Kafando et al. Afr. J. Clin. Exper. Microbiol. 2024; 25 (3): xxxx

https://www.afrjcem.org

African Journal of Clinical and Experimental Microbiology. ISSN 1595-689X AJCEM/2347. https://www.ajol.info/index.php/ajcem

Jul 2024; Vol.25 No.3

(A)

Copyright AJCEM 2024:

Original Article

Open Access

Bacteraemia at the tertiary care University Hospital Yalgado Ouedraogo: Bacterial species and their antibiotic resistance profiles

*1,2Kafando, H., ^{3,4}Diallo, I., ⁵Sanou, G., ⁶Lompo, P., ¹Ouédraogo, G. S., ^{4,7}Sanou, I., ^{4,8}Koeta, F., and ^{2,9}Ouédraogo, A. S.

¹Laboratory of Bacteriology-Virology, University Hospital Yalgado Ouedraogo, 03 BP 7022, Ouagadougou, Burkina Faso

²National Reference Laboratory for Antimicrobial Resistance Control (NRL-AMR), Bobo Dioulasso, Burkina Faso ³Department of Infectious Diseases, University Hospital Yalgado Ouedraogo, Ouagadougou, Burkina Faso ⁴Training and Research Unit in Health Science, University Joseph Ki-Zerbo, Ouagadougou, Burkina Faso ⁵Departement of Nephrology-Haemodialysis, University Hospital Yalgado Ouedraogo, Ouagadougou, Burkina Faso

⁶Institut de Recherche en Sciences de la Sante, Clinical Research Unit of Nanoro (IRSS-URCN), Nanoro, Burkina Faso

⁷Department of Laboratory, University Hospital of Tengandogo, Ouagadougou, Burkina Faso ⁸Department of Paediatrics, University Hospital Yalgado Ouedraogo, Ouagadougou, Burkina Faso ⁹National Institute of Health Sciences, University Nazi Boni, Bobo Dioulasso, Burkina Faso *Correspondence to: hervekafando7@qmail.com; +22676146695

Abstract:

Background: Bloodstream infections are serious health problem because of the significant morbidity and mortality they cause. The number of deaths increases in the presence of multidrug resistant bacteria. The aim of this study was to determine the bacteriological and resistance profiles of bacteria isolated from blood cultures. **Methodology:** This is a retrospective descriptive study over 3 years (1st January 2019 to 31st December 2021) of all blood cultures received in the Bacteriology-Virology Laboratory at CHU-YO. Bacteria were isolated from blood cultures after routine processing in automated BD BACTEC FX40 machine. Bacteria identification and antibiotic susceptibility test (AST) was by conventional biochemical tests and API 20E, and Kirby-Bauer disc diffusion method respectively from Jan to Sept 2019, and by BD Phoenix M50 from Sept 2019 to Dec 2021. All proven cases of bacteraemia documented by culture, identification and AST were included in the study. Data analysis was done using EPI-INFO 7.2.4.0 software.

Results: A total of 335 pathogenic bacteria were isolated from non-duplicate blood cultures collected from a total of 2345 patients, with 1209 males and 1136 females, giving a male to female ratio of 1.06. Gram-negative bacilli accounted for 63.6% (n=213) with a predominance of Enterobacteriaceae (40.6%, n=136). The leading species were Klebsiella spp (18.5%, n=62) followed by E. coli (14.0%, n=47). Gram-positive cocci accounted for 36.4% (n=122), mostly Staphylococcus aureus (22.1%, n=74). Klebsiella spp and E. coli strains showed high levels of resistance to beta-lactams (60 to 71.0% for piperacillin-tazobactam, 87 to 89.0% for amoxicillin-clavulanic acid and 79 to 90.0% for ceftriaxone), fluoroquinolones (75 to 78.0% for ciprofloxacin) and sulphonamides (82 to 96.0% for cotrimoxazole). The lowest levels of resistance were observed with cefoxitin (5-20.0%) and imipenem (5-7.0%). Strain sensitivity to aminoglycosides was highly variable, ranging from 0-5.0% for amikacin to 54-67.0% for gentamicin. The main mechanism of resistance of Klebsiella spp and E. coli strains to beta-lactam antibiotics was ESBL production; 64.5% (40/62) and 60.0% (28/47), respectively. Staphylococcus aureus strains were resistant to methicillin (MRSA) in 13.0% of cases. All were sensitive to fusidic acid and vancomycin. Conclusion: Klebsiella pneumoniae, E. coli and S. aureus are the main bacteria responsible for bacteremia in Burkina Faso. Their resistance to antibiotics is very high and remains of concern. The introduction of rapid tests to detect resistant bacteria directly from blood culture broths is essential for the early adaptation of empirical antibiotic therapy.

Keywords: Blood culture; Bacteraemia; Antibiotic resistance

Received Apr 22, 2024; Revised May 09, 2024; Accepted may 10, 2024

Copyright 2024 AJCEM Open Access. This article is licensed and distributed under the terms of the Creative Commons Attrition 4.0 International License <a rel="license" href="http://creativecommons.org/licenses/by/4.0/", which permits unrestricted use, distribution and reproduction in any medium, provided credit is given to the original author(s) and the source. Editor-in-Chief: Prof. S. S. Taiwo

Bactériémies au Centre Hospitalier Universitaire Yalgado

Ouedraogo: Espèces bactériennes et leur profil de résistance aux antibiotiques

*1,2Kafando, H., ^{3,4}Diallo, I., ⁵Sanou, G., ⁶Lompo, P., ¹Ouédraogo, G. S., ^{4,7}Sanou, I., ^{4,8}Koeta, F., et ^{2,9}Ouédraogo, A. S.

¹Service de Bactériologie-Virologie, Centre Hospitalier Universitaire Yalgado Ouédraogo, 03 BP 7022, Ouaqadougou, Burkina Faso

²Laboratoire National de Référence de Lutte Contre la Résistance aux Antimicrobiens (LNR-RAM), Bobo Dioulasso, Burkina Faso

³Service de Maladies Infectieuses, Centre Hospitalier Universitaire Yalgado Ouédraogo, Ouagadougou, Burkina Faso

⁴Unité de Formation et de Recherche en Science de la Santé, Université Joseph Ki-Zerbo, Ouagadougou, Burkina Faso

⁵Service de Néphrologie-Hémodialyse, Centre Hospitalier Universitaire Yalgado Ouédraogo, Ouagadougou, Burkina Faso

⁶Institut de Recherche en Sciences de la Santé, Unité de Recherche Clinique de Nanoro (IRSS-URCN), Nanoro, Burkina Faso

Département des Laboratoires, Centre Hospitalier Universitaire de Tengandogo, Ouagadougou, Burkina Faso 8Service de Pédiatrie, Centre Hospitalier Universitaire Yalgado Ouédraogo, Ouagadougou, Burkina Faso 9Institut National des Sciences de la Santé, Université Nazi Boni, Bobo Dioulasso, Burkina Faso *Correspondance à: hervekafando7@gmail.com; +22676146695

Résumé:

Contexte: Les bactériémies sont des infections graves du fait des taux de morbidité et de mortalité significatives qu'elles engendrent. Les décès sont multipliés par deux ou trois si les patients sont atteints d'infections bactériennes résistantes aux antibiotiques. Le but de ce travail est de déterminer le profil bactériologique et de résistance actuelle des bactéries isolées dans les hémocultures.

Méthodologie: Il s'est agi d'une étude descriptive rétrospective sur 3 ans (1er Janvier 2019 au 31 Décembre 2021) de toutes les hémocultures reçues au laboratoire de bactériologie-virologie du CHU-YO. Les bactéries ont été isolées à partir des hémocultures après traitement de routine dans l'automate BD BACTEC FX40. L'identification des bactéries et l'antibiogramme ont été réalisés respectivement par des tests biochimiques classiques et API 20E, et par la méthode de diffusion du disque de Kirby-Bauer de janvier à septembre 2019, et par BD Phoenix M50 de Septembre 2019 à Décembre 2021. Tous les cas avérés de bactériémie documentés par culture, identification et antibiogramme ont été inclus dans l'étude. L'analyse des données a été réalisée à l'aide du logiciel EPI-INFO 7.2.4.0

Résultats: Au total, 335 bactéries pathogènes ont été isolées à partir d'hémocultures non redondantes sur un total de 2345 patients, dont 1209 hommes et 1136 femmes, soit un ratio homme/femme de 1,06. Les bacilles à Gram négatif représentaient 63,6% (n=213) avec une prédominance d'entérobactéries (40,6%, n=36). Les principales espèces étaient *Klebsiella* spp (18,5%, n=62) suivies par *E. coli* (14.0%, n=47). Les cocci à Gram positif représentaient 36,4% (n=122), principalement *S. aureus* (22,1%, n=74). Les souches de *Klebsiella* spp et *d'E. coli* ont montré des niveaux élevés de résistance aux bêtalactamines (60 à 71.0% pour la pipéracilline-tazobactam, 87 à 89.0% pour l'amoxicilline-acide clavulanique et 79 à 90.0% pour la ceftriaxone), aux fluoroquinolones (75 à 78.0% pour la ciprofloxacine) et aux sulfamides (82 à 96.0% pour le cotrimoxazole). Les niveaux de résistance les plus faibles ont été observés avec la céfoxitine (5 à 20.0%) et l'imipénème (5 à 7.0%). La sensibilité des souches aux aminosides était très variable, allant de 0-5% pour l'amikacine à 54-67.0% pour la gentamicine. Le principal mécanisme de résistance des souches de *Klebsiella* spp et *d'E. coli* aux bêtalactamines était la production de BLSE; 64,5% (40/62) et 60.0% (28/47), respectivement. Les souches de *S. aureus* étaient résistantes à la méthicilline (SARM) dans 13.0% des cas. Toutes étaient sensibles à l'acide fusidique et à la vancomycine.

Conclusion: Klebsiella pneumoniae, E. coli et S. aureus sont les principales bactéries responsables des bactériémies dans Burkina Faso. Leur résistance aux antibiotiques est très élevée et reste préoccupante. L'introduction de tests rapides de détection des bactéries résistantes directement à partir des bouillons d'hémoculture est essentielle pour l'adaptation précoce de l'antibiothérapie probabiliste.

Mots clés: Hémoculture; Bactériémie; Résistance aux antibiotiques

Introduction:

Bacteremia is defined as the presence of bacteria in the blood of a patient with systemic signs of infection. It may be secondary to a localized and documented infection or primary i.e. without an identified origin (1). In developed countries, 40% of community-acquired and nosocomial bacteremia progress to sepsis or septic shock, compared to 20% in

intensive care units (2). Whatever the cause, bacteremia is most often associated with a high mortality rate of up to 36% (3). Factors associated with an increased risk of mortality include the absence of appropriate early antibiotic therapy and poor control of the infection site (3-5).

Increasing bacterial resistance to antibiotics is a major problem in the management of invasive infections. In practice, conventional bacteriological diagnostic methods take 48-72 hours to obtain an antibiogram, and 20-30% of patients receive inadequate initial antibiotic therapy, with a 7.6% increase in mortality for each hour of delayed antibiotic therapy (6). For clinicians, knowledge of the bacterial species most frequently encountered in infectious diseases and their susceptibility to the main antibiotics is essential for early and appropriate antibiotic therapy (7). This is more than necessary in the case of invasive infections such as sepsis which cause 30% of hospital deaths in developed countries (8) and where empirical antibiotic therapy determines the vital prognosis.

The management of sepsis is based on urgent and appropriate empirical antibiotic therapy. The choice of molecules used requires knowledge of the local bacterial ecology and their sensitivity to antibiotics, which needs to be regularly updated. The aim of this study is to describe the bacteriological and resistance profiles of the main bacteria involved in bacteraemia at the University Hospital Yalgado Ouedraogo (CHUYO) from 2019 to 2021.

Materials and method:

Study setting, design and period:

This is a retrospective descriptive study over a 3-year period (1st January 2019 to 31st December 2021) of blood cultures received at the CHUYO. All proven cases of bacteraemia documented by culture, identification and antibiotic susceptibility testing carried out and validated in the bacteriology-virology laboratory of the CHUYO were included in this study. Duplicates that had been clearly identified (the same species identified in the same patient with same sensitivity profile) were excluded.

Ethics statement:

The study was approved by the National Ethics Committee for Health Research (Reference no: 2023-04-096). The personal data collected on the patients were not disclosed.

Isolation and identification of bacteria:

Blood samples were routinely inoculated in BD BACTEC bottles (aerobic, anaerobic and paediatric) and incubated in the BD BACTEC FX40 (Becton Dickinson, New Jersey) following a 5-day protocol. All positive broths were cultured on Chocolate + PolyViteX agar. A selective medium was added according to the results of Gram staining (e. g. presence of Gram-negative bacilli, EMB medium was used, while in the presence of Gram-positive cocci in clusters, CHAPMAN medium was used).

From January to August 2019, identification was carried out using conventional microbiology methods, including morphological and biochemical characteristics (API20E, catalase, oxidase), and the antibiotic susceptibility

testing (AST) was performed using the Kirby-Bauer disc diffusion method on Mueller-Hinton (MH) agar. From September 2019 to December 2021, identification and antibiotic susceptibility testing were performed on BD Phoenix M50 (Becton Dickinson, New Jersey) using panels for Gram-negative (NMIC) and Grampositive (PMIC) bacteria.

The following antibiotics were routinely used for the sensitivity testing; penicillin G (PG), ampicillin (AMP), amoxicillin-clavulanic acid (AMC), ticarcillin-clavulanic acid (TCC), piperacillin-tazobactam (PTZ), ceftriaxone (CRO), ceftazidime (CAZ), cefepime (FEP), imipenem (IMI), meropenem (MEM), ertapenem (ERT), gentamicin (GEN), tobramycin (TOB), amikacin (AN), moxifloxacin (MOX), levofloxacin (LEV), ciprofloxacin (CIP), trimethoprim-sulfamethoxazole (SXT), erythromycin (E), clindamycin (DA), fusidic acid (FA), and vancomycin (VAN). The results of AST were interpreted in accordance with the recommendations of the 2021 European Committee on Antimicrobial Susceptibility Testing (EUCAST 2021).

ESBL production was detected by the double disc synergy test involving a central amoxicillin-clavulanic acid disc placed 30 mm away from a 3rd or 4th generation cephalosporin disc (ceftazidime, ceftriaxone, cefepime) on MH agar, with characteristic 'champagne cork' appearance. For AST performed in liquid media, ESBL production was detected by the Expert System of the BD Phoenix M50 automated system (Becton Dickinson, New Jersey). Cefoxitin was used to detect methicillin resistance in *S. aureus* isolates.

Statistical analysis:

The data from the study were entered into Excel 2013 and analyzed using EPI-INFO 7.2.4 software. The Chi-square test was used to make comparisons between the different proportions, with a value of p < 0.05 as the threshold of statistical significance.

Results:

Patient characteristics:

A total of 2345 non-redundant blood cultures from 2345 patients were included during the study period. There were a total of 1209 males, giving a sex ratio of 1.06. Nearly 64.0% (n=1498) of patients were aged \leq 17 years. Children under one year of age were the most represented (34.6%, n=812). The majority of blood samples came from the departments of paediatrics (61.2%, n=1436), nephrology-haemodialysis (8.1%, n=189), gynaecology-obstetrics (5.1%, n=120), internal medicine (4.8%, n=112), medical emergencies (4.2%, n=99), intensive care (3.9%, n=91) and infectious diseases (2.4% n=55) (Table 1).

Microbiological profiles of the microorganisms isolated in blood cultures:

A total of 715 non-redundant bacterial and fungal species were isolated, giving a microbiological yield of 30.5% (715/2345). These isolates belonged to almost fifty different species, of which clinically significant bacteria accounted for 46.8% (n=335). Gram-negative bacilli (GNB) were the most frequent (63.6%, n=213), with predominance of Enterobacteriaceae (40.6%, n=136). More than 80.0% of the Enterobacteriaceae were *Klebsiella* spp (45.6%, n=62), followed by *Escherichia coli* (34.5%, n=47). Gram-positive cocci (GPC) accounted for 36.4% (n=122) of all clinically significant isolates, with predominance of *Staphylococcus aureus* (22.1%, n=74), followed by *Enteroco-*

ccus species (8.6%, n=29) and Streptococcus spp (5.7%, n=19) (Table 2). Staphylococcus aureus accounted for 60.7% (74/122) of clinically significant Gram-positive cocci.

The rate of potential contamination of blood cultures was about 16.0% (373/2345), which represented 52.1% of all isolates (373/715) and were essentially coagulase-negative staphylococci (38.7%, n=277) and Gram-positive bacilli of the genus *Bacillus* (10.7%, n=77) (Table 2). The trends in clinical categories show that the rate of isolation of potential contaminants decreased significantly with patients' age (p<0.001), from 20.0% in children aged ≤ 1 year, to 12.0% in patients aged 60 years and above (Fig 1).

Table 1: demographic characteristics of patients with clinical suspicion of bacteraemia at CHUYO, Ouagadougou, Burkina Faso

Characteristics	Number	Percentage
Age group (years)		
≤ 1	812	34.6
1-17	686	29.3
18-60	630	26.8
≥ 60	217	9.3
Gender		
Female	1136	48.4
Male	1209	51.6
Departments		
Paediatric	1436	61.2
Nephrology-haemodialysis	189	8.1
Gynecology-obstetrics	120	5.1
Internal medicine	112	4.8
Medical emergencies	99	4.2
Intensive care units	91	3.9
Other departments	69	2.9
Infectious diseases	55	2.3
Cardiology	37	1.6
Dermatology	37	1.6
Neurosurgery	32	1.4
Neurology	30	1.3
Surgery (orthopedics and visceral)	24	1.0
Hepato-Gastro-Enterology	14	0.6

Antibiotic resistance of the main bacteria isolates:

The antibiotic resistance of the main bacteria isolated from blood cultures is shown in Table 3. *Klebsiella* spp and *E. coli* showed high levels of resistance to beta-lactam antibiotics; penicillins + beta-lactamase inhibitors (60 to 71.0% for piperacillin-tazobactam versus 87 to 89.0% for amoxicillin-clavulanic acid), 3rd generation cephalosporins (79 to 90.0% for ceftriaxone), fluoroquinolones (75 to 78.0% for ciprofloxacin) and sulphonamides

(82 to 96.0% for trimethoprim-sulfamethoxazole). The lowest levels of resistance were observed with cefoxitin (5 to 20.0%) and imipenem (5 to 7.0%).

The sensitivity of isolates to aminoglycosides varied widely, ranging from 0 to 5.0% for amikacin, to 54 to 67.0% for gentamicin (Table 3). The main mechanism of resistance of *Klebsiella* spp and *E. coli* isolates to beta-lactam antibiotics was ESBL production (64.5%, 40/62) and (60%, 28/47) respectively.

Table 2: Distribution of micro-organisms isolated from blood cultures at CHUYO, Ouagadougou, Burkina Faso

Bacterial family and specie	es	Number of isolates	Percentage	Clinical categorization			
Enterobacterales (n=136)	Klebsiella spp	62	8.67	Clinically significant			
	Escherichia coli	47	6.57	organisms (n=335)			
	Enterobacter cloacae complex	15	2.10				
	Morganella morganii	3	0.42				
	Raoultella ornithinolytica	2	0.28				
	Citrobacter spp	2	0.28				
	Yersinia pseudotuberculosis	1	0.14				
	Serratia odorifera	1	0.14				
	Proteus mirabilis	1	0.14				
	Providencia stuartii	1	0.14				
	Salmonella spp	1	0.14				
Other Gram-negative bacilli (n=77)	Acinetobacter baumannii	38	5.31				
	Pseudomonas spp	21	2.94				
	Burkholderia cepacia	9	1.26				
	Pantoea agglomerans	4	0.56				
	Comamonas testosteroni	2	0.28				
	Aeromonas hydrophila	1	0.14				
	Chromobacterium violaceum	1	0.14				
	Tatumella ptyseos	1	0.14				
Gram-positive cocci (n=410)	Staphylococcus aureus	74	10.35				
	Enterococcus spp	29	4.06				
	Streptococcus spp	19	2.66				
	Coagulase negative staphylococci	277	38.74	Potential contaminants (n=373)			
	Aerococcus spp	5	0.70				
	Micrococcus spp	5	0.70				
	Rhodococcus equi	1	0.14				
Gram-positive bacilli (n=85)	Bacillus spp	77	10.77				
	Corynebacterium spp	8	1.12				
Fungi (n=7)	Candida spp	7	0.98	Fungemia (n=7)			
Total		715	100.00				

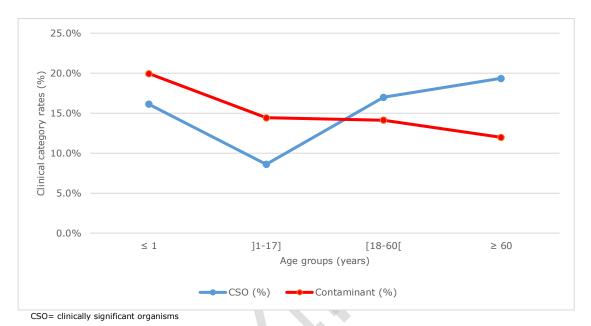


Fig 1: Distribution of clinical categories of bacteria isolated according to patients' age

Table 3: Antibiotic resistance of the four main bacterial pathogens isolated from blood cultures of patients with bloodstream infection at CHUYO, Ouagadougou, Burkina Faso

Number of isolates tested to the antibiotics	Percentage of antibiotic-resistant isolates																
	AMP	AMC	TCC	PTZ	CRO	CAZ	IMI	SXT	AN	GEN	CIP	FOX	PG	E	DA	FA	VAN
Klebsiella spp (n=62)	-	87	87	71	90	89	7	82	0	67	75	10	-	-	-	-	-
Escherichia coli (n= 47)	96	89	89	60	79	79	5	96	5	54	78	20	-	-	-	-	-
Acinetobacter baumannii (n=38)	-		45	32	-	42	34	76	16	52	61	-	-	-	-	-	-
Staphylococcus aureus (n=74)	-			-	-	-	-	29	-	12	23	13	88	28	12	0	0

AMP: ampicillin; AMC: amoxicillin-clavulanic acid; TCC: ticarcillin -clavulanic acid; PTZ: piperacillin-tazobactam; CRO: ceftriaxone; CAZ: ceftazidime; IMI: imipenem; SXT: cotrimoxazole; AN: amikacin; GEN: gentamicin; CIP: ciprofloxacin; FOX: cefoxitin; PG: penicillin G; E: erythromycin; DA: clindamycin; FA: fusidic acid; VAN: vancomycin

As for Gram-negative non-Enterobacteriaceae isolates, *Acinetobacter baumannii* was particularly resistant to beta-lactam antibiotics, with 34.0% resistant to imipenem. Amikacin was the most active antibiotic, with only 16.0% of bacterial isolates resistant to it. *Sta-phylococcus aureus* isolates were highly resistant to penicillin G (88.0%) and cotrimoxazole (29.0%). Methicillin-resistant strains (MRSA) accounted for 13.0% of all *S. aureus* isolates. Macrolides and related drugs were relatively active, with resistance rates ranging from 12% for clindamycin to 28.0% for erythromycin. No resistance to vancomycin or fusidic acid was reported (Table 3).

Discussion:

In this study, clinically significant bacteria responsible for bacteremia were Gramnegative bacilli (63.6%) dominated by Enterobacteriaceae (40.6%), mainly Klebsiella spp and E. coli, while S. aureus accounted for 22.1%. The rate of potential contamination of blood cultures was very high at 16.0%. High proportion of Gram-negative bacilli in bacteraemia, particularly Enterobacteriaceae, has been reported in several studies, with rates of between 40 to 70.0% (9-12). Over 80.0% of Enterobacteriaceae isolated were Klebsiella species (45.6%) and *E. coli* (34.5%). This trend in the bacteriological profile of bacteraemias caused by Enterobacteriaceae had already been described by Ebonque et al., (10) in Cameroon, who reported that Klebsiella were in first place at 27.8%, followed by E. coli at 12.0% of all isolates from blood cultures. Boughattas et al., (9) reported the same observation regarding the high involvement of Enterobacteriaceae in both nosocomial and community-acquired bacteraemias, with frequencies of 33.3% and 52.5% respectively.

Among the clinically significant Grampositive cocci, S. aureus was the most frequently seen in our study (60.7%). Data from the French national observatory on the epidemiology of bacterial resistance to antibiotics also show that it is the main species isolated (45.4%) among Gram-positive cocci involved in nosocomial bacteraemia (13). Staphylococcus aureus is generally considered to be the second pathogen involved in bacteremia after Enterobacteriaceae (14). In Morocco, Badaoui et al., (12) reported the same finding, with S. aureus bacteremia occurring in 26.5% of cases. In Tunisia, similar trends were also reported by Boughattas et al., (9) with 30.6% and 22.5% respectively in nosocomial and community-acquired bacteraemias. Staphylococcus aureus bacteraemias are common in healthcare-associated infections and is most often linked to a variety of clinical situations, the most frequent being catheter-related in

poly-pathological patients (14). They constitute diagnostic and therapeutic emergencies due to their high mortality rates. Mortality is estimated at 20-25.0% at one month, and is very often associated with the initial presence of sepsis, the location of the primary infection (neurological, pulmonary, and cardiac) (15).

In this study, over 52.0% of isolates were potential contaminants, consisting mainly of coagulase-negative staphylococci (38.7%) and Gram-positive bacilli of the genus Bacillus (10.8%). This high frequency highlights the quality challenges in the microbiological diagnosis of bacteraemia in our context, and is attributable to two main factors; (i) the working environment where contamination of blood cultures in countries with limited resources often originates in the environment, as Bacillus spp are known to be present in the air (as aerobic spore bearers) and have been described in epidemics of pseudo-bacteremia originating in the environment (16), and (ii) failure to follow good blood culture practice, making it difficult to distinguish between contaminants and pathogens, because certain contaminants typical of blood cultures, such as coagulasenegative staphylococci, which accounted for over 38.0% of isolates in this study, can cause catheter-related infections.

Clinical categorization of organisms is generally established by the number of blood cultures positive for the particular organisms (16). Often, a coagulase-negative staphylococcus is only considered clinically significant if it is isolated from at least two separate blood cultures, as the probability of contaminating both cultures with the same pathogen is very low (17-18). However, this approach is often very difficult to implement in low- and middleincome countries, where in majority of cases, only a single pair of blood cultures is taken because of the low purchasing power of the population and the lack of health insurance to facilitate access to microbiological diagnosis. The time taken for detection can also help with interpretation, as it has been shown that contaminants develop more slowly than true pathogens. In this concept, it is established that a bacteraemic patient will have a much higher inoculum of bacteria than a contaminated culture. Theoretically, it follows that a larger inoculum will develop more rapidly than a smaller one (19).

The rate of isolation of potential contaminants in our study was around 16.0%, with a significant variation according to patients' age, ranging from 20.0% in children aged ≤ 1 year of age to 12.0% in patients aged 60 years and above. The high level of contamination of paediatric blood cultures was reported by Brunet et al., (20) who described contamination rates of over 10.0%, with coagulase-negative staphylococci topping the list. It is gener-

ally accepted that contamination of blood cultures by skin flora, particularly coagulase-negative staphylococci, is essentially due to poor antisepsis of the skin during venipuncture (16). This could account for the high rate of potential contamination in paediatric patients, who are less cooperative during venipuncture and are subject to a variety of manipulations that can lead to contamination of blood cultures.

In terms of antibiotic resistance, the most frequently isolated Enterobacteriaceae (Klebsiella spp and E. coli) exhibited very high levels of resistance to amoxicillin-clavulanic acid and to the 3rd generation cephalosporins (3GCs). The main mechanism of resistance was the production of extended-spectrum beta lactamase (ESBL) in 60.0% and 64.5% of cases respectively in E. coli and Klebsiella spp. Similar results were reported in a Madagascan hospital in 2020, with ESBL-producing strains occurring in 62.2% of cases (21). In Casablanca Morocco and Tunisia respectively, prevalence rates of 62.0% and 60.3% ESBL-producing Enterobacteriaceae were reported in bacteraemias (22-23). The strong involvement of ESBL-producing Enterobacteriaceae in bacteraemia no longer needs to be demonstrated, leading to the empirical prescription of carbapenems, which remain the antibiotics of 'last resort'. However, the widespread use of carbapenems has led to the emergence of carbapenemase-producing strains. In this study, the resistance of strains to imipenem was 5.0% and 7.0% for E. coli and Klebsiella spp respectively. Dridi et al., (23) reported that 6.4% of Klebsiella strains were resistant to carbapenems. Boughattas et al., (9) and Cattoen et al., (24) described near-total sensitivities of E. coli to imipenem. In developed countries, the current trend is to use therapeutic alternatives that avoid the use of carbapenems, such as piperacillin-tazobactam (25) or new antibiotics such as ceftazidime-avibactam and ceftolozane-tazobactam (26-27) which are not yet available in the West African countries.

Methicillin-resistant *S. aureus* (MRSA) accounted for 13.0% of all isolates, and 87.0% were methicillin-susceptible (MSSA). Antibiotic susceptibility data for *S. aureus* isolates from infections in France show the same trend with 86.0% of MSSA in hospital settings (14). Whereas in the case of MSSA bacteraemia, there is ample room for maneuver in terms of choice of antibiotics, the presence of MRSA bacteraemia considerably reduces the therapeutic options, with the exception of vancomycin or daptomycin-based monotherapy and the use of the new 5th generation cephalosporins such as ceftaroline and ceftobiprole (28-29). But like ceftazidime-avibactam and

ceftolozane-tazobactam, 5th generation cephalosporins are not yet available in our country.

Conclusion:

Escherichia coli, K. pneumoniae and S. aureus are the main bacteria responsible for bacteraemia in our hospital. The antibiotic resistance of these bacteria is very high. The introduction of rapid tests to detect resistant bacteria directly from blood culture broths is proving essential for the early adaptation of empirical antibiotic therapy. However, the high level of potential contaminants in blood cultures is not conducive to the optimal use of antibiotics. There is an urgent need to improve local blood culture practice and to assess the impact of contaminants on therapeutic decisions.

Acknowledgements:

The authors would like to thank the Bacteriology-Virology Technical Team for their contribution to the analysis of the samples in this study.

Contributions of authors:

HK, PL, SGO and IS were involved in study conceptualization; SGO, HK and IS were involved in the methodology; HK and IS were involved in study validation; HK and SGO were involved in data collection, cleaning and analysis; HK, SG, SGO and ID were involved in original manuscript draft preparation; HK, SG, ID, PL, IS and ASO reviewed the article. All authors read and agreed to the submitted version of the manuscript.

Source of funding:

No funding was provided for this study

Conflicts of interest:

The authors declare that they have no conflicts of interest in connection with this study.

References:

- National HealthCare Safety Network. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-central Line Associated Blood stream Infection).
 - https://www.cdc.qov/nhsn/pdfs/pscmanual/4psc cla bscurrent.pdf; 2024. (Accessed January 22, 2024).
- Timsit, J. F., Ruppé, E., Barbier, F., Tabah, A., and Bassetti, M. Bloodstream infections in critically ill patients: an expert statement. Intensive Care Med. 2020; 46 (2): 266-284. https://doi.org/10.1007/s00134-020-05950-6
- 3. Tabah, A., Koulenti, D., Laupland, K., et al. Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study.

- Intensive Care Med. 2012; 38 (12): 1930-1945. https://doi.org/10.1007/s00134-012-2695-9
- Adrie, C., Garrouste-Orgeas, M., Ibn Essaied, W., et al. Attributable mortality of ICU-acquired bloodstream infections: Impact of the source, causative microorganism, resistance profile and antimicrobial therapy. J Infect. 2017; 74 (2):131-141. https://doi.org/10.1016/j.jinf.2016.11.001
- Zahar, J. R., Timsit, J. F., Garrouste-Orgeas, M., et al. Outcomes in severe sepsis and patients with septic shock: Pathogen species and infection sites are not associated with mortality. Crit Care Med. 2011; 39 (8):1886.doi:10.1097/CCM.0b013e31821b827c
- Kumar, A., Roberts, D., Wood, K. E., et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006; 34 (6):1589. doi:10.1097/01.CCM.0000217961.75225.E9
- Da, G., Ra, W., Rp, W., et al. Strategies to Prevent and Control the Emergence and Spread of Antimicrobial-Resistant Microorganisms in Hospitals. A challenge to hospital leadership. JAMA. 1996; 275 (3). https://pubmed.ncbi.nlm.nih.gov/8604178/.
 Abbara, S., Guillemot, D., El Oualydy, S., et al.
- Abbara, S., Guillemot, D., El Oualydy, S., et al. Caractéristiques clinico-microbiologiques et mortalité des épisodes avec bactériémie nosocomiale dans 14 hôpitaux universitaires en France, 2016-2019. MMI Formation. 2022; 1 (2): S31-32. doi: 10.1016/j.mmifmc.2022.03.069
- Boughattas, S., El Haddad, N., Azouzi, F., et al. Bacteremia in paediatrics. Infect Dis Now. 2021; 51 (5): S140. https://doi.org/10.1016/j.idnow.2021.06.222
- Ebongue, C. O., Mefo'o, J. N., Dongho, E. N., Moukoko, E. E., Adiogo, D., and Beyihabd, G. Bacteriological profile and antibiotic susceptibility of blood culture isolates (2006-2011) in Douala, Cameroon. Rev Mali Infect Microbiol. 2014; 27-39. https://doi.org/10.53597/remim.vi2.365
- Savadogo, M., Diallo, I., Diendéré, A., Sondo, K., and Sawadogo, A. Sepsis observed in the infectious diseases department of the CHU Yalgado Ouédraogo in Ouagadougou: epidemiological, clinical and evolutionary aspects. Rev Mali Infect Microbiol. 2021; 16 (2):32-35. http://dx.doi.org/10.53597/remim.v16i2.1867
- Badaoui, L., Lahsen, A. O., Daoudi, N., et al. Current profile of bacteremia in the Department of Infectious Diseases: About 216 cases. Rev Mali Infect Microbiol. 2016:7-11.
- http://dx.doi.org/10.53597/remim.v6i0.825

 13. Bertrand, X., Costa, Y., and Pina, P. Surveillance of antimicrobial resistance of bacteria isolated from bloodstream infections: data of the French National Observatory for Epidemiology of Bacterial Resistance to Antibiotics (ONERBA), 1998-2003. Med Mal Infect. 2005; 35 (6):329-334.

 doi: 10.1016/j.medmal.2005.05.002.
- Moing, V. L. Staphylococcus aureus bacteremia and infective endocarditis. MMI Formation. 2022; 1 (4): 172-179.doi:10.1016/j.mmifmc.2022.09.006
- Braquet, P., Alla, F., Cornu, C., et al. Factors associated with 12-week case-fatality in Staphylococcus aureus bacteraemia: a prospective cohort study. Clin Microbiol Infect. 2016; 22 (11):948.e1-948.e7. doi:10.1016/j.cmi.2016.07.034
- Ombelet, S., Barbé, B., Affolabi, D., et al. Best Practices of Blood Cultures in Low-and-Middle-Income Countries. Front Med. 2019; 6: 131. doi: 10.3389/fmed.2019.00131

- Weinstein, M. P. Blood Culture Contamination: Persisting Problems and Partial Progress. J Clin Microbiol. 2003; 41 (6): 2275-2278.
 doi: 10.1128/jcm.41.6.2275-2278.2003
- Isabelle, A., Murielle, C., and Brigitte, L. Bacteremia and fungemia - Blood culture. In: REMIC. French Microbiology Society. 5th Edition, 2015: 125-128.
- Hall, K. K., and Lyman, J. A. Updated Review of Blood Culture Contamination. Clin Microbiol Rev. 2006; 19 (4): 788-802. doi: 10.1128/cmr.00062-05
- Brunet, C. Impact of contaminated blood cultures in paediatric emergencies, retrospective study at Bordeaux University Hospital. Thesis Doctorate in Medicine. 2019.
- Rakotovao-Ravahatra, Z. D., Randriatsarafara, F. M., Rakotovao, A. L., and Rasamindrakotroka, A. Prevalence and factors associated with extended-spectrum β-lactamase producing Enterobacteriaceae bacteraemia in University Hospital of Befelatanana, Madagascar. Afr J Clin Exper Microbiol. 2021; 22 (1): 52-59.doi:10.4314/ajcem.v22i1.7
- 22. Jarmoumi, A., Bencharef, H., Hasnane, S., Lamchaheb, M., Zerouali, K., and Quessar, A. Bacteraemia in neutropenic patients during acute myeloblastic leukaemia at the Casablanca haematology center. Poster, Biology Innovation Day. 2019
- Dridi, K., Gdoura, S., and Houimli, S. Bacteriological profile and sensitivity of blood culture isolates at Hôpital F.S.I la Marsa. Poster 0555, 30th National Congress of the Tunisian Society of Infectious Pathology. 2021
- Cattoen, C., Descamps, D., Vachée, A., and Wallet, F: ESBL-producing Escherichia coli bacteremia in Nord -Pas-de-Calais: patient characteristics, antibiotic susceptibility, and therapeutic management. Med Mal Infect. 2014; 44(6):41. doi:10.1016/S0399-077X (14)70160-X
- Henderson, A., Paterson, D. L., Chatfield, M. D., et al. Association Between Minimum Inhibitory Concentration, Beta-lactamase Genes and Mortality for Patients Treated With Piperacillin/Tazobactam or Meropenem From the MERINO Study. Clin Infect Dis. 2021; 73 (11):e3842-3850.doi:10.1093/cid/ciaa1479
- Isler, B., Ezure, Y., Romero, J. L. G. F., Harris, P., Stewart, A. G., and Paterson, D. L. Is Ceftazidime/ Avibactam an Option for Serious Infections Due to Extended-Spectrum-β-Lactamase-and Amp C-Producing Enterobacterales? a Systematic Review and Metaanalysis. Antimicrob Agents Chemother. 2020; 65 (1): doi:10.1128/aac.01052-20.
- Hirsch, E. B., Brigman, H. V., Zucchi, P. C., et al. Ceftolozane-tazobactam and ceftazidime-avibactam activity against β-lactam-resistant *Pseudomonas aerruginosa* and extended-spectrum β-lactamase-producing Enterobacterales clinical isolates from US medical centres. J Glob Antimicrob Resist. 2020; 22: 689-694. doi: 10.1016/j.jqar.2020.04.017
- Tong, S. Y. C., Lye, D. C., Yahav, D., et al. Effect of Vancomycin or Daptomycin With vs Without an Antistaphylococcal β-Lactam on Mortality, Bacteremia, Relapse, or Treatment Failure in Patients with MRSA Bacteremia: A Randomized Clinical Trial. JAMA. 2020; 323(6):527-537.doi:10.1001/jama.2020.0103
 Jacqueline, C., and Tattevin, P. Ceftaroline, a new
- Jacqueline, C., and Tattevin, P. Ceftaroline, a new cephalosporin active against methicillin-resistant Sta-phylococcus aureus: experimental and clinical data, therapeutic prospects. J Anti-Infect. 2012;14(1):3-10 doi: 10.1016/j.antinf.2012.01.001