphy SL, Xu J, Kochanek KD. Deaths: final data for 2008. *Natl Vital Stat Rep.* 2011;59(10):1-126.
- [4]. Zaragoza R, Artero A, Camarena JJ, Sancho S, González R, Nogueira JM. The influence of inadequate empirical antimicrobial treatment on patients with bloodstream infections in an intensive care unit. *Clin Microbiol Infect.* 2003;9(5):412-8.
- [5]. Marschall J, Agniel D, Fraser VJ, Doherty J, Warren DK. Gram-negative bacteraemia in non-ICU patients: factors associated with inadequate antibiotic therapy and impact on outcomes. *J Antimicrob Chemother.* 2008;61(6):1376-83.
- [6]. Carpentier J-P, Petrognani R, Morillon M. Bacteremia. *EMC - Mal infect.* 2004;1:1-7.

- [7]. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. *Chest*. 1999;115(2):462-74.
- [8]. Lakhe A, Sylla K, Mbaye K, Ndiaye R, Cisse V, KA D, et al. Bacteremia: Profile and Antibiotic Resistance at the Infectious and Tropical Diseases Clinic in Fann Hospital, Dakar, Senegal. *J Infect Dis Ther*. 2018;06.
- [9]. Hill PC, Onyeama CO, Ikumapayi UN, Secka O, Ameyaw S, Simmonds N, et al. Bacteraemia in patients admitted to an urban hospital in West Africa. *BMC Infect Dis*. 2007;7(1):2.
- [10]. Akoua-Koffi C, Tia H, Plo JK, Monemo P, Cissé A, Yao C, et al. Epidemiology of community-onset bloodstream infections in Bouaké, central Côte d'Ivoire. *New Microbes and New Infect*. 2015;7:100-4.
- [11]. Anderson DJ, Moehring RW, Sloane R, Schmader KE, Weber DJ, Jr VGF, et al. Bloodstream Infections in Community Hospitals in the 21st Century: A Multicenter Cohort Study. *PLOS ONE*. 2014;9(3):e91713.
- [12]. Ngoyi ENO, Otiobanda GF, Mahoungou-Guimbi CK, Obengui, Moyen R, Moyen GM. Apport de l'hémoculture dans le diagnostic des bactériémies au Centre (...) - Société de l'Anesthésie Réanimation d'Afrique Francophone. *RAMUR*. 2014;19(1):15-8.
- [13]. Huson MAM, Stolp SM, van der Poll T, Grobusch MP. Community-acquired bacterial bloodstream infections in HIV-infected patients: a systematic review. *Clin Infect Dis*. 2014;58(1):79-92.
- [14]. Seydi M, Sow AI, Soumaré M, Diallo HM, Hatim B, Tine R, et al. Place des bactériémies à *Staphylococcus aureus* au CHU de Fann à Dakar. *Med Mal Infect*. 2004;34(5):210-5.
- [15]. Omezzine Letaief A, Battikh R, Bahri F, Hmouda H, Jemni L. Epidemiological and evolutionary aspects of bacteremia in an internal medicine department: 148 cases. *Med Mal Infect*. 1997;27(8):778-81.
- [16]. Seydi M, Sow PS, Soumaré M, Ndour CT, Dia NM, Diop BM, et al. Bacteremia during AIDS in Dakar, Senegal. *Med Mal Infect*. 2003;33(6):323-6.
- [17]. Martinez RM, Wolk DM. Bloodstream Infections. *Microbiol Spectr*. 2016;4(4). 10.1128/microbiolspec.DMIH2-0031-2016. PMID: 27726765.
- [18]. Mbaye K, Lakhe A, Sylla K, Ndiaye A, Cisse V, Ka D, et al. Enterobacterial Infections Diagnosed at the Clinic of Infectious Diseases of Fann Hospital (2013-2014) Dakar, Senegal. *Adv in Infect Dis*. 2018; 08:217-28
- [19]. Choo EJ, Chambers HF. Treatment of Methicillin-Resistant *Staphylococcus aureus* Bacteremia. *Infect Chemother*. 2016;48(4):267-73.

[20]. Daneman N, Shore K, Pinto R, Fowler R. Antibiotic treatment duration for bloodstream infections in critically ill patients: a national survey of Canadian infectious diseases and critical care specialists. *Int J Antimicrob Agents*. 2011;38(6):480-5.

[21]. Havey TC, Fowler RA, Pinto R, Elligsen M, Daneman N. Duration of antibiotic therapy for critically ill patients with bloodstream infections: A retrospective cohort study. *Can J Infect Dis Med Microbiol*. 2013;24(3):129-37.

[22]. Timsit J-F, Soubirou J-F, Voiriot G, Chemam S, Neuville M, Mourvillier B, et al. Treatment of bloodstream infections in ICUs. *BMC Infect Dis*. 2014; 14:489.

UNDER PEER REVIEW