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Original Research Article

Bacteremias in Intensive Care Unit: A Two-Year Retrospective Study

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Abstract: Nosocomial infections, particularly bacteremias, are a significant concern in intensive care units (ICUs) due to their invasive nature and the severity of patient's conditions. This retrospective study aimed to investigate the epidemiological and resistance profile of bacteria isolated from blood cultures in patients admitted to the intensive care units of Ibn Sina University Hospital in Rabat. The study spanned over 24 months, from January 2021 to December 2022. Data from 725 positive blood cultures were analyzed, and 423 cases met the criteria for bacteremia. Gram-negative bacilli were more frequently isolated than gram-positive cocci, with *Klebsiella pneumoniae* and *Acinetobacter baumannii* being the most prevalent species. The resistance profile of the isolated bacteria was assessed using various techniques, including automated systems and disk diffusion. The findings underscore the importance of identifying the responsible bacterial species and their resistance patterns in ICU settings to guide appropriate treatment strategies and improve patient outcomes. Further research and interventions are needed to address the challenges posed by nosocomial infections in ICUs and reduce their associated morbidity and mortality rates.

Keywords: Bacteremia, Intensive Care Unit, Retrospective Study, Nosocomial Infections, Resistance Profile, Blood Cultures.

INTRODUCTION

Nosocomial infections (NIs) pose a significant public health challenge affecting both developed and resource-poor countries, with their highest prevalence observed in intensive care units due to the invasive nature of procedures and the severity of patient conditions [1, 2].

Bacteremias are defined by the presence of at least one positive blood culture. However, for certain bacteria with lower pathogenic potential, such as coagulase-negative staphylococci, Bacillus spp., Corynebacterium spp., Propionibacterium spp., Micrococcus spp., and other saprophytic or commensal bacteria, at least two positive blood culture bottles from different punctures are required [3].

Bacteremias represent the second most common infection in terms of frequency among nosocomial infections in intensive care, after pneumonia. Their high lethality rate emphasizes the importance of identifying the responsible bacterial species and their resistance profile [2].

This study aims to determine the epidemiological and resistance profile of bacteria isolated from blood cultures in patients hospitalized in the various intensive care units of the Ibn Sina University Hospital of Rabat.

MATERIALS AND METHODS

This retrospective study was conducted at the Central Laboratory of Bacteriology-Serology and Hygiene of the Ibn Sina University Hospital in Rabat. The study period spanned from January 1, 2021, to December 31, 2022 (24 months). Ethical approval was granted by the ethical committee of CHU Ibn Sina University Hospital, Rabat.

We included isolates from aerobic and anaerobic blood cultures received from various intensive care units of the CHU hospitals. The following criteria were used for exclusion:

- Duplicate isolates with the same resistance profile from the same patient within a five-day period.
- The following bacterial species when isolated only once:
- Coagulase-negative staphylococci
- Bacillus spp.
- Corynebacterium spp.
- Propionibacterium spp.
- Micrococcus spp.

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Blood culture bottles were incubated at 37°C in the BD BACTEC FX system. In the absence of growth after 7 days of incubation, a negative result was reported.

For positive bottles, the following procedures were performed:

- Microscopic examination in the fresh state
- Gram staining
- Subculturing on selected agar media according to context

Identification of bacteria was performed based on cultural, morphological, and biochemical characteristics of colonies, using both manual and automated BD PHOENIX galleries.

The resistance profile study was conducted using the automated BD PHOENIX system and by the disk diffusion technique on Mueller-Hinton agar for non-fastidious bacteria and on PolyViteX® chocolate agar for fastidious bacteria.

The interpretive reading and detection of various resistance phenotypes, based on quantitative and qualitative methods, were performed according to the recommendations described by the Antibiogram Committee of the French Society of Microbiology (SFM) [4].

RESULTS

Out of a total of 2067 blood cultures, 725 were positive (35.1%), among which 423 (20.4%) met the definition of bacteremia and thus the inclusion criteria. 61 patients were hospitalized in pediatric intensive care (14.4%), and 362 in adult intensive care (85.6%), with a male-to-female sex ratio of 1.84.

Gram-negative bacilli (GNB) 55.80% (N=236) were more isolated than gram-positive cocci (GPC) 44,2% (N=187). The most isolated bacterial species were *Klebsiella pneumoniae* and *Acinetobacter baumannii*, accounting for 19.15% (N=81) and 15.84% (N=67) of cases, respectively. The distribution and resistance profile of bacterial species are reported in Tables I, II, and III.

Table I: *Distribution of the different isolated species*

			N	%
GNB N=236 (55.8%)	Enterobacteria N=153 (36.2%)	*Citrobacter braakii*	1	0,2%
		Citrobacter freundii	1	0,2%
		Enterobacter aerogenes	4	0,9%
		Enterobacter cloacae	12	2,8%
		Escherichia coli	32	7,6%
		Klebsiella pneumoniae	81	19,1%
		Morganella morganii	5	1,2%
		Proteus mirabilis	5	1,2%
		Providencia stuartii	5	1,2%
		Serratia marcescens	7	1,7%
	Non fermenting N=83 (19.6%)	*Acinetobacter baumannii*	67	15,8%
		Pseudomonas aeruginosa	16	3,8%
GPC N=187 (44.2%)	Staphylococcus N=135 (31.9%)	*Staphylococcus aureus*	46	10,9%
		Staphylococcus capitis	1	0,2%
		Coagulase_negative staphylococcus	56	13,2%
		Staphylococcus cohnii	5	1,2%
		Staphylococcus epidermidis	18	4,3%
		Staphylococcus equorum	1	0,2%
		Staphylococcus haemolyticus	4	0,9%
		Staphylococcus hominis	4	0,9%
	Streptococcus N=8 (1.9%)	*Streptococcus spp.*	8	1.9%
	Enterococcus N=44 (10.4%)	*Enterococcus faecalis*	32	7,6%
		Enterococcus faecium	12	2,8%
Total			423	100%

Table II: Resistance profile of isolated enterobacteria

	***C. braakii* 0.2%(N=1)**		***C. freundii* 0.2%(N=1)**		***E. aerogenes* 0.9%(N=4)**		***E. cloacae* 2.8%(N=12)**		***E. coli* 7.6%(N=32)**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
AMX	1	100	1	100	4	100	12	100	20	63
TIC	1	100	1	100	3	75	9	75	28	88
AMC	1	100	1	100	4	100	12	100	18	56

	***C. braakii* 0.2%(N=1)**		***C. freundii* 0.2%(N=1)**		***E. aerogenes* 0.9%(N=4)**		***E. cloacae* 2.8%(N=12)**		***E. coli* 7.6%(N=32)**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
TIM	1	100	1	100	2	50	2	16.6	18	56
PPT	0	0	1	100	2	50	1	8	9	28
CLT	1	100	1	100	4	100	12	100	24	75
CXT	1	100	1	100	4	100	12	100	7	22
CTZ	1	100	1	100	2	50	2	16.6	13	41
CTR	1	100	1	100	2	50	2	16.6	13	41
CFP	1	100	1	100	2	50	2	16.6	12	38
ERT	0	0	0	0	1	25	1	8	1	3
IMI	0	0	0	0	0	0	1	8	1	3
AMI	0	0	0	0	0	0	0	0	2	6
GEN	1	100	0	0	2	50	2	16.6	8	25
SXT	1	100	0	0	2	50	2	16.6	5	16
FOS	1	100	0	0	0	0	1	8	8	25
FUR	0	0	0	0	2	50	3	25	1	3
CIP	1	100	0	0	2	50	2	16.6	9	28
NAL	1	100	0	0	2	50	2	16.6	16	50

(AMX: Amoxicillin, TIC: Ticarcillin, AMC: Amoxicillin + Clavulanic acid
TIM: Ticarcillin + Clavulanic acid ; PPT: Piperacillin + Tazobactam
CLT: Cephalothin ; CXT: Cefoxitin ; CTZ: Ceftazidime ; CTR: Ceftriaxone
CFP: Cefepim ; ERT: Ertapenem ; IMI: Imipenem ; AMI: Amikacin
GEN: Gentamicin ; SXT: Trimethoprim-sulfamethoxazole ; FOS: Fosfomycin
FUR: Nitrofurantoin ; CIP: Ciprofloxacin ; NAL: Nalidixic acid

Table III: Resistance profile of isolated enterobacteria.

	***K. pneumoniae* 19.1%(N=81)**		***M. morganii* 1.2%(N=5)**		***P. mirabilis 1.2%*(N=5)**		***P. stuartii 1.2%*(N=5)**		***S. marcescens 1.7%*(N=7)**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
AMX	81	100	5	100	3	60	5	100	7	100
TIC	81	100	1	20	3	60	5	100	5	71
AMC	58	72	5	100	1	20	5	100	7	100
TIM	58	72	0	0	1	20	4	80	1	14
PPT	45	56	0	0	1	20	2	40	2	29
CLT	53	65	5	100	0	0	5	100	7	100
CXT	37	46	0	0	0	0	3	60	7	100
CTZ	51	63	0	0	0	0	3	60	1	14
CTR	51	63	0	0	0	0	4	80	1	14
CFP	48	59	0	0	0	0	3	60	1	14
ERT	20	25	0	0	0	0	2	40	1	14
IMI	20	25	0	0	0	0	2	40	1	14
AMI	8	10	0	0	0	0	0	0	0	0
GEN	43	53	3	60	3	60	5	100	1	14
SXT	40	49	1	20	1	20	2	40	1	14
FOS	28	35	0	0	1	20	0	0	1	14
FUR	23	28	2	40	5	100	5	100	7	100
CIP	43	53	2	40	2	40	1	20	3	43
NAL	50	62	4	80	3	60	1	20	1	14

AMX: Amoxicillin, TIC: Ticarcillin, AMC: Amoxicillin + Clavulanic acid
TIM: Ticarcillin + Clavulanic acid ; PPT: Piperacillin + Tazobactam
CLT: Cephalothin ; CXT: Cefoxitin ;CTZ: Ceftazidime ;CTR: Ceftriaxone
CFP: Cefepim ; ERT: Ertapenem ; IMI: Imipenem ; AMI: Amikacin
GEN: Gentamicin ; SXT: Trimethoprim-sulfamethoxazole ; FOS: Fosfomycin
FUR: Nitrofurantoin ; CIP: Ciprofloxacin ; NAL: Nalidixic acid

The incidence of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae was 46.4%(N=71), primarily isolated in *Klebsiella pneumoniae* (62.96%), *Escherichia coli* (40.62%), and

Enterobacter sp. (25%). This same mechanism was detected only once in each of the other Enterobacteriaceae species, except for *Morganella morganii*, *Proteus mirabilis*, and *Providencia stuartii*. 26 strains of Enterobacteriaceae were resistant to carbapenems, accounting for 16.99%, with *Klebsiella pneumoniae* representing the potential producer at 24.69%.

Beta-lactams naturally active against *Pseudomonas aeruginosa* maintained better antibacterial activity, with approximately 75% sensitivity, while this sensitivity was only 21% even to carbapenems in *Acinetobacter baumannii* isolates (Figure 1).

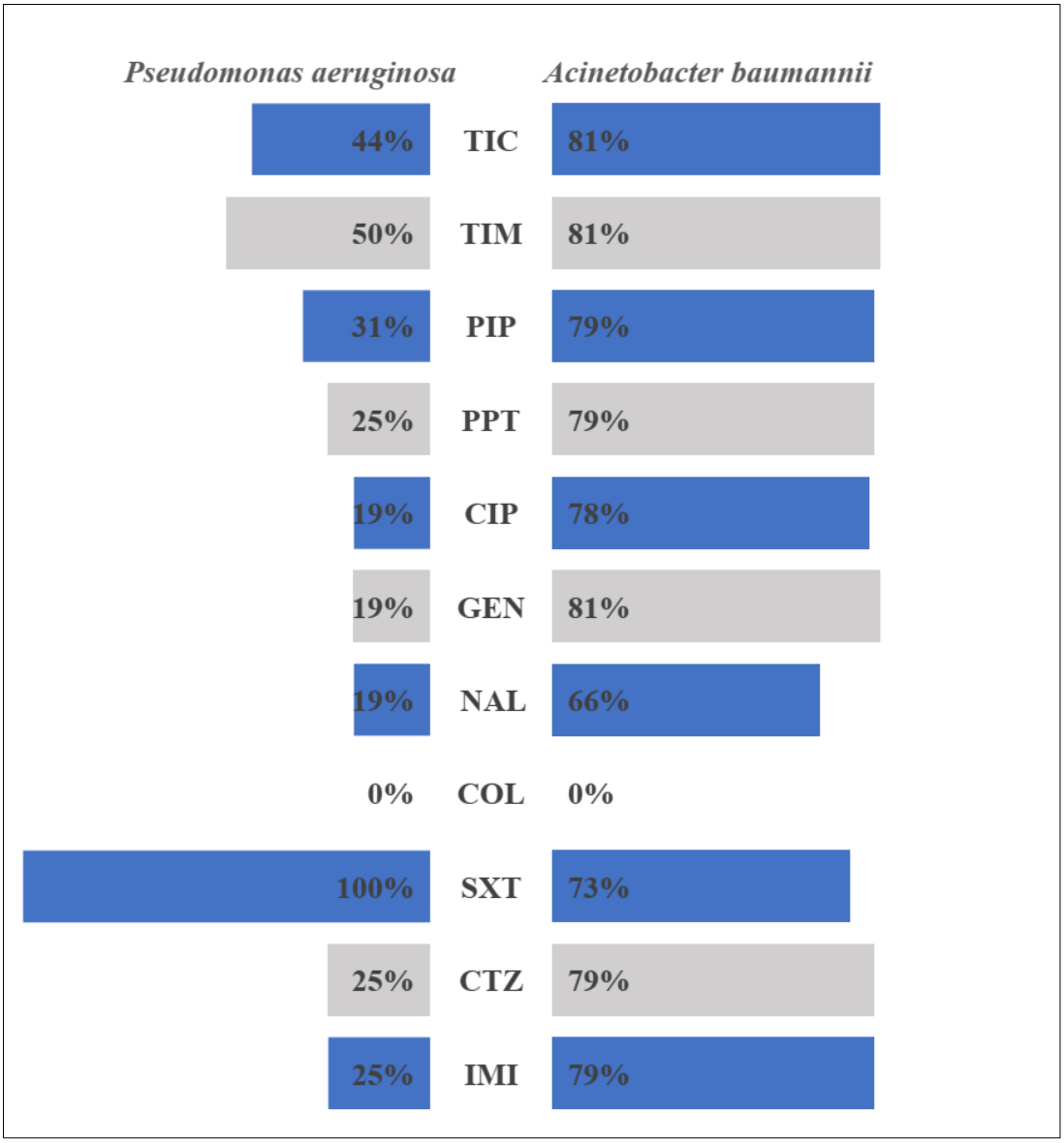

Figure 1: Resistance profile of non-fermenting GNB (Gram-Negative Bacteria)
(TIC: Ticarcillin; TIM: Ticarcillin + Clavulanic acid; PIP: Piperacillin
PPT: Piperacillin + Tazobactam; CIP: Ciprofloxacin; GEN: Gentamicin
NAL: Nalidixic acid; COL: Colistin SXT: Trimethoprim-sulfamethoxazole
CTZ: Ceftazidime; IMI: Imipenem

We identified 135 isolates of staphylococci in our series, among which 46 were *Staphylococcus aureus* (34%), with seven being methicillin-resistant *Staphylococcus aureus* (MRSA), accounting for 15.22% of *Staphylococcus aureus* isolates. No resistance to daptomycin and linezolid was observed (Figure 2).

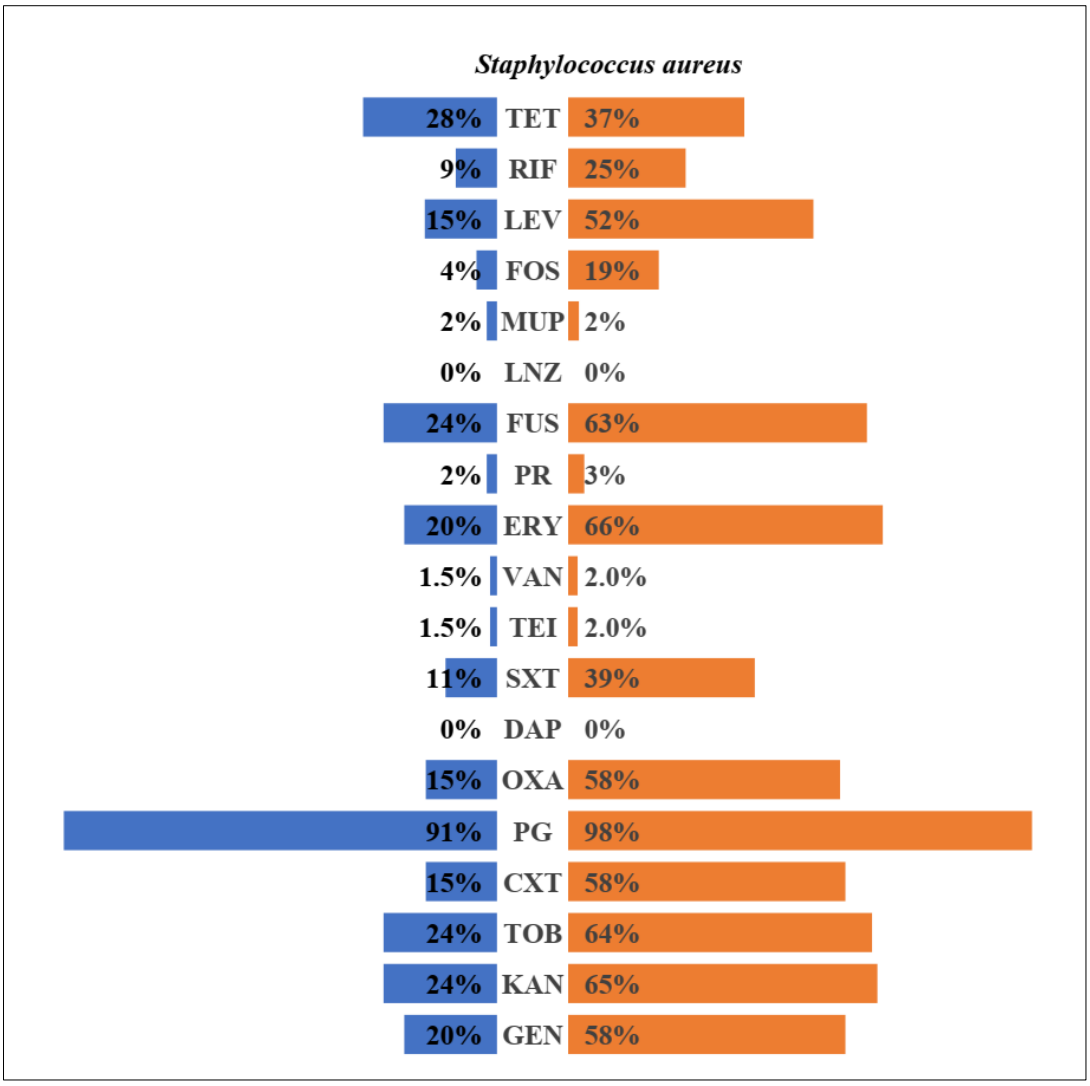

Figure 2: Resistance profile of Staphylococci

(TET: Tetracycline, RIF: Rifampicin, LEV: Levofloxacin, FOS: Fosfomycin, MUP: Mupirocin, LNZ: Linezolid, FUS: Fusicid acid, PR: Pristinamycin, ERY: Erythromycin, VAN: Vancomycin, TEI: Teicoplanin, SXT: Triméthoprim-sulfaméthoxazole, DAP: Daptomycin, OXA: Oxacillin, PG: Penicillin G, CXT: Cefoxitin, TOB: Tobramycin, KAN: Kanamycin, GEN: Gentamicin)

DISCUSSION

Bacteremias are severe infections, leading to significant morbidity and mortality in the absence of adequate treatment, particularly in intensive care units. They remain a public health concern in the modern world despite advancements in antibiotics and bacteremia management [5]. In the United States, where they are ranked as the 11th leading cause of mortality, with nearly 36,000 deaths, 19.1% of bacteremias are nosocomial in origin, this figure is higher in Canada (28%) [6]. In our study, the positivity rate of blood cultures was 20.4%. This figure is significantly higher than that found in a Tunisian study where the rate was 11.3%, while it is comparable to that of a burn intensive care unit (21.3%) [7,8]. This high frequency is explained by both endogenous and exogenous factors: chronic illnesses, visceral failures, immunosuppression, the use of respiratory devices, vascular catheters, and urinary catheters.

The predominance of Gram-negative bacilli (GNB) among the isolated bacteria in our series is consistent with Tunisian studies and an Indian study but contrasts with the multicenter cohort conducted in the United States by Deverick *et al.*, where Gram-positive cocci (GPC) predominated at 54.4% [7-10]. This predominance of GNB is mainly attributed to pulmonary and urinary entry points in ventilated patients or those with urinary catheters, challenges in maintaining hygiene conditions, and manual handling. Regarding the bacterial species identified, our results align with a study conducted at the Ibn Rochd University Hospital, in which *Klebsiella pneumoniae* and *Acinetobacter baumannii* were the most isolated, in contrast to two

French studies where *Escherichia coli* predominated [11-13].

Gram-negative bacteremias have been recognized as a growing reservoir of resistance mechanisms such as ESBLs, as illustrated by our study, which revealed the detection of these enzymes in 46.4% of Enterobacteriaceae. This rate is significantly higher than those reported by Kallel *et al*., (24.5%) and Frigui *et al*., (22.9%) [7-14]. In our series, the main producer of ESBLs was *Klebsiella pneumoniae*, followed by *Escherichia coli*, with a prevalence of 62.96% and 40.62%, respectively, contrasting with the study conducted by Ko Chang *et al*., where *Escherichia coli* was the most isolated ESBL-producing Enterobacteriaceae [15]. The isolation of these ESBL-producing Enterobacteriaceae has been steadily increasing in recent years according to the REA-Raisin network survey published in 2019 [16]. This worrying trend affects the choice of antibiotic therapy, leading to increased use of carbapenems as the first-line therapeutic choice for severe infections caused by ESBL-producing Enterobacteriaceae, consequently resulting in the emergence of carbapenemase producing Enterobacteriaceae (CPE). The rate of these CPE was 16.99% in our study, which is consistent with the result of the cohort study by Tabah *et al*., (18.6%) [17]. *Klebsiella pneumoniae* accounted for 76.92% of CPE, with this resistance mechanism detected in 24.69% of isolates of this species, which is lower compared to the cohort study by Tabah *et al*., (38%) [17].

Acinetobacter baumannii, on the other hand, can be found in various sites within the patient's environment, including bedsheets, curtains, and furniture, where it can survive for extended periods. However, contamination through manual handling is the most common route [7-18]. Literature data indicate a significant increase in the incidence of *Acinetobacter baumannii* infections [19]. This explains the rate found in our study (15.8%), which is consistent with the cohort study by Tabah *et al*., (16.3%) [17]. The multidrug resistance of *Acinetobacter baumannii* is well illustrated by our results, revealing a resistance rate of 79.1%, both to third-generation cephalosporins and carbapenems. Literature data show higher rates, limiting therapeutic options and resulting in increased mortality [20].

In our study, *Pseudomonas aeruginosa* represents only 3.8% of isolates, a lower rate than that found in the literature, where mortality related to *Pseudomonas aeruginosa* bacteremias ranges from 20% to 50% [11-22]. Carbapenem resistance has steadily increased in recent years, with surveillance by the REA-Raisin network revealing a rise of 11.1% between 2013 and 2016 [16]. Our study identified a resistance rate of 25%, both to imipenem and ceftazidime, which is lower compared to the cohort study by Tabah *et al*., (37%) [17].

Furthermore, in our study, coagulase-negative staphylococci (CoNS) accounted for 21% of all isolates, with their rate varying from 5.6 to 35% in the literature [11-23]. These bacteria, which are increasingly isolated and were long considered contaminants, are now recognized as true pathogens, potentially implicated in nosocomial bacteremias [24, 25].

Staphylococcus aureus bacteremias, associated with significant morbidity and mortality approaching 25%, accounted for 10.9% of bacteremias in our study, which is comparable to the literature [13-26]. Understanding the factors contributing to the emergence of these infections has significantly progressed, but the appearance and evolution of methicillin-resistant strains in the hospital setting pose a significant public health problem [27]. The rate of methicillin-resistant *Staphylococcus aureus* (MRSA) was approximately 15.22% in our study, while various studies reported widely disparate rates (Table IV).

Tableau IV: Prevalence of MRSA rates in various studies
MRSA (Methicillin-resistant Staphylococcus aureus)

	Country	**N *S.aureus***	**Prevalence of MRSA**
Tabah *et al*., (2012) [17]	Multinational	119	48 %
Network REA-Raisin (2018) [16]	France	1531	15.2 %
Kim *et al*., (2020) [28]	South Korea	529	82.6 %
Our study	Morocco	46	15.22 %

These concerning rates prompt control measures, including decolonization with chlorhexidine baths, whose effectiveness was demonstrated in a study conducted in the United States between 2002 and 2006, where MRSA nosocomial infections were reduced by 75% in a surgical intensive care unit [29]. Similarly, the meta-analysis by Frost *et al*., showed a 36% decrease in MRSA bacteremias after implementing chlorhexidine baths [30].

The increased use of vancomycin in MRSA bacteremias, as recommended by the Infectious Diseases Society of America and la Société de Pathologie Infectieuse de Langue Française (SPILF), has led to the emergence of strains with reduced susceptibility to glycopeptides (GISA) [31, 32]. While the rate of GISA was 1.5% in our series, its estimation is nevertheless challenging due to the numerous diagnostic methods, with highly heterogeneous sensitivity and specificity. Prevalence of 1 to 5% have been reported in Europe, the United States, and Asia [27]. In France, the REA-Raisin

network found 0.5% of GISA in 2016 [16]. Although the proportion of GISA may seem small, they can lead to treatment failures in patients for whom the therapeutic arsenal is already limited.

CONCLUSION

In addition to the high frequency of nosocomial bacteremia in our setting, our work illustrates the multidrug resistance of isolated strains, notably *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, justifying the use of broad-spectrum antibiotics. All these elements underscore the importance of implementing preventive measures, including hand hygiene, environmental disinfection, staff education, prudent antibiotic prescribing, epidemiological monitoring of resistance, and isolation of patients carrying multidrug-resistant bacteria.

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