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Antimicrobial Susceptibility Patterns of Gram-negative Bacteria, Gram-positive Bacteria and Fungi Species Isolated from Blood Culture Bottles in Yaounde, Cameroon

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Abstract **Background:** Bloodstream infections (BSIs) are the leading cause of mortality and morbidity worldwide. The aim of this study was to determine the prevalence of germs isolated from blood culture bottles, to see if age and sex are a risk factor for infection, and to present sensitivity and resistance profiles of the germs most represented during the study period. **Methods:** This was a retrospective and observational study. It carried out in Yaounde, at the Centre Pasteur of Cameroon from January 2010 to December 2019. Samples from patients with a clinical picture of a bloodstream infection were contained in the Bact/Alert FA, FN, and PF Plus bottles and incubated in the Bact/Alert 3D automaton. Antimicrobial susceptibility testing was performed immediately for positive cultures using the diffusion method and the Vitek 2-Compact device. **Results:** A total of 5687 samples were analyzed during the study period for a prevalence of contaminated samples of 95.4%. The male sex was the most represented with 3011 samples (55.5%) and 2336 samples (43.1%) for the female sex. The mean age of infected patients was 15 years ± 19.1 standard deviation (SD) with the <20 years who were most infected. The distribution differences by sex and age group were statistically significant ($p<0.0001$). Among the germs isolated from blood culture bottles, the most represented were: *Staphylococcus sp.* (13.3%), *Klebsiella pneumoniae* (11.9%), *Micrococcus sp.* (6.3%), *Staphylococcus epidermidis* (6.2%), *Staphylococcus aureus* (5.3%), *Staphylococcus haemolyticus* (4.7%), *Escherichia coli* (4.6%), *Enterobacter cloacae* (4.2%) and *Acinetobacter baumannii* (4.0%), *Staphylococcus hominis* (3.6%). This study showed that a statistically significant association exists between the isolated organisms and age groups ($p<0.0001$). Antimicrobial susceptibility testing showed that *Enterobacter cloacae, Enterococcus faecium, Klebsiella oxytoca, Klebsiella pneumoniae, Serratia marcescens, Staphylococcus aureus* and *Staphylococcus epidermidis* were the most resistances in the antibiotics of penicillin family. In the cephalosporin family, the most important resistances were observed for *Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae* and *Serratia marcescens*. As for sulfamides, the bacterial species most resistant to cotrimoxazole were *Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Salmonella typhimurium*. Concerning yeasts, *Candida sp.* and *Candida parapsilosis* were the most represented with higher resistances for amphotericin B. **Conclusion:** The results of this research with the high prevalence of a bloodstream infections and the high rates of antibiotic resistance show the need to expand the surveillance of multidrug resistance in all regions of the country and to initiate research aimed at understanding the genetic mechanisms involved in the increase of resistance.

Keywords: *bloodstream infections, antimicrobial susceptibility testing, Vitek 2-compact, multidrug resistance surveillance, genetic mechanisms*

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1. Introduction

Bloodstream infections (BSIs) are a major cause of mortality and morbidity worldwide and are associated with duration in hospitals and high costs of healthcare systems [1-4]. In addition, epidemiological data reveal that approximately 250,000 cases of BSIs occur annually in the United States [3] with more than 1.2 million episodes of BSIs reported and 157,000 deaths per year in Europe [5]. Among these infections is sepsis, which is defined as a fatal condition and a functional failure of several organs caused by deregulation of the host's response to infection that damages its own tissues [6-8]. Sepsis is extremely widespread and is a severe disease with a mortality rate in hospitals ranging from 28.3% to 41.1%, and therefore represents one of the leading causes of death in hospitalized patients in Europe [6]. According to reports from the Centers for Disease Control and Prevention, more than 1 million cases of sepsis occur each year and it is the ninth leading cause of death in the United States [9].

Several pathogenic germs are responsible for BSIs. These include Gram-negative bacteria (GNB) such as *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Klebsiella spp.*, *Neisseria meningitidis* (*N. meningitidis*), *Haemophilus influenzae* (*H. influenzae*), and Gram-positive bacteria (GPB) such as coagulase-negative staphylococci (CoNS), *Staphylococcus aureus* (*S. aureus*), *Streptococcus pneumoniae* (*S. pneumoniae*), *Streptococcus pyogenes* (*S. pyogenes*), *Streptococcus agalactiae* (*S. agalactiae*), and *Enterococcus faecium* (*E. faecium*) [10,11]; these two groups of bacteria have been found in several studies in febrile patients. In middle- and low-income countries, high mortality and morbidity rates are due to community-acquired bacteremia, with the highest incidence in children under 5 years of age [12]. The germs most responsible for cases of bacteremia in Africa are: *S. pneumoniae*, *S. aureus*, typhoidal and non-typhoidal *Salmonella enterica* serotypes, *H. influenzae*, *N. meningitidis*, *K. pneumoniae* and *E. coli* [12]. *E. coli*, *S. aureus*, *K. pneumoniae* and *S. pneumoniae* are also involved in more than 70% of cases of community-acquired bloodstream infections (CA-BSIs) although the distribution of pathogens varies and depends on the site of infection and the characteristics of the patient concerned [13]. It should be noted that *P. aeruginosa* causes up to 5% of CA-BSIs, mainly in patients with severe underlying conditions (e.g. immunosuppression) and/or exposed to medical services and suffering from urinary tract infection (UTI) [13]. Still within the framework of the *Enterobacteriaceae* family of germs responsible for BSIs, *Salmonella enterica* subspecies *enterica* serotype Typhi (*Salmonella Typhi*) responsible for typhoid fever remains widespread in developing countries with more than 10 million new cases worldwide and 160,000 deaths in 2017 [14]. In Africa, south of the Sahara, *Salmonella Typhi* is the predominant species of BSIs in children and adults, along with typhoid fever, which globally causes 17 million illnesses and 178,000,000 deaths each year [15]. Apart from BSIs caused by bacterial species, those caused by fungi, particularly *Candida* species, are also the major cause of mortality and morbidity, more specifically in patients admitted to intensive care units (ICUs) and in those with hematological malignancies [16]. Moreover, although *Candida spp.* are believed to be the fourth most common pathogen isolated from blood culture, the crude mortality rate of *Candida* infections is very high among all nosocomial BSIs [16].

The emergence of antimicrobial resistance, specifically multidrug resistance (MDR) to drugs such as ampicillin, chloramphenicol and cotrimoxazole, is a major public health problem that makes the treatment of BSIs, including typhoid fever and sepsis, difficult [15]. Indeed, the latest studies conducted in China have shown, for example, that methicillin-resistant *Staphylococcus aureus* (MRSA) is widespread worldwide with a resistance rate of 63.2% to oxacillin compared to 76.2% for CoNS [17]. For *Salmonella enterica*, MDR to traditionally used antibiotics (ampicillin, chloramphenicol, cotrimoxazole) has led to the use of fluoroquinolones as the drug of choice. However, it is also known that fluoroquinolone-resistant *Salmonella* Typhi is widespread in Asia and parts of Africa [15]. This led the World Health Organization (WHO) in 2017 to identify fluoroquinolone-resistant *Salmonella enterica as a* priority pathogen for research and development of new antimicrobial drugs. And more recently, extended spectrum β-lactamases (ESBLs) produced from *Salmonella* Typhi have emerged and spread in South Asia [15].

In view of the multiplicity of germs involved in BSIs and organisms that are multi-resistant to antimicrobials, it is therefore more than necessary to know precisely which germs come from a blood culture in order to find the appropriate treatment in case of BSIs and more particularly in case of typhoid fever or sepsis [18,19]. In order to contribute to the improvement of the follow-up of patients with a clinical picture of a BSI, the aim of this research was to present the profile of bacterial and fungal species isolated from blood culture bottles; to investigate the association of these germs with age and sex as a risk factor for infection; and to provide information on the sensitivity profiles of the antimicrobials tested during the study period.

2. Materials and Methods

2.1. Place and Period of Study

We conducted a retrospective study over a period of 10 years (from January 2010 to December 2019) in Yaounde, capital of the Central region, at the Centre Pasteur of Cameroon (CPC), a reference and public health laboratory, technical body of the Ministry of Public Health of Cameroon and Member of the International Network of Pasteur Institutes.

2.2. Collection of Samples

Samples from patients with a clinical picture of a BSI were collected in aerobic (Bact/Alert FA Plus), anaerobic (Bact/Alert FN Plus) and pediatric (Bact/Alert PF Plus) bottles. After collection, each bottle was carefully labeled by the staff of the collection department and the samples were carried directly to the Bacteriology laboratory for analysis.

2.3. Biological Analysis of Samples

At the laboratory, samples are first recorded in the draining board registers with an identification number.

Once registered, they are incubated in Bact/Alert 3D automated system (bioMerieux, France) for the detection of microorganism growth. When the Bact/Alert 3D buzzer signals positive growth of the microorganisms, identification is performed on appropriate culture media (PolyViteX Chocolate agar, Blood agar, Mac Conkey agar, Chapman agar, Methylene Blue Eosin agar, Sabouraud + Chloramphenicol agar, etc.) that were incubated for 24 or 48 hours. The study of biochemical characteristics was also carried out using API 20E [20] and API 20C [21]. After identification, antimicrobial susceptibility testing was performed by the diffusion method and the use of the Vitek 2-compact device [22,23].

The antibiotics tested in this study were : PEN: penicillin (6 µg); AMP: ampicillin (10 µg); AMO/ACM: amoxicillin (25 µg); AMC: amoxicillin + clavulanic acid (20 µg/10 µg); TIC: ticarcillin (75 µg); TCC : ticarcillin + clavulanic acid (75 µg/10 µg); PIC: piperacillin (100 µg); AME: enterococcal ampicillin (10 µg); PIT/TZP: piperacillin + tazobactam (100 µg/10 µg); SAM/FAM : ampicillin + sulbactam (10 µg/10 µg); OXA: oxacillin (1 µg); ETP: ertapenem (10 µg); IMI: imipenem (10 µg); MER: meropenem (10 µg); CFT: cephalotin (30 µg); CXM: cefuroxime (30 µg); CXT: cefoxitin (30 µg); CTX/CCM: cefotaxime (30 µg); CAZ: ceftazidime (30 µg); CFM: cefixime (5 µg); FEP: cefepime (30 µg); CRO: ceftriaxone (30 µg); ATM/AZT: aztreonam (30 µg); GEN : gentamicin (10 µg); SPT: spectinomycin (10 µg); KAN: kanamycin (30 µg); TOB: tobramycin (10 µg); AKN: amikacin (30 µg); NET: netilmicin (30 µg); GEH: gentamicin 500; GE2 : gentamicin 250; S: streptomycin (10 µg); STH: streptomycin HC (300 µg); CMP: chloramphenicol (30 µg); TET: tetracycline (30 µg); MIN: minocycline (30 µg); DOT: doxycycline (30 µg); TGC: tigecycline (15 µg) ERY: erythromycine (15 µg); LIN: lincomycin (15 µg); CLI/CM: clindamycin (2 µg); QDA: quinupristin + dalfopristin (15 µg); PRI : pristinamycin (15 µg); COL: colistin (50 µg); VAN: vancomycin (30 µg); TEC: teicoplanin (30 µg); PB: polymixin (300 IU); TSU/SXT: trimethoprim + sulfamethoxazole (1.25 µg + 23.75 µg); FUR: nitrofurantoin (300 µg); NAL: nalidixic acid (30 µg); OFL: ofloxacin (5 µg); PEF: pefloxacin (5 µg); NOR: norfloxacin (10 µg); CIP: ciprofloxacin (5 µg); LEV : levofloxacin (5 µg); MXF: moxifloxacin (5 µg); RFA: rifampicin (5 µg); FUC: fusidic acid (10 µg); FOS: fosfomycin (200 µg); LIZ: linezolid (30 µg) and TEL: telithromycin (15 µg). In the context of antifungal agents, those used in this study were: miconazole, econazole, ketoconazole, fluconazole, amphotericin B, 5-fluorocytosine, voriconazole and clotrimazole. Antibiotic and antifungal susceptibility interpretations were in accordance with the recommendations of the Clinical Laboratory Standard Institute (CLSI) [24-29]. The quality control strains used for antimicrobial susceptibility testing were: *E. coli* ATCC 25922, *S. pneumoniae* ATCC 49619, *S. aureus* ATCC 25923, *E. faecalis* ATCC 29212, *K. pneumoniae* ATCC 700603, *P. aeruginosa* ATCC 27853 *and C. parapsilosis* ATCC 22019.

2.4. Data Collection and Statistical Analysis

The data were retrieved from the GLIMS software (data management system of CPC). The database contained the variables date of collection, gender, number of bottles used for culture, germs identified, patient age (years) and antibiotics and antifungals tested (represented by their 3 letters codes). After extraction of the data from GLIMS, the database was cleaned with Microsoft Office Excel 2019 and the statistical analyses were performed using R language version 3.6.1 (2019-07-05) [30]. Within the framework of the presentation of the data, the finalfit package was used to produce the tables [31]. The statistical tests used in this research were: Pearson's Chi-square and Fischer's exact tests for comparing proportions and associations between qualitative variables; the non-parametric Kruskal-Wallis test for comparing means of patient age by age group and gender. The logistic regression model was used to evaluate the association between the identified germs and sex with the Odds-ratio (OR) values that were determined to see if sex is a risk factor for infection. The significance level was set at $p<0.05$.

3. Results

3.1. Characteristics of Study Population

From January 2010 to December 2019, 5687 samples were analyzed for a prevalence of infection of 95.4% (5424 samples positive for the presence of a pathogenic bacterial or fungal germ). The most represented sex was male with 3011 samples (55.5%) versus 2336 samples (43.1%) for female. The difference in distribution of samples by sex was statistically significant ($p<0.0001$). The mean age of infected participants was 15.0 years ± 19.1 standard deviations (SD). The most represented age group was under 20 years of age with 4373 (80.6%) infected samples from this group with a mean age of 7.2 years ± 4.5 SD (Table 1). The difference in sample distribution across age groups was statistically significant ($p<0.0001$). The year 2019 was the most represented in terms of infection followed by the years 2015-2017. A significant difference in the proportion of contaminated samples according to the years of the study was also observed ($p<0.0001$).

3.2. Prevalence of Germs Isolated from Blood Culture Bottles

The results in Table 2 show the prevalence of germs isolated from blood culture bottles during the study period. The prevalence of the most represented bacterial species was 83.5% while the prevalence of the most represented fungal species was 1.5%. Among the bacteria, the most represented (prevalence > 5%) were: *Staphylococcus sp.* (13.3%); *K. pneumoniae* (11.9%); *Micrococcus sp.* (6.3%); *S. epidermidis* (6.2%) and *S. aureus* (5.3%). As for fungi, only *Candida sp.* (0.9%) and *C. parapsilosis* (0.5%) were the most represented. Table 2 also shows the other species isolated from blood culture bottles during the study period.

3.3. Association of Identified Germs with Age Groups and Gender

A statistically significant association between age groups and isolated germs was found in this study ($p<0.0001$). The

germs for which the difference in distribution was significant between the age groups were: *E. cloacae* (p<0.0001); *E. faecalis* (p = 0.02358); *E. coli* (p<0.0001); *K. oxytoca* (p<0.0001); *K. pneumoniae* (p = 0.002289); *S. enteritidis* (p = 0.0376); *Salmonella sp.* (p = 0.002776); *S. Typhi* (p<0.0001); *S. epidermidis* (p = 0.008207); *Staphylococcus sp.* (p<0.0001) and other organisms (p = 0.005093); with the youngest group (<20 years) being at highest risk of infection (Table 3).

According to the results in Table 4, gender was not associated with infection caused by germs isolated from blood culture bottles (p = 0.942), in other words, gender was not a risk factor for BSIs.

Table 1. Presentation of socio-demographic variables

Variables	Age groups (years)				Total (n=5687) No. (%)	p-value	Sex		Total (n=5687) No. (%)	p-value
	<20 (n=4596) No. (%)	20-39 (n=330) No. (%)	40-59 (n=333) No. (%)	≥60 (n=330) No. (%)			Men (n=3170) No. (%)	Women (n=2433) No. (%)		
Age										
mean (SD)	7.2 (4.5)	29.9 (6.2)	49.5 (5.9)	72.8 (8.9)	15.0 (19.1)	**<0.0001***	14.3 (18.2)	16.0 (20.1)	15.0 (19.1)	0.1574*
Origin										
Bottle №1	4304 (93.6)	285 (86.4)	268 (80.5)	295 (89.4)	5152 (90.6)	**<0.0001**	2909 (91.8)	2255 (92.7)	5164 (90.8)	0.8649
Bottle № 2	55 (1.2)	27 (8.2)	45 (13.5)	25 (7.6)	152 (2.3)		84 (2.6)	69 (2.8)	153 (2.7)	
Bottle № 3	14 (0.3)	2 (0.6)	9 (2.7)	5 (1.5)	30 (0.5)		18 (0.6)	12 (0.5)	30 (0.5)	
Years										
2010	147 (3.2)	25 (7.6)	9 (2.7)	20 (6.0)	201 (3.5)	**<0.001**	129 (4.1)	73 (3.0)	202 (3.6)	0.1781
2011	228 (5.0)	20 (6.1)	15 (4.5)	24 (7.3)	287 (5.0)		146 (4.6)	143 (5.9)	289 (5.1)	
2012	226 (4.9)	21 (6.4)	13 (3.9)	23 (7.0)	283 (5.0)		166 (5.2)	118 (4.8)	284 (5.0)	
2013	301 (6.5)	19 (5.8)	13 (3.9)	20 (6.0)	353 (6.2)		215 (6.8)	140 (5.8)	355 (6.2)	
2014	450 (9.8)	31 (9.4)	32 (9.6)	34 (10.3)	547 (9.6)		306 (9.7)	242 (9.9)	548 (9.6)	
2015	635 (13.8)	56 (17.0)	68 (20.4)	56 (17.0)	815 (14.3)		452 (14.3)	364 (15.0)	816 (14.3)	
2016	560 (12.2)	38 (11.5)	42 (12.6)	37 (11.2)	677 (11.9)		379 (12.0)	301 (12.4)	680 (12.0)	
2017	541 (11.8)	37 (11.2)	33 (9.9)	25 (7.6)	636 (11.2)		361 (11.4)	275 (11.3)	636 (11.2)	
2018	466 (10.1)	27 (8.2)	35 (10.5)	33 (10.0)	561 (9.9)		318 (10.0)	244 (10.0)	562 (9.9)	
2019	819 (17.8)	40 (12.1)	62 (18.6)	53 (16.1)	974 (17.1)		539 (17.0)	436 (17.9)	975 (17.1)	
Overall prevalence	4373 (95.1)	314 (95.2)	322 (96.7)	325 (98.5)	5334 (93.8)	**<0.0001**	3011 (95.0)	2336 (96.0)	5347 (94.0)	**<0.0001**

p-value: p-value of Pearson's Chi-squared test
*: p-value of Kruskal-Wallis rank sum test

Table 2. Prevalence of the 28 most represented species during the study period

Ranking	Organism	No. of isolates	% of total
	Bacteria		
1	*Staphylococcus sp.*	759	13.3
2	*Klebsiella pneumoniae*	679	11.9
3	*Micrococcus sp.*	358	6.3
4	*Staphylococcus epidermidis*	350	6.2
5	*Staphylococcus aureus*	304	5.3
6	*Staphylococcus haemolyticus*	265	4.7
7	*Escherichia coli*	263	4.6
8	*Enterobacter cloacae*	241	4.2
9	*Acinetobacter baumannii*	227	4.0
10	*Staphylococcus hominis*	203	3.6
11	*Bacillus sp.*	122	2.1
12	*Serratia marcescens*	96	1.7
13	*Enterococcus faecalis*	93	1.6
14	*Staphylococcus saprophyticus*	86	1.5
15	*Corynebacterium sp.*	84	1.5
16	*Salmonella typhi*	83	1.5
17	*Salmonella sp.*	76	1.3
18	*Acinetobacter calcoace*	75	1.3
19	*Streptococcus sp.*	70	1.2
20	*Streptococcus pneumoniae*	56	1.0
21	*Klebsiella oxytoca*	52	0.9
22	*Enterococcus faecium*	51	0.9
23	*Salmonella enteritidis*	46	0.8
24	*Salmonella typhimurium*	44	0.8
25	*Pseudomonas aeruginosa*	43	0.8

Ranking	Organism	No. of isolates	% of total
26	*Staphylococcus sciuri*	26	0.5
	Total	4752	83.5
	Fungi		
27	*Candida sp.*	52	0.9
28	*Candida parapsilosis*	31	0.5
	Total	83	1.5
	Other*	589	10.4
	Total	5424	95.4

*Other organisms included the following (No): Candida albicans (21); Cryptococcus neoformans (21); Pseudomonas sp. (18); *Staphylococcus simulans* (18); *Burkholderia cepacia* (17); *Serratia liquefaciens* (17); *Enterobacter aerogenes* (16); *Pantoea sp*. (16); *Streptococcus agalactiae* (16); *Salmonella Dublin* (15); *Streptococcus mitis* (15); *Micrococcus luteus* (14); *Candida guillermondii* (13); *Citrobacter freundii* (13); *Sphingomonas paucimobilis* (13); *Haemophilus influenzae* (12); *Enterococcus sp.* (11); *Chryseomonas luteola* (10); *Aerococcus viridans* (9); *Candida famata* (9); *Staphylococcus cohnii* (9); *Staphylococcus aureus* resistant à la meticillin (8); *Staphylococcus xylosus* (8); *Stenotrophomonas maltophilia* (8); *Streptococcus pyogenes* (8); *Acinetobacter lwoffii* (7); *Acinetobacter sp.* (7); *Aeromonas hydrophila* (7); *Proteus mirabilis* (7); *Streptococcus arlettae* (7); *Citrobacter koserii* (6); *Enterobacter sakazakii* (6); *Kocuria sp.* (6); *Staphylococcus lugdunensis* (6). Other organisms were isolated but they were weakly represented.

Table 3. Distribution of the most represented germs according to age group

Organism	Age groups (years) <20 (n=4596) No. (%)	20-39 (n=330) No. (%)	40-59 (n=333) No. (%)	≥60 (n=330) No. (%)	Total (n=5687) No. (%)	p-value
Bacteria						
Acinetobacter baumannii	182 (4.0)	12 (3.6)	14 (4.2)	13 (3.9)	221 (3.9)	0.9871
Acinetobacter calcoace	59 (1.3)	4 (1.2)	3 (0.9)	8 (2.4)	74 (1.3)	0.3754*
Bacillus sp.	108 (2.3)	4 (1.2)	3 (0.9)	5 (1.5)	120 (2.1)	0.132
Corynebacterium sp.	70 (1.5)	3 (0.9)	5 (1.5)	6 (1.8)	84 (1.5)	0.8368*
Enterobacter cloacae	170 (3.7)	20 (6.1)	29 (8.7)	15 (4.5)	234 (4.1)	**<0.0001**
Enterococcus faecalis	72 (1.6)	5 (1.5)	1 (0.3)	11 (3.3)	89 (1.6)	**0.02358**
Enterococcus faecium	46 (1.0)	1 (0.3)	0 (0.0)	2 (0.6)	49 (0.9)	0.1441
Escherichia coli	164 (3.6)	23 (7.0)	30 (9.0)	40 (12.1)	257 (4.5)	**<0.0001**
Klebsiella oxytoca	38 (0.8)	5 (1.5)	5 (1.5)	4 (1.2)	52 (0.9)	**<0.0001**
Klebsiella pneumoniae	513 (11.2)	51 (15.5)	55 (16.5)	49 (14.8)	668 (11.7)	**0.002289**
Micrococcus sp.	304 (6.6)	17 (5.2)	19 (5.7)	15 (4.5)	355 (6.2)	0.2759
Pseudomonas aeruginosa	33 (0.7)	4 (1.2)	1 (0.3)	5 (1.5)	43 (0.8)	0.2144*
Salmonella enteritidis	45 (1.0)	1 (0.3)	0 (0.0)	0 (0.0)	46 (1.0)	**0.0376***
Salmonella sp.	68 (1.5)	6 (1.8)	0 (0.0)	0 (0.0)	74 (1.3)	**0.002776***
Salmonella typhi	66 (1.4)	16 (4.8)	1 (0.3)	0 (0.0)	83 (1.5)	**<0.0001***
Salmonella typhimurium	36 (0.8)	2 (0.6)	5 (1.5)	1 (0.3)	44 (0.8)	0.411*
Serratia marcescens	73 (1.6)	7 (2.1)	5 (1.5)	10 (3.0)	95 (1.7)	0.2738
Staphylococcus aureus	240 (5.2)	21 (6.4)	23 (6.9)	19 (5.8)	303 (5.3)	0.5323
Staphylococcus epidermidis	302 (6.6)	13 (3.9)	19 (5.7)	9 (2.7)	343 (6.0)	**0.008207**
Staphylococcus haemolyticus	231 (5.0)	9 (2.7)	12 (3.6)	11 (3.3)	263 (4.6)	0.08349
Staphylococcus hominis	172 (3.7)	10 (3.0)	12 (3.6)	7 (2.1)	201 (3.5)	0.3978
Staphylococcus saprophyticus	78 (1.7)	2 (0.6)	1 (0.3)	4 (1.2)	85 (1.5)	0.08994
Staphylococcus sciuri	23 (0.5)	1 (0.3)	0 (0.0)	1 (0.3)	25 (0.4)	0.7767*
Staphylococcus sp.	662 (14.4)	20 (6.1)	30 (9.0)	34 (10.3)	746 (13.1)	**<0.0001**
Streptococcus pneumoniae	41 (0.9)	4 (1.2)	1 (0.3)	7 (2.1)	53 (0.9)	0.1004*
Streptococcus sp.	57 (1.2)	3 (0.9)	3 (0.9)	4 (1.2)	67 (1.2)	0.9672*
Fungi						
Candida parapsilosis	28 (0.6)	1 (0.3)	1 (0.3)	0 (0.0)	30 (0.5)	0.5049*
Candida sp.	48 (1.0)	2 (0.6)	1 (0.3)	0 (0.0)	51 (0.9)	0.1271*
Other organisms	444 (9.7)	47 (14.2)	43 (12.9)	45 (13.6)	579 (10.2)	**0.005093**
Overall prevalence	4373 (95.1)	314 (95.2)	322 (96.7)	325 (98.5)	5334 (93.8)	**<0.0001**

p-value: p-value of Pearson's Chi-squared test
*: p-value of Fisher's exact test

3.4. Antimicrobial Susceptibility Patterns of the Most Represented Bacterial and Fungi Species during the Study Period

In the penicillin family, the highest resistances were in favor of ticarcillin with 100% resistance for *K. oxytoca*, 99.3% resistance for *K. pneumoniae*, 95.4% for *E. coli*, 84.1% for *S. typhimurium* and 80.0% for *E. cloacae*. *E. cloacae* was also the most resistant to amoxicillin + clavulanic acid with a resistance of 97.5%. As for *S. aureus*, its resistance rate was also the highest for penicillin (87.5%). In the cephalosporin family, the highest resistance was in favor of cephalotin with 98.9% resistance for *Serratia marcescens* (*S. marcescens*), 94.6% resistance for *E. cloacae*, 79.2% resistance for *K. pneumoniae* and 75.7% resistance for *E. coli*. *K. pneumoniae* was also resistant to cefotaxime at 77.6% as

well as *E. cloacae* which was 71.4% resistant to this antibiotic. For the aminoglycoside family, the highest resistances were observed for *K. pneumoniae* and *E. cloacae* with 74.7% and 62.7% resistance to gentamicin respectively, *E. faecium* with 66.7% resistance to gentamicin 500, 64.7% resistance to kanamycin high load and *E. cloacae* with 63.1% resistance to tobramycin. For tetracyclines, *S. pneumoniae* was the most resistant to tetracycline (60.7%) followed by *Streptococcus sp.*, *S. epidermidis* and *S. haemolyticus* which were resistant to the same antibiotic (57.1%, 53.1% and 51.3% respectively). Within macrolides, *E. faecalis* and *E. faecium* were the most resistant (57.0% and 54.9% resistant to erythromycin respectively). Quinupristin + dalfopristin which belongs to the streptogramine family was the only antibiotic of this family for which high resistance was observed (39.8% resistance for *E. faecalis*). Trimethoprim + sulfamethoxazole (cotrimoxazole) of the sulfamide family showed strong resistance to *E. coli* (84.4%), *K. pneumoniae* (83.8%), *S. typhimurium* (79.5%) and *E. cloacae* (75.5%). Inhibitors of nucleic acid synthesis (fluoroquinolones) were more resistant for *E. coli* with 58.2% resistance to ofloxacin and 48.7% resistance to nalidixic acid and *E. cloacae* with 45.2% resistance to ofloxacin. Finally, the highest resistances were also recorded for *P. aeruginosa* to fosfomycin and rifampicin (62.8% and 58.1% respectively).

In terms of sensitivity, Table 5 showed that most of the germs identified were sensitive to a wide variety of antibiotics. Among penicillins, *S. enteritidis* was the most sensitive with 93.5% sensitivity to amoxicillin + clavulanic acid, 87.0% sensitivity to ticarcillin and 80.4% sensitivity to amoxicillin; *S. Typhi* was next most sensitive to amoxicillin + clavulanic acid (79.5%); *Acinetobacter calcoace* with 78.7% sensitivity to ticarcillin + clavulanic acid and *E. faecalis* with 68.8% sensitivity to enterococcal ampicillin. For carbapenems, the highest sensitivities were in favor of imipenem with 85.3% sensitivity to *K. pneumoniae*, 82.6% sensitivity to *E. cloacae*, 78.7% sensitivity to *E. coli* and 76.0% sensitivity to *A. calcoace.*

Table 4. Distribution of the most represented germs by gender

Organism	Sex		OR (95%-CI)	Total (n=5687) No. (%)	p-value
	Men (n=3170) No. (%)	Women (n=2433) No. (%)			
Bacteria					
Acinetobacter baumannii	118 (3.7)	105 (4.3)	1.15 (0.87-1.52)	223 (3.9)	0.2961
Acinetobacter calcoace	40 (1.3)	34 (1.4)	1.10 (0.67-1.78)	74 (1.3)	0.6933
Bacillus sp	75 (2.4)	45 (1.8)	0.77 (0.52-1.13)	120 (2.1)	0.1669
Corynebacterium sp	47 (1.5)	37 (1.5)	1.01 (0.64-1.60)	84 (1.5)	0.9466
Enterobacter cloacae	134 (4.2)	101 (4.2)	0.97 (0.74-1.27)	235 (4.1)	0.8226
Enterococcus faecalis	50 (0.2)	39 (1.6)	1.00 (0.64-1.57)	89 (1.6)	0.9798
Enterococcus faecium	29 (0.9)	20 (0.8)	0.89 (0.47-1.63)	49 (0.9)	0.6839
Escherichia coli	138 (4.4)	120 (4.9)	1.13 (0.87-1.46)	258 (4.5)	0.3486
Klebsiella oxytoca	27 (0.9)	25 (1.0)	1.20 (0.66-2.15)	52 (0.9)	0.5214
Klebsiella pneumoniae	382 (12.1)	288 (11.8)	0.97 (0.82-1.14)	670 (11.8)	0.6949
Micrococcus sp	208 (6.6)	147 (6.0)	0.91 (0.72-1.13)	355 (6.2)	0.3701
Pseudomonas aeruginosa	23 (0.7)	20 (0.8)	1.12 (0.58-2.14)	43 (0.8)	0.7078
Salmonella enteritidis	24 (0.8)	22 (0.9)	1.18 (0.63-2.21)	46 (0.8)	0.5698
Salmonella sp	46 (1.5)	28 (1.2)	0.78 (0.47-1.28)	74 (1.3)	0.3069
Salmonella typhi	51 (1.6)	32 (1.3)	0.81 (0.50-1.28)	83 (1.5)	0.3419
Salmonella typhimurium	20 (0.6)	24 (1.0)	1.55 (0.82-2.97)	44 (0.8)	0.1448
Serratia marcescens	50 (1.6)	45 (1.8)	1.16 (0.76-1.78)	95 (1.7)	0.4656
Staphylococcus aureus	179 (5.6)	124 (5.1)	0.89 (0.69-1.13)	303 (5.3)	0.3179
Staphylococcus epidermidis	194 (6.1)	151 (6.2)	1.00 (0.80-1.26)	345 (6.1)	0.9753
Staphylococcus haemolyticus	146 (4.6)	117 (4.8)	1.03 (0.80-1.34)	263 (4.6)	0.7889
Staphylococcus hominis	108 (3.4)	93 (3.8)	1.11 (0.83-1.49)	201 (3.5)	0.4521
Staphylococcus saprophyticus	44 (1.4)	42 (1.7)	1.23 (0.79-1.94)	86 (1.5)	0.3318
Staphylococcus sciuri	15 (0.5)	10 (0.4)	0.86 (0.34-2.04)	25 (0.4)	0.7094
Staphylococcus sp	430 (13.6)	319 (13.1)	0.99 (0.81-1.11)	749 (13.2)	0.5136
Streptococcus pneumoniae	32 (1.0)	21 (0.9)	0.84 (0.46-1.51)	53 (0.9)	0.5487
Streptococcus sp.	37 (55.2)	30 (1.2)	1.04 (0.62-1.75)	67 (1.2)	0.8566
Fungi					
Candida parapsilosis	17 (0.5)	13 (0.5)	0.99 (0.44-2.16)	30 (0.5)	0.9687
Candida sp	34 (1.1)	17 (0.7)	0.64 (0.34-1.18)	51 (0.9)	0.1341
Other organisms	313 (9.9)	267 (11.0)	1.11 (0.93-1.32)	580 (10.2)	0.2276
Overall prevalence	3011 (95.0)	2336 (96.0)		5347 (94.0)	0.942

p-value: p-value of Pearson's Chi-squared test
*: p-value of Fisher's exact test
OR: Odd ratio
CI: Confidence interval

In the cephalosporin family the most sensitive germs were: *S. enteritidis* with 97.8% sensitivity to cefotaxime, 91.3% sensitivity to ceftazidime, 80.4% sensitivity to cephalotin; *Salmonella sp.* with 89.5% sensitivity to cefotaxime, 84.2% sensitivity to ceftazidime; *S. Typhi* with 97.6% sensitivity to cefotaxime and 96.4% sensitivity to ceftazidime; *S. typhimurium* with 95.5% sensitivity to cefotaxime and 86.4% sensitivity to ceftazidime; *S. marcescens* with 74.0% sensitivity to cefotaxime and 74.0% sensitivity to ceftazidime. In the family of aminoglycosides, we obtained higher sensitivity rates for : *A. baumannii* with 88.1% sensitivity to amikacin, 72.2% sensitivity to tobramycin and 69.2% sensitivity to gentamicin; *A. calcoace* with 94.7% sensitivity to amikacin, 82.7% sensitivity to tobramycin and 74.7% sensitivity to gentamicin; *E. cloacae* with 88.8% sensitivity to amikacin; *E. coli* with 84.8% sensitivity to amikacin; *K. oxytoca with* 92.3% sensitivity to amikacin; *K. pneumoniae* with 94.7% sensitivity to amikacin; *P. aeruginosa with* 90.7% sensitivity to amikacin and 74.4% sensitivity to tobramycin; *S. enteritidis* with 100.0% sensitivity to amikacin; *Salmonella sp.* with 92.1% sensitivity to amikacin; *S.* Typhi with 95.2% sensitivity to amikacin; *S. typhimurium with* 95.5% sensitivity to amikacin; *S. marcescens with* 79.2% sensitivity to amikacin and *S. aureus* with 77.0% sensitivity to gentamicin. Among the tetracyclines, only *Staphylococcus epidermidis* had the highest sensitivity to minocycline (60.6%). For macrolides, sensitivity was high for *S. pneumoniae* and *S. aureus* to erythromycin (69.6% and 64.8% respectively) and for lincosamides, *S. aureus* was the most sensitive (78.9% sensitivity to lincomycin). In the streptogramines family, quinupristin + dalfopristin was more effective against *S. aureus* (89.5%) and *S. epidermidis* (74.6%); pristinamycin belonging to the same family was more effective against *S. aureus* (77.3%) and *S. epidermidis* (70.9%). Vancomycin from the glycopeptide family was more effective against: *E. faecalis* (96.8%), *E. faecium* (98.0%), *S. aureus* (96.4%), *S. epidermidis* (76.6%), *S. pneumoniae* (98.2%) and *Streptococcus sp.* (90.0%). Teicoplanin another glycopeptide was also effective against *E. faecalis* (93.5%), *E. faecium* (98.0%), *S. aureus* (82.6%) and *Streptococcus sp.* (87.1%). As for colistin, the highest sensitivity was in favour of *P. aeruginosa* (76.7%). For sulfamides, trimethoprim + sulfamethoxazole (cotrimoxazole) was more effective against *S. enteritidis* (89.1% sensitivity), *S. marcescens* (88.5% sensitivity) and *A. calcoace* (60.0% sensitivity). For nitrofurans, the most sensitive species to nitrofurantoin were: *E. faecalis* (82.8%), *E. faecium* (68.6%) and *Streptococcus sp.* (65.7%).

Table 5. Antimicrobial susceptibility patterns of the most represented bacterial species during the study period

Antibiotics	*Acinetobacter Baumannii* (n=227)	*Acinetobacter calcoace* (n=75)	*Bacillus sp.* (n=122)	*Enterobacter cloacae* (n=241)	*Enterococcus faecalis* (n=93)	*Enterococcus faecium* (n=51)	*Escherichia coli* (n=263)	*Klebsiella oxytoca* (n=52)
	%I/%R/%S							
PEN	NA	NA	NA	NA	9.7/7.5/4.3	0/7.5/0	NA	NA
AMP	NA	NA	NA	0/29.9/0	1.1/10.7/10.7	0/13.7/2.0	0/32.7/0.8	0/34.6/0
AMO/ACM	0/0.9/0	0/0.8/0	NA	0/65.6/0	NA	NA	0/63.5/3.0	0/65.4/0
AMC	0/0/0.9	0/1.3/0	NA	0.4/97.5/0.4	NA	NA	4.6/65.4/28.9	17.3/42.3/40.4
TIC	0.4/42.7/55.9	1.3/30.7/68.0	NA	0.8/80.1/18.7	NA	NA	0/95.4/4.6	0/100.0/0
TCC	0.9/32.6/56.4	1.3/18.7/78.7	NA	0/5.8/2.1	NA	NA	0/4.9/2.7	1.9/11.5/5.8
PIC	2.6/35.7/52.0	0/30.7/68.0	NA	0.8/56.0/12.4	NA	NA	0/66.5/4.6	1.9/73.1/3.8
AME	NA	NA	NA	NA	0/7.5/68.8	1.9/78.4/1.9	NA	NA
PIT/TZP	4.0/18.1/55.5	0/12.0/50.7	NA	18.3/14.5/24.9	NA	NA	8.0/20.2/31.6	15.4/5.8/26.9
SAM/FAM	0/0.4/0	0/2.7/4.0	NA	NA	NA	NA	NA	NA
OXA	NA	NA	NA	NA	NA	NA	NA	NA
ETP	0/0/0.4	NA	NA	0/0/13.7	NA	NA	0/0/11.4	0/0/7.7
IMI	4.0/7.5/67.4	1.3/1.3/76.0	0/0/0.8	0.4/2.1/82.6	0/0/2.2	NA	0/3.0/78.7	1.9/0/69.2
MER	3.5/7.0/52.0	0/0/36.0	NA	0/0/6.6	NA	NA	0/0/4.9	0/0/7.7
CFT	0/1.3/0	0/1.3/0	NA	0/94.6/0.8	NA	NA	6.5/75.7/15.2	0/57.7/38.5
CXM	NA	NA	NA	0/19.9/4.1	NA	NA	0/12.9/10.6	0/17.3/9.6
CXT	0/0.9/0	0/1.3/0	NA	0/61.0/2.1	NA	NA	1.5/14.4/40.3	0/3.8/50.0
CTX/CCM	0/1.3/0.4	0/1.3/0	NA	0.8/71.4/27.8	2.2/15.1/0	0/7.8/0	0.8/52.9/46.4	5.8/51.9/42.3
CAZ	8.4/20.7/70.0	16.0/20.0/64.0	NA	7.9/63.9/27.8	NA	NA	5.3/49.0/45.2	9.6/38.5/48.1
CFM	0/0.4/0	NA	NA	0/22.4/0	NA	NA	0/12.7/9.9	0/13.4/15.4
FEP	3.1/13.2/45.8	5.3/13.3/32.0	NA	5.8/11.6/8.3	NA	NA	1.9/14.8/10.6	5.8/3.8/9.6
CRO	0/0.9/0	NA	NA	NA	NA	NA	NA	NA
ATM/AZT	0/0/0.4	NA	NA	NA	NA	NA	NA	NA
GEN	0/30.4/69.2	0/25.3/74.7	0/0/0.8	0/62.7/37.3	NA	NA	0.8/45.2/54.0	0/53.8/46.2
SPT	NA	NA	NA	NA	NA	NA	NA	NA
KAN	NA	NA	NA	NA	0/4.3/0	0/5.9/0	NA	NA
TOB	0/25.6/72.2	1.3/16.0/82.7	NA	0/63.1/35.3	NA	NA	0.4/48.3/46.8	0/40.4/59.6
AKN	3.1/5.3/88.1	1.3/4.0/94.7	0/0/0.8	4.6/6.6/88.8	NA	NA	4.2/11.0/84.8	3.8/3.8/92.3
NET	0/0.4/1.3	0/4.0/34.7	NA	0/2.5/2.1	NA	NA	0/0.8/2.7	0/3.8/17.3
KAH	NA	NA	NA	NA	30.1/45.2/9.7	13.7/64.7/1.9	NA	NA
GEH	NA	NA	NA	NA	44.1/30.1/20.4	21.6/66.7/5.9	NA	NA
GE2	NA	NA	NA	NA	NA	NA	NA	NA

Antibiotics	*Acinetobacter Baumannii* (n=227)	*Acinetobacter calcoace* (n=75)	*Bacillus sp.* (n=122)	*Enterobacter cloacae* (n=241)	*Enterococcus faecalis* (n=93)	*Enterococcus faecium* (n=51)	*Escherichia coli* (n=263)	*Klebsiella oxytoca* (n=52)
S	NA	NA	NA	NA	NA	NA	NA	NA
STH	NA	NA	NA	NA	2.2/1.1/2.2	5.9/0/0	NA	NA
CMP	0/0.4/0.4	NA	NA	0/0/0.4	NA	NA	0/0/1.9	NA
TET	NA	NA	NA	0/21.2/7.9	0/46.2/17.2	0/49.0/5.9	0/22.8/6.5	0/13.5/15.4
MIN	0/0/2.6	NA	NA	NA	0/4.3/0	0/5.9/0	NA	NA
DOT	NA	NA	NA	NA	NA	NA	NA	NA
TGC	NA	NA	NA	NA	0/0/14.0	0/0/11.8	NA	NA
ERY	NA	NA	NA	NA	2.2/57.0/3.2	2.0/54.9/0	NA	NA
LIN	NA	NA	NA	NA	0/5.4/0	0/13.7/0	NA	NA
CLI/CM	NA	NA	0/0.8/0	NA	0/1.1/0	0/5.9/0	NA	NA
QDA	NA	NA	NA	NA	9.7/39.8/10.8	5.9/2.0/58.8	NA	NA
PRI	NA	NA	NA	NA	0/22.6/2.2	0/0/5.9	NA	NA
COL	0.4/6.6/69.6	0/4.0/50.7	NA	NA	NA	NA	NA	NA
VAN	NA	NA	0/0/0.8	NA	0/3.2/96.8	0/2.0/98.0	NA	NA
TEC	NA	NA	NA	NA	0/2.2/93.5	0/2.0/98.0	NA	NA
PB	NA	NA	NA	NA	NA	NA	NA	NA
TSU/SXT	0.4/56.8/37.0	2.7/33.3/60.0	NA	0/75.5/21.2	0/46.2/19.4	0/52.9/5.9	0/84.4/10.3	0/55.8/42.3
FUR	NA	NA	NA	0/0/1.2	1.1/7.5/82.8	0/19.6/68.6	0/0.8/7.2	0/0/3.8
NAL	0/0/0.9	0/0/1.3	NA	0.4/39.4/31.1	NA	NA	0/48.7/21.7	0/21.2/46.2
OFL	0.4/4.4/23.8	1.3/0/54.7	NA	5.4/45.2/48.5	NA	NA	2.7/58.2/35.4	3.8/21.2/75.0
PEF	NA	NA	NA	NA	NA	NA	NA	NA
NOR	NA	NA	NA	0/1.2/0	NA	NA	0/1.1/0.4	0/0/5.8
CIP	2.2/14.1/81.9	1.3/4.0/88.0	0/0/0.8	17.8/16.2/65.6	NA	NA	2.3/46.4/51.3	7.7/11.5/80.8
LEV	NA	NA	NA	0/0/0.4	0/9.7/18.3	2.0/7.8/2.0	NA	NA
MXF	NA	NA	NA	NA	0/2.2/7.5	0/5.9/0	NA	NA
RFA	26.0/4.4/37.9	18.7/21.3/30.7	0/0/0.8	NA	0/23.7/3.2	0/11.8/5.9	NA	NA
FUC	NA	NA	NA	NA	NA	NA	NA	NA
FOS	0/44.5/6.6	0/45.3/1.3	NA	0/20.3/47.3	NA	NA	0/1.1/70.0	0/3.8/75.0
LIZ	NA	NA	NA	NA	0/3.2/84.9	0/0/82.4	NA	NA
TEL	NA	NA	NA	NA	0/4.3/18.3	0/5.9/9.8	NA	NA

PEN: penicillin; AMP: ampicillin; AMO/ACM: amoxicillin; AMC: Amoxicillin + Clavulanic Acid; FAM/SAM: ampicillin + sulbactam; TIC: ticarcillin; TCC: ticarcillin + clavulanic acid; PIC: piperacillin; AME: ampicillin enterocoque; PIT/TZP: piperacillin + tazobactam; SAM/FAM: ampicillin + sulbactam; OXA: oxacillin; ETP: ertapenem; IMI: imipenem; MER: meropenem; CFT: cephalotin; CXM: cefuroxime; CXT: cefoxitin; CTX/CCM: cefotaxime; CAZ: ceftazidime; CFM: cefixime; FEP: cefepime; CRO: ceftriaxone; ATM/AZT: aztreonam; GEN: gentamicin; SPT: spectinomycin; KAN: kanamycin; TOB: tobramycin; AKN: amikacin; NET: netilmicin; KAH: kanamycin (high load); GEH: gentamicin 500; GE2: gentamicin 250; S: streptomycin; STH: streptomycin HC; CMP: chloramphenicol; TET: tetracycline; MIN: minocycline; DOT: doxycycline; TGC: tigecycline; ERY: erythromycine; LIN: lincomycin; CLI/CM: clindamycin; QDA: quinupristin-dalfopristin; PRI: pristinamycin; COL: colistin; VAN: vancomycin; TEC: teicoplanin; PB: polymixin; SXT/TSU: trimethoprim + sulfamethoxazole (Cotrimoxazole); FUR: nitrofurantoin; NAL: nalidixic acid; OFL: ofloxacin; PEF: pefloxacin; NOR: norfloxacin; CIP: ciprofloxacin; LEV: levofloxacin; MXF: moxifloxacin; RFA: Rifampicin; FUC: fusidic acid; FOS: fosfomycin; LIZ: Linezolid; TEL: telithromycin; I: Intermediate; S: Susceptibility; R: Resistance; NA: not available

Table 5. Antimicrobial susceptibility patterns of the most represented bacterial species during the study period (continued)

Antibiotics	*Klebsiella Pneumoniae* (n=679)	*Micrococcus sp.* (n=358)	*Pseudomonas aeruginosa* (n=43)	*Salmonella enteritidis* (n=46)	*Salmonella sp.* (n=76)	*Salmonella typhi* (n=83)	*Salmonella typhimurium* (n=44)	*Serratia marcescens* (n=96)
	%I/%R/%S							
PEN	NA	0/0.6/0	NA	NA	NA	NA	NA	NA
AMP	0/25.9/0	NA	NA	0/2.1/4.3	0/7.9/9.2	0/1.2/1/2	0/18.2/2.3	0/28.1/0
AMO/ACM	0/73.9/0.1	NA	NA	2.2/10.9/80.4	0/30.3/52.6	0/63.9/33.7	0/65.9/13.6	0/67.7/4.2
AMC	9.7/62.0/27.7	NA	NA	0/6.5/93.5	7.9/18.4/73.7	13.3/7.2/79.5	9.1/36.4/54.5	1.0/92.7/6.3
TIC	0.3/99.3/0.4	NA	2.3/44.2/48.8	0/13.0/87.0	0/36.8/60.5	0/61.4/37.3	0/84.1/15.9	3.1/33.3/62.5
TCC	0/9.1/3.1	NA	4.7/39.5/55.8	0/0/19.6	0/9.2/7.9	0/0/20.5	0/9.1/0	0/0/8.3
PIC	0.9/64.9/4.4	NA	4.7/30.2/62.8	0/6.5/32.6	0/17.1/32.9	0/27.7/19.3	0/43.2/11.4	0/27.1/53.1
AME	NA	NA	NA	NA	NA	NA	NA	NA
PIT/TZP	16.9/16.8/25.2	NA	4.7/25.6/44.2	2.2/0/52.2	1.3/1.3/36.8	0/0/57.8	0/6.8/43.2	2.1/4.2/55.2
SAM/FAM	NA	NA	NA	NA	NA	NA	NA	NA
OXA	NA	0/0.6/0	NA	NA	NA	NA	NA	NA
ETP	0/0.3/12.5	NA	NA	0/0/10.9	0/0/5.3	0/0/6.0	0/0/6.8	0/0/2.1
IMI	0.4/2.4/85.3	NA	0/9.3/65.1	0/0/58.7	0/0/63.2	0/0/38.6	0/0/47.7	0/3.1/46.9
MER	0/0.1/5.9	NA	0/4.7/65.1	0/0/2.2	0/0/1.3	NA	0/0/2.3	NA
CFT	0.1/79.2/18.0	NA	NA	0/15.2/80.4	0/30.3/68.4	2.4/15.7/77.1	0/36.4/61.4	0/98.9/1.0
CXM	0/18.6/3.4	NA	NA	0/0/2.2	0/1.3/9.2	NA	0/2.3/9.1	0/16.7/0
CXT	0/9.9/47.7	NA	NA	0/6.5/60.9	0/6.6/55.3	0/4.8/39.8	0/0/43.2	0/17.7/11.5

Antibiotics	*Klebsiella Pneumoniae* (n=679)	*Micrococcus sp.* (n=358)	*Pseudomonas aeruginosa* (n=43)	*Salmonella enteritidis* (n=46)	*Salmonella sp.* (n=76)	*Salmonella typhi* (n=83)	*Salmonella typhimurium* (n=44)	*Serratia marcescens* (n=96)
CTX/CCM	0.3/77.6/21.6	NA	NA	0/2.2/97.8	0/10.5/89.5	0/1.2/97.6	0/4.5/95.5	1.0/25.0/74.0
CAZ	15.0/63.8/20.8	NA	9.3/20.9/69.8	0/2.2/91.3	2.6/9.2/84.2	2.4/0/96.4	6.8/4.5/86.4	2.1/24.0/74.0
CFM	0/18.4/2.2	NA	NA	0/0/4.3	0/1.3/9.2	NA	0/2.3/13.6	0/5.2/8.3
FEP	10.3/9.7/6.5	NA	7.0/11.6/41.9	0/0/21.7	0/1.3/14.5	0/0/33.7	0/2.3/6.8	2.1/9.4/9.4
CRO	NA	NA	NA	NA	NA	NA	NA	NA
ATM/AZT	NA	NA	2.3/0/0	0/0/8.7	1.3/1.3/3.9	1.2/0/3.6	2.3/0/0	NA
GEN	0/74.7/25.0	0/0.6/0	0/23.3/76.7	0/0/100.0	1.3/13.2/85.5	1.2/2.4/95.2	0/6.8/93.2	0/42.7/57.3
SPT	NA	NA	NA	NA	NA	NA	NA	NA
KAN	NA	0/0.6/0	NA	NA	NA	NA	NA	NA
TOB	0.6/59.9/36.7	0/0.6/0	0/23.3/74.4	0/0/65.2	0/10.5/60.5	0/2.4/63.9	0/6.8/72.7	7.3/58.3/30.2
AKN	2.7/2.4/94.7	NA	2.3/4.7/90.7	0/0/100.0	0/3.9/92.1	0/2.4/95.2	0/2.3/95.5	0/20.8/79.2
NET	0/3.2/5.4	NA	0/0/11.6	0/0/13.0	0/6.6/6.6	0/0/14.5	0/0/6.8	0/0/4.2
KAH	NA	NA	NA	NA	NA	NA	NA	NA
GEH	NA	NA	NA	NA	NA	NA	NA	NA
GE2	NA	NA	NA	NA	NA	NA	NA	NA
S	NA	NA	NA	NA	NA	0/0/1.2	NA	NA
STH	NA	NA	NA	NA	NA	NA	NA	NA
CMP	0/0.3/0.9	NA	NA	2.2/0/15.2	0/6.6/10.5	0/9.6/20.5	0/11.4/4.5	NA
TET	0/18.3/7.7	0/0.3/0.3	NA	2.2/4.3/23.9	1.3/13.2/19.7	1.2/22.9/6.0	2.3/4.5/29.5	0/26.0/0
MIN	NA	NA	NA	NA	NA	NA	NA	NA
DOT	NA	NA	NA	NA	NA	NA	NA	NA
TGC	NA	NA	NA	NA	NA	NA	NA	NA
ERY	NA	0/0.6/0	NA	NA	NA	NA	NA	NA
LIN	NA	0/0/0.6	NA	NA	NA	NA	NA	NA
CLI/CM	NA	0/0/0.6	NA	NA	NA	NA	NA	NA
QDA	NA	0/0.3/0.3	NA	NA	NA	NA	NA	NA
PRI	NA	0/0/0.6	NA	NA	NA	NA	NA	NA
COL	0/0/0.1	NA	0/4.7/76.7	NA	NA	NA	NA	NA
VAN	NA	0/0/0.6	NA	NA	NA	NA	NA	NA
TEC	NA	0/0/0.6	NA	NA	NA	NA	NA	NA
PB	NA	NA	NA	NA	NA	NA	NA	NA
TSU/SXT	0/83.8/15.8	0/0.3/0.3	0/55.8/7.0	0/8.7/89.1	0/38.2/59.2	0/61.4/36.1	0/79.5/20.5	0/9.4/88.5
FUR	0.1/0.3/1.2	0/0/0.6	NA	NA	0/0/1.3	NA	NA	0/2.1/0
NAL	0.1/27.7/45.2	NA	NA	0/10.9/78.2	3.9/14.5/63.2	0/4.8/95.2	0/2.3/75.0	0/5.2/67.7
OFL	2.4/35.5/59.5	0/0.6/0	2.3/4.7/14.0	0/8.7/60.9	3.9/14.5/55.3	0/1.2/67.5	0/2.3/81.8	0/5.2/90.6
PEF	NA	NA	NA	NA	NA	NA	NA	NA
NOR	0/0.4/0.7	NA	NA	NA	0/0/1.3	NA	NA	0/0/2.1
CIP	10.8/20.8/67.9	NA	4.7/4.7/79.1	0/8.7/89.1	5.3/9.2/85.5	0/1.2/98.8	0/2.3/97.7	2.1/2.1/95.8
LEV	0/0/0.4	NA	NA	NA	NA	NA	NA	NA
MXF	NA	NA	NA	NA	NA	NA	NA	NA
RFA	NA	0/0/0.6	11.6/58.1/7.0	NA	NA	NA	NA	NA
FUC	NA	0/0/0.6	NA	NA	NA	NA	NA	NA
FOS	0/5.9/61.1	0/0/0.6	0/62.8/20.9	0/2.2/34.8	0/1.3/51.3	0/0/48.2	0/0/43.2	0/3.1/75.0
LIZ	NA	NA	NA	NA	NA	NA	NA	NA
TEL	NA	NA	NA	NA	NA	NA	NA	NA

PEN: penicillin; AMP: ampicillin; AMO/ACM: amoxicillin; AMC: Amoxicillin + Clavulanic Acid; FAM/SAM: ampicillin + sulbactam; TIC: ticarcillin; TCC: ticarcillin + clavulanic acid; PIC: piperacillin; AME: ampicillin enterocoque; PIT/TZP: piperacillin + tazobactam; SAM/FAM: ampicillin + sulbactam; OXA: oxacillin; ETP: ertapenem; IMI: imipenem; MER: meropenem; CFT: cephalotin; CXM: cefuroxime; CXT: cefoxitin; CTX/CCM: cefotaxime; CAZ: ceftazidime; CFM: cefixime; FEP: cefepime; CRO: ceftriaxone; ATM/AZT: aztreonam; GEN: gentamicin; SPT: spectinomycin; KAN: kanamycin; TOB: tobramycin; AKN: amikacin; NET: netilmicin; KAH: kanamycin (high load); GEH: gentamicin 500; GE2: gentamicin 250; S: streptomycin; STH: streptomycin HC; CMP: chloramphenicol; TET: tetracycline; MIN: minocycline; DOT: doxycycline; TGC: tigecycline; ERY: erythromycine; LIN: lincomycin; CLI/CM: clindamycin; QDA: quinupristin-dalfopristin; PRI: pristinamycin; COL: colistin; VAN: vancomycin; TEC: teicoplanin; PB: polymixin; SXT/TSU: trimethoprim + sulfamethoxazole (Cotrimoxazole); FUR: nitrofurantoin; NAL: nalidixic acid; OFL: ofloxacin; PEF: pefloxacin; NOR: norfloxacin; CIP: ciprofloxacin; LEV: levofloxacin; MXF: moxifloxacin; RFA: Rifampicin; FUC: fusidic acid; FOS: fosfomycin; LIZ: Linezolid; TEL: telithromycin; I: Intermediate; S: Susceptibility; R: Resistance; NA: not available.

Table 5. Antimicrobial susceptibility patterns of the most represented bacterial species during the study period (continued)

Antibiotics	*S. aureus* (n=304)	*S. epidermidis* (n=350)	*S. haemolyticus* (n=265)	*S. hominis* (n=203)	*S. saprophyticus* (n=86)	*S. sciuri* (n=26)	*Staphylococcus sp.* (n=759)	*S. pneumoniae* (n=56)	*Streptococcus sp.* (n=70)
	%I/%R/%S								
PEN	0.3/87.5/3.6	0/75.4/1.7	0/59.6/0.4	0/53.7/1.0	0/52.3/2.3	0/61.5/3.8	0/8.7/0.1	12.5/8.9/26.8	8.6/28.6/48.6
AMP	NA	NA	NA	NA	NA	NA	NA	1.8/0/3.6	4.3/11.4/40/0

Antibiotics	*S. aureus* (n=304)	*S. epidermidis* (n=350)	*S. haemolyticus* (n=265)	*S. hominis* (n=203)	*S. saprophyticus* (n=86)	*S. sciuri* (n=26)	*Staphylococcus sp.* (n=759)	*S. pneumoniae* (n=56)	*Streptococcus sp.* (n=70)
AMO/ACM	NA	NA	NA	NA	NA	NA	NA	3.6/5.3/76.8	NA
AMC	NA	NA	NA	NA	NA	NA	NA	0/0/53.6	NA
TIC	NA	NA	NA	NA	NA	NA	NA	NA	NA
TCC	NA	NA	NA	NA	NA	NA	NA	NA	NA
PIC	NA	NA	NA	NA	NA	NA	NA	NA	NA
AME	NA	NA	NA	NA	NA	NA	NA	0/0/1.8	1.4/4.3/10.0
PIT/TZP	NA	NA	NA	NA	NA	NA	NA	NA	NA
SAM/FAM	NA	NA	NA	NA	NA	NA	NA	NA	NA
OXA	0.3/36.2/63.5	0/57.7/19.1	0/55.5/2.6	0/44.3/9.9	0/33.7/19.8	0/53.8/11.5	0/7.9/1.2	0/0/1.8	NA
ETP	NA	NA	NA	NA	NA	NA	NA	NA	NA
IMI	NA	NA	NA	NA	NA	NA	NA	NA	NA
MER	NA	NA	NA	NA	NA	NA	NA	NA	NA
CFT	NA	NA	NA	NA	NA	NA	NA	NA	NA
CXM	NA	NA	NA	NA	NA	NA	NA	NA	NA
CXT	NA	NA	NA	NA	NA	NA	NA	NA	NA
CTX/CCM	NA	NA	NA	NA	NA	NA	NA	0/0/44.6	2.9/25.7/54.3
CAZ	NA	NA	NA	NA	NA	NA	NA	NA	NA
CFM	NA	NA	NA	NA	NA	NA	NA	NA	NA
FEP	NA	NA	NA	NA	NA	NA	NA	NA	NA
CRO	NA	NA	NA	NA	NA	NA	NA	0/0/26.8	NA
ATM/AZT	NA	NA	NA	NA	NA	NA	NA	NA	NA
GEN	0/21.4/77.0	0.3/33.1/43.4	0/47.5/12.1	0/24.1/30.0	0/19.8/34.9	0/3.8/61.5	0/5.5/3.6	0/0/1.8	NA
SPT	NA	NA	NA	NA	NA	NA	NA	NA	NA
KAN	0.7/27.6/38.8	0/42.8/25.4	0/43.8/4.5	0/24.6/10.3	0/22.1/29.1	0/7.7/11.5	0/5.9/2.1	NA	NA
TOB	0.3/15.8/44.1	0/31.4/32.3	0/22.3/4.9	0/15.3/12.8	0/19.8/19.8	0/3.8/11.5	0/5.1/2.8	NA	NA
AKN	NA	NA	NA	NA	NA	NA	NA	NA	NA
NET	NA	NA	NA	NA	NA	NA	NA	NA	NA
KAH	NA	NA	NA	NA	NA	NA	NA	3.6/0/1.8	52.9/10.0/20.0
GEH	NA	NA	NA	NA	NA	NA	NA	62.5/1.8/16.1	60.0/10.0/24.3
GE2	NA	NA	NA	NA	NA	NA	NA	NA	NA
S	NA	NA	NA	NA	NA	NA	NA	NA	NA
STH	NA	NA	NA	NA	NA	NA	NA	NA	NA
CMP	NA	NA	NA	NA	NA	NA	NA	0/12.5/62.5	0/0/4.3
TET	0/42.4/55.6	0/53.1/23.4	0.4/51.3/7.9	0/45.8/8.4	0/31.4/23.3	0/26.9/38.5	0/7.0/1.8	0/60.7/30.4	1.4/57.1/27.1
MIN	3.3/71.7	0/4.6/60.6	0/3.4/26.4	0/1.0/28.6	0/4.7/38.4	0/0/26.9	0/0.5/7.5	NA	NA
DOT	NA	NA	NA	NA	NA	NA	NA	NA	NA
TGC	0/0/4.3	0/0/2.0	0/1.9/3.8	0/0/0.5	0/0/2.3	0/0/11.5	0/0/0.1	NA	NA
ERY	0/28.3/64.8	0/37.7/39.4	0/36.6/22.3	0/35.0/20.2	0/25.6/29.1	0/23.1/42.3	0/4.9/4.2	5.4/14.3/69.6	2.9/40.0/50.0
LIN	0/10.5/78.9	0/18.6/58.3	0.4/15.5/41.9	0/12.8/40.4	0/20.9/30.2	0/34.6/0	0/1.6/7.1	0/1.8/5.4	0/0/1.4
CLI/ CM	0/1.0/23.7	0/5.7/25.7	0/1.1/6.0	0/3.0/3.4	0/9.3/11.6	0/7.7/0	0/0/0.1	0/5.4/44.6	0/1.4/2.9
QDA	0/2.0/89.5	0.3/0.6/74.6	0.4/0/58.5	0/1.0/54.2	0/2.3/48.8	0/0/61.5	0.3/0/8.0	0/0/3.6	1.4/1.4/24.3
PRI	0/1.0/77.3	0.3/0.6/70.9	0/0/44.9	0/0.5/46.3	0/2.3/39.5	0/0/15.4	0.1/0/7.5	0/0/78.6	0/0/15.7
COL	NA	NA	NA	NA	NA	NA	NA	NA	NA
VAN	0.3/1.6/96.4	0/0.3/76.6	0/0.8/59.6	0/1.0/53.2	0/0/54.7	0/0/65.4	0/0.1/9.0	0/1.8/98.2	0/4.3/90.0
TEC	0.3/1.3/82.6	6.9/6.3/45.4	0.4/0.4/26.8	0/1.5/28.6	0/2.3/45.3	0/0/26.9	0.3/0.7/6.3	0/0/7.1	1.4/4.3/87.1
PB	NA	NA	NA	NA	NA	NA	NA	NA	NA
TSU/SXT	1.6/13.8/9.5	5.7/24.6/11.7	0/5.7/0	0.5/4.4/0.5	3.5/12.8/8.1	0/0/7.7	0.1/0.1/0	0/8.9/1.8	0/58.6/25.7
FUR	0/0.7/54.3	0/0.6/61.1	0/0/26.4	0/0.5/26.1	0/0/52.3	0/0/15.4	0/0/7.2	0/0/3.6	0/8.6/65.7
NAL	NA	NA	NA	NA	NA	NA	NA	NA	NA
OFL	0/1.6/18.1	0/7.7/23.4	0/4.2/1.5	0/0.5/4.9	0/5.8/15.1	0/0/7.7	0/0/0.1	NA	NA
PEF	NA	NA	NA	NA	NA	NA	NA	NA	NA
NOR	0/0/1.3	NA	NA	NA	NA	NA	NA	0/1.8/30.4	NA
CIP	0.7/1.6/5.3	0/0.9/1.7	0/5.7/0.8	0.5/0/1.0	0/1.2/1.2	0/0/11.5	NA	41.1/3.6/19.6	NA
LEV	0/16.1/45.4	0.9/8.0/25.1	0/34.0/17.7	0/7.9/41.4	0/4.7/25.6	0/0/57.7	0.1/3.2/5.1	1.8/3.6/76.8	1.4/15.7/68.6
MXF	0/0/3.9	0.3/0.3/1.7	1.9/3.4/0.8	NA	0/1.2/1.2	3.8/0/7.7	NA	NA	NA
RFA	30.3/3.0/54.6	9.4/8.6/54.0	17.0/19.2/16.2	18.2/4.4/23.6	1.2/4.7/32.6	0/0/11.5	0.8/1.7/5.4	0/0/23.2	1.4/12.9/58.6
FUC	0.7/3.3/52.3	2.6/13.4/43.4	0/6.0/19.2	0/10.8/15.8	0/16.3/22.1	0/15.4/0	0/2.0/5.3	NA	NA
FOS	0/1.6/54.9	0/6.9/54.3	0/2.6/23.8	0/4.4/22.7	0/34.9/3.5	0/0/15.4	0/1.2/6.7	NA	NA
LIZ	0/0.7/65.1	0/0.9/32.9	0/0.8/52.8	0/2.0/47.8	0/3.5/26.7	0/0/57.7	0/0/8.0	0/0/8.9	2.9/2.9/77.1
TEL	0/1.6/38.8	1.4/1.7/24.6	0/4.2/26.0	0/2.5/26.6	0/2.3/10.5	0/0/11.5	0/0/2.1	0/0/7.1	1.4/5.7/64.3

PEN: penicillin; AMP: ampicillin; AMO/ACM: amoxicillin; AMC: Amoxicillin + Clavulanic Acid; FAM/SAM: ampicillin + sulbactam; TIC: ticarcillin; TCC: ticarcillin + clavulanic acid; PIC: piperacillin; AME: ampicillin enterocoque; PIT/TZP: piperacillin + tazobactam; SAM/FAM: ampicillin + sulbactam; OXA: oxacillin; ETP: ertapenem; IMI: imipenem; MER: meropenem; CFT: cephalotin; CXM: cefuroxime; CXT: cefoxitin; CTX/CCM: cefotaxime; CAZ: ceftazidime; CFM: cefixime; FEP: cefepime; CRO: ceftriaxone; ATM/AZT: aztreonam; GEN: gentamicin; SPT: spectinomycin; KAN: kanamycin; TOB: tobramycin; AKN: amikacin; NET: netilmicin; KAH: kanamycin (high load); GEH: gentamicin 500; GE2: gentamicin 250; S: streptomycin; STH: streptomycin HC; CMP: chloramphenicol; TET: tetracycline; MIN: minocycline; DOT: doxycycline; TGC: tigecycline; ERY: Erythromycine; LIN: Lincomycin; CLI/CM: clindamycin; QDA: quinupristin-dalfopristin; PRI: pristinamycin; COL: colistin; VAN: vancomycin; TEC: teicoplanin; PB: polymixin; SXT/TSU: trimethoprim + sulfamethoxazole (Cotrimoxazole); FUR: nitrofurantoin; NAL: nalidixic acid; OFL: ofloxacin; PEF: pefloxacin; NOR: norfloxacin; CIP: ciprofloxacin; LEV: levofloxacin; MXF: moxifloxacin; RFA: Rifampicin; FUC: fusidic acid; FOS: fosfomycin; LIZ: Linezolid; TEL: telithromycin; I: Intermediate; S: Susceptibility; R: Resistance; NA: not available; *S. aureus*: *Staphylococcus aureus*; *S. epidermidis*: *Staphylococcus epidermidis*; *S. haemolyticus*: *Staphylococcus haemolyticus*; *S. hominis*: *Staphylococcus hominis;* *S. saprophyticus*: *Staphylococcus saprophyticus*; *S. sciuri*: *Staphylococcus sciuri*; *S. pneumoniae*: *Streptococcus pneumoniae*.

Table 6. Antimicrobial susceptibility patterns of the most represented fungal species during the study period

Isolated organism (No.)	%I/%R/%S							
	MIC	**ECO**	**KET**	**FLU**	**AMB**	**5FC**	**VRC**	**CLO**
				Fungi				
Candida parapsilosis (31)	6.5/3.2/77.4	3.2/3.2/80.6	0/0/80.6	0/0/16.1	0/25.8/58.1	0/3.2/0	0/0/9.7	0/0/93.5
Candida sp. (52)	7.7/1.9/86.5	9.6/1.9/82.7	0/1.9/82.7	0/3.8/11.5	0/15.4/76.9	NA	0/0/3.8	13.5/15.4/61.5

MIC: miconazole; ECO: econazole; KET: ketoconazole; FLU: fluconazole; AMB: amphotericin B; 5FC: 5-fluorocytosine; VRC: voriconazole; CLO: clotrimazole; I: Intermediate; S: Susceptibility; R: Resistance; NA: not available

Ciprofloxacin (systemic quinolone) inhibitor of nucleic acid synthesis was highly effective against: *S. Typhi* (98.8% sensitivity), *S. typhimurium* (97.7% sensitivity), *S. marcescens* (95.8% sensitivity), *S. enteritidis* (89.1% sensitivity), *A. calcoace* (88.0% sensitivity), *Salmonella sp*. (85.5% sensitivity), *A. baumannii* (81.9% sensitivity), *K. oxytoca* (80.8% sensitivity), *P. aeruginosa* (79.1% sensitivity) and *K. pneumoniae* (67.9% sensitivity). The germs most sensitive to levofloxacin were *S. pneumoniae* (76.8%) and *Streptococcus sp.* (68.6%). Fosfomycin was very effective against: *K. oxytoca* (75.0% sensitivity), *S. marcescens* (75.0% sensitivity) and *E. coli* (70.0% sensitivity). Linezolid, the only oxazolidinone antibiotic represented, was more effective against *E. faecalis* (84.9%), *E. faecium* (82.4%), *Streptococcus sp.* (77.1%) and *S. aureus* (65.1%). The ketolide family showed that only *Streptococcus sp.* was the most sensitive to telithromycin (64.3%).

For fungi, sensitivity was high for most of the antifungal agents tested (Table 6). Within the azole family, the highest sensitivities were in favor of miconazole with 77.4% and 86.5% sensitivity respectively for *C. parapsilosis* and *Candida sp*; econazole with 80.6% and 82.7% sensitivity respectively for *C. parapsilosis* and *Candida sp*; ketoconazole with the same percentages of sensitivity as for econazole; clotrimazole with 93.5% and 61.5% sensitivity respectively for *C. parapsilosis* and *Candida sp*. For the polyene family, *Candida sp.* were more sensitive to amphotericin B than *C. parapsilosis* (76.9% versus 58.1%).

4. Discussion

BSIs and resistance to antibacterial agents that are a real challenge worldwide lead to high mortality and morbidity in clinical situations [32]. This study showed that out of 5687 samples analyzed during the study period, the prevalence of infection was 95.4%. This result is different from those obtained in other studies [10,33-38] where the prevalences of BSIs were 18.2%, 31.2%, 6.97%, 27.0%, 14.2%, 29.4% and 28.0% respectively. This difference in prevalence obtained in the present study compared to the others could be explained by the difference in methodology used with regard to blood culture systems, the difference in the place and period of study, the target population, the epidemiological difference in etiological agents, seasonal variations as stated by Dagnew *et al.* [10] or Sana *et al.* [35] or Wasihun *et al.* [38]. This study also showed that the difference in distribution of positive samples by sex was significant ($p<0.0001$) with 55.5% for males and 43.1% for females. The mean age of infected participants was 15.0 years ± 19.1 SD with those <20 years who were most affected by the infection. These results are similar to those obtained in the study by Jain and Das Chugh [39], in which 61.9% of male patients had enteric fever with a mean age of 14.2 years and the <15 year old group was the most represented. In the study by Msemo *et al.* [15], conducted in northeastern Tanzania between 2008-2016 in children aged 1.0-59.99 months, males were also the most represented with a proportion of 62.8% among those positive for *S. Typhi* and 61.9% among those positive for non-typhoidal *Salmonella*. In the research conducted by Popoola *et al.* [12] in Nigeria, female sex was the most represented (51.3%) with a mean age of participants of 15.2 years ± 0.6 SD with patients aged 1-17 years (68.5%) being the most represented.

Among the germs isolated in this study, Gram-positive Cocci were the most represented followed by GNB. As for fungi, they were less represented among the identified germs. The most represented Gram-positive Cocci were: *Staphylococcus sp.* (13.3%), *Micrococcus sp.* (6.3%), *S. epidermidis* (6.2%), *S. aureus* (5.3%), *S. haemolyticus* (4.7%), *S. hominis* (3.6%), *E. faecalis* (1.6%), *S. saprophyticus* (1.5%), *Streptococcus sp.* (1.2%), *S. pneumoniae* (1.0%), *E. faecium* (0.9%) and *Staphylococcus sciuri* (0.5%). Among GNB, *Enterobacteriaceae* and non-fermentative Gram-negative bacilli were the most represented. In the *Enterobacteriaceae* group, the most abundant were *K. pneumoniae* (11.9%), *E. coli* (4.6%), *E. cloacae* (4.6%), *S. marcescens* (1.7%), *S. Typhi* (1.5%), *Salmonella sp.* (1.3%), *K. oxytoca* (0.9%), *S. enteritidis* (0.8%) and *S. typhimurium* (0.8%). For the group of non-fermentative Gram-negative bacilli *A. baumannii* (4.0%),

Corynebacterium sp. (1.5%), *A. calcoace* (1.3%) and *P. aeruginosa* (0.8%) were the most abundant. These results are close to those obtained in most previous studies [8,10,34,35,37,38,40-42] where the most represented germs in BSIs were Cocci Gram positive with *S. aureus*, CoNS, *S. epidermidis*, *S. pneumoniae*; *Enterobacteriaceae* with *E. coli*, *K. pneumoniae*, *Salmonella enterica* (*S.* Typhi, *Salmonella paratyphi* A, B), *S. marcescens*; Gram negative non-fermentative bacilli with *A. baumannii*, *A. calcoace* and *P. aeruginosa*. Our study showed that the fungi most represented in BSIs were *C. parapsilosis* and Candida *spp.*; a result close to the study by Sana *et al.* [35] where *C. parapsilosis* was the most represented followed by *C. albicans*, *C. glabrata*, *C. tropicalis* and *C. krusei*. In the study by Oz and Gokbolat [16] on the other hand, *C. albicans* was the most represented followed by the non-*albicans C. parapsilosis*, *C. tropicalis*, *C. glabrata* and *C. krusei* which were represented in the same proportions.

A statistically significant association between the germs isolated and the age of the participants was found in this study ($p<0.0001$) with the <20 years old who were most concerned by BSI. Significant differences in distributions for this age group compared to the others were found for *E. cloacae* ($p<0.0001$), *E. faecalis* ($p = 0.02358$), *E. coli* ($p<0.0001$), *K. oxytoca* ($p<0.0001$), *K. pneumoniae* ($p = 0.002289$), *S. enteritidis* ($p = 0.0376$), *Salmonella sp.* ($p = 0.002776$), *S.* Typhi ($p<0.0001$), *S. epidermidis* ($p = 0.008207$), *Staphylococcus sp.* ($p<0.0001$) and other organisms ($p = 0.005093$). Concerning sex, no association was found with BSIs in this study ($p = 0.942$). These results are close to those of Dagnew *et al.* [10], where age was associated with BSI ($p = 0.0004$) with the majority of patients who were older than 15 years (>15 years). Also, as in the present study, gender was not associated with infection ($p = 0.526$). The germs most represented in the >15 years olds in their study were CoNS, *S. aureus*, *E. coli*, *Klebsiella spp.*, *P. aeruginosa*, *S. pyogenes*, *Enterobacter spp.* and *Acinetobacter spp.*. In the published article by Jain and Das Chugh [39], sex was also a risk factor for infection in children under 15 years of age (66.3%) with enteric fever caused by *Salmonella enterica* serotype Typhi, *Salmonella enterica* serotype *paratyphi* A and *Salmonella enterica* serotype *paratyphi* B compared to young adults 20-30 years of age (18%). Another study by Seni *et al.* [36], also showed that age was a risk factor for BSIs with the neonatal period (≤ 1 month) being a risk factor for BSIs [Multivariate OR (95% CI): 1.93 (1.07-3.48); $p = 0.030$]. However, sex was not a risk factor for infection [Univariate OR (95% CI): 0.97 (0.67-1.41); $p = 0.894$]. The study by Ahmed *et al.* [43], also showed an association between age groups and infection for some pathogenic organisms including *Pseudomonas sp.* [OR (95% CI): 0.383 (0.341-0.430); $p<0.001$], *S. paratyphi* A, B [OR (95% CI): 0.510 (0.449-0.579); $p<0.001$] and *Serratia sp.* [OR (95% CI): 0.592 (0.373-0.941); $p<0.05$]; significant association for the group of patients older than 5 years (>5 years). In the less than 5 years (<5 years) group of this study [43], the association was significant for non-typhoidal *Salmonella sp.* [OR (95% CI): 5.082 (3.171-8.146); $p<0.001$] and *S. pneumoniae* [OR (95% CI): 3.827 (2.922-5.012); $p<0.001$]. In contrast to the present study, Ahmed *et al.* [43], also found an association between sex and infection for *S. aureus* [OR (95% CI): 1.348 (1.019-1.783); $p<0.05$] significantly associated with male sex and *E. coli* [OR (95% CI): 0.705 (0.581-0.855); $p<0.001$] significantly associated with female sex. In the study by Al-Mulla *et al.* [44], carried out in children with cancer and bacteremia, and the study by Li et *al.* [45], carried out in neonatal sepsis patients, sex was not a risk factor for infection, as in the present study, with p-values of 0.555 and 0.81 respectively. The fact that age is a risk factor for infection of BSI with younger infants, particularly those with bacteremia, enteric fever or neonatal sepsis, could be explained by a weak immune response in this age group, the socio-economic status of their parents, or poor hygiene and consumption of contaminated food usually prepared outside the home or consumed on the street as shown in the studies by Dagnew *et al.* [10] or Jain and Das Chugh [39]. In the study by Seni *et al.* [36], carried out in northwestern Tanzania, the status of children, especially those infected with HIV, is a major risk factor for BSIs.

Antimicrobial susceptibility testing showed that in this study the highest rates of resistance were in favor of penicillin antibiotics, cephalosporins, aminoglycosides and sulfamides. In the penicillin family, the highest resistance rates were in favour of ticarcillin, amoxicillin + clavulanic acid and penicillin with the bacterial species *E. cloacae*, *E. coli*, *K. oxytoca*, *K. pneumoniae*, *S. typhimurium* and *S. aureus* being the most concerned. In the cephalosporin family, the most important resistances were in favor of cephalotin and cefotaxime with *E. cloacae*, *E. coli*, *K. pneumoniae* and *S. marcescens* being the most resistant. For the aminoglycoside family, the most important resistances were in favor of gentamicin, tobramycin, kanamycin high load and gentamicin 500 with *K. pneumoniae* and *E. cloacae* being more resistant to gentamicin, *E. cloacae* more resistant to tobramycin and *E. faecium* more resistant to kanamycin high load and gentamicin 500. As for the sulfamide family, the highest resistances were recorded for trimethoprim + sulfamethoxazole with *E. cloacae*, *E. coli*, *K. pneumoniae* and *S. typhimurium* being the most resistant. These results are close to those of Pokhrel *et al.* [46], who found high resistance to most of the antibiotics tested, particularly those of the beta-lactam family, aminoglycosides, fluoroquinolones and glycopeptides. In the study by Seni *et al.* [36], the isolated germs notably *K. pneumoniae*, *S. aureus*, *E. coli*, *Acinetobacter spp*, other GPB and other GNB were multi-resistant to most of the antibiotics tested: *K. pneumoniae*, which was the most represented was multi-resistant to ampicillin (100%), cotrimoxazole (96.3%), gentamicin (78.2%), ciprofloxacin (29.1%), amoxicillin + clavulanic acid (94.6%), ceftazidime (90.9%) and ceftriaxone (95.7%); *S. aureus* was more resistant to ampicillin (100%), cotrimoxazole (82.6%) and erythromycin (65.2%); *E. coli* was more resistant to ampicillin (100%), cotrimoxazole (94.1%) and amoxicillin + clavulanic acid (94.1%). *Acinetobacter spp.* was more resistant to cotrimoxazole (90.0%) and ceftazidime (100%). Another research team, that of Ahmed *et al.* [43], who worked on bacterial agents responsible for BSIs and antimicrobial resistance in Dhaka, Bangladesh between 2005-2014 found high rates of resistance of the identified germs to the majority of antimicrobials tested with *S.* Typhi, which showed high resistance to ampicillin (24-

62%), cotrimoxazole (21-63%) and ciprofloxacin (87-96%); *S. paratyphi* A, B which was highly resistant to ciprofloxacin (91-100%); *E. coli* highly resistant to ampicillin (71-96%), cotrimoxazole (56-76%), ciprofloxacin (41-73%) and ceftriaxone (32-76%); as for *S. pneumoniae*, their study showed that it was more resistant to cotrimoxazole (70-91%). The study by Sorsa *et al.* [37] also showed results similar to those of the present study. In their study, *E. coli* was highly resistant to penicillin and aminoglycoside antibiotics with 66.7% resistance to ampicillin and 55.6% resistance to gentamycin; *Klebsiella spp.* was highly resistant to these two first-line antibiotics in the treatment of neonatal sepsis (91% resistance to ampicillin and 82% resistance to gentamycin). As for the other GPB and GNB isolated, their resistance rate was high for 3rd generation cephalosporins and 72% of the bacteria isolated were multi-resistant. The study conducted in northern Ethiopia by Wasihun *et al.* [38], also showed that the antimicrobial resistance patterns were 0-83.3% and 0-100% respectively for GPB and GNB with higher resistance rates for trimethoprim + sulfamethoxazole (70.1%), oxacillin (62.5%), ceftriaxone (58.9%) and doxycycline (49.3%). In the study by Maham *et al.* [41], the prevalence of multidrug resistance (MDR) was 83.4% with a higher MDR rate in GPB compared to GNB (85% vs. 70.4%); that of Deku *et al.* [47] showed that isolated bacteria were more resistant to tetracyclines (73.4%), penicillins (76.8%) and sulfamides. The multiresistance observed in the present and previous studies could be justified by the presence of resistance enzymes found in the germs responsible for BSIs as stated by Akova [32] in his article with for example the community-acquired bloodstream infections (CA-BSIs) caused by methicillin-resistant *Staphylococcus aureus* (MRSA), of which 5 major clones including multilocus sequences are associated with multiresistance: the sequence type 1 (ST-1), ST-8, ST-59, ST-80 and ST-30; *Streptococcus spp.* including *S. pneumoniae* and *S. viridans streptococci* which are resistant to antibiotics of the beta-lactam family due to alteration of the penicillin-binding protein; *Enterococcus spp.* including *E. faecium* which is resistant to antibiotics of the beta-lactam family due to the production of PBP5 which has a low affinity for penicillins; *Escherichia coli* whose resistance is associated with the production of CTX-M-15 extended spectrum beta-lactamases (ESBLs), the production of beta lactamase inhibitory enzymes (OXA-1) which confer resistance to beta-lactamase inhibitors, notably amoxicillin + clavulanic acid and piperacillin + tazobactam, the presence of carbapenemases and the *mcr-1* gene which confers resistance to colistin; *P. aeruginosa* whose resistance is associated with the production of AmpC beta lactamases and metallo-beta-lactamases (PER-1) whose production confers high resistance to cephalosporins, particularly ceftazidime; *A. baumannii* whose resistance is associated with the production of class A ESBLs which confer resistance to cephalosporins and class B ESBLs which confer resistance to carbapenems but also to cephalosporins and penicillins. In addition, other factors of multiresistance, notably the wrong use of antibiotics and their indiscriminate use, are increasingly contributing to the emergence of treatment failures in the context of BSIs, as Thapa and Sapkota point out [48].

Despite the multidrug resistance observed during this study, most of the germs represented were also sensitive to penicillin antibiotics with high sensitivity rates for ticarcillin + clavulanic acid, enterococcal ampicillin, amoxicillin, amoxicillin + clavulanic acid and ticarcillin. In the cephalosporin family, this study showed that *Salmonella* species were more sensitive to cefotaxime and ceftazidime. In terms of aminoglycosides, the most effective antibiotic was amikacin with high sensitivity rates (79%-100%) for *A. baumannii*, *A. calcoace*, *E. cloacae*, *E. coli*, *K. oxytoca*, *K. pneumoniae*, *P. aeruginosa*, *S. enteritidis*, *Salmonella sp.*, *S* Typhi, *S. typhimurium* and *S. marcescens*. In the streptogramine family, the antibiotics quinupristin + dalfopristin and pristinamycin were highly effective against *S. aureus* (89.5% sensitivity for quinupristin + dalfopristin and 77.3% sensitivity for pristinamycin) and *S. epidermidis* (74.6% sensitivity for quinupristin + dalfopristin and 70.9% sensitivity for pristinamycin). This study also showed that in the family of polypeptides, vancomycin was very effective (76.6%-98.2% sensitivity) against the Gram-positive Cocci *E. faecalis*, *E. faecium*, *S. aureus*, *S. epidermidis*, *S. pneumoniae* and *Streptococcus sp.*. As for teicoplanin, its efficacy was also important for *E. faecalis* (93.5%), *E. faecium* (98%), *S. aureus* (82.6%) and *Streptococcus sp.* (87.1%). Concerning the fluoroquinolone family, ciprofloxacin was highly effective against BSIs caused by *K. pneumoniae* (67.9%), *P. aeruginosa* (79.1%), *S. enteritidis* (89.1%), *Salmonella sp.* (85.5%), *S. Typhi* (98.8%), *S. typhimurium* (97.7%), *S. marcescens* (95.8%), *A. baumannii* (81.9%), *A. calcoace* (88%) and *K. oxytoca* (80.8%). These results are close to those of Vasudeva *et al.* [33] who found high sensitivities for most of the antibiotics tested with the majority of Gram-positive Cocci which were sensitive to vancomycin and linezolid and Gram negative Cocci which were more sensitive to cefoperazone/sulbactam. Marcello *et al.* [49], in a meta-analysis of the prevalence of community onset-bloodstream infections (CO-BSIs) in hospitalized patients in Africa and Asia, found similar results in terms of antimicrobial susceptibility. Indeed, their study showed that ciprofloxacin was highly effective against Gram-negative bacilli during the periods before 2008 and those of 2008-2018. As for GPB, sensitivity was high to erythromycin and vancomycin for *S. aureus*; and to erythromycin, penicillin and chloramphenicol for *S. pneumoniae*. In the study by Popoola *et al.* [12] in febrile patients in Nigeria, the sensitivity of *S. aureus* was high for gentamycin (91.4%), ciprofloxacin (79.4%), clindamycin (82.1%) and chloramphenicol (76.8%). Another study by Savage *et al.* [50] in patients diagnosed in 14 intensive care units (ICU) in Canada showed that GNB (*Enterobacteriaceae* and non-*Enterobacteriaceae*), which were most represented in BSIs, were more sensitive to amikacin (97.8% for *Enterobacteriaceae* and 96.8% for non-*Enterobacteriaceae*), carbapenems (98.6% for *Enterobacteriaceae* and 80.9% for non-*Enterobacteriaceae*), gentamycin (94.3% for *Enterobacteriaceae* and 89.0% for non-*Enterobacteriaceae*) and tobramycin (90.9% for *Enterobacteriaceae* and 93.0% for non-*Enterobacteriaceae*). Several other studies [44,45,47,48,51-54] have also shown that sensitivity to the antimicrobials tested was high for most germs isolated from blood culture bottles, which is justified

by the improvement of therapeutic protocols and the efficiency of treatment lines that take into account the use of several families of antibiotics. Indeed, as confirmed by Popoola *et al.* [12], Banik *et al.* [51] and Mamtora *et al.* [53], the use of carbapenems (imipenem and meropenem), amikacin, gentamycin for the treatment of BSIs caused by *Enterobacteriaceae* or vancomycin and linezolid for the treatment of BSIs caused by MRSA and *Enterococcus spp*. is a treatment of choice in the follow-up and management of infected patients. For the fungi most represented in this study (*C. parapsilosis* and *Candida sp.*), this study showed that azole antifungal agents were highly effective in candidemia with miconazole, which had an efficacy rate of 77.4% and 86.5% respectively against *C. parapsilosis* and *Candida sp.*; econazole and ketoconazole were 80.6% and 82.7% effective against *C. parapsilosis* and *Candida sp.* and clotrimazole was 93.5% and 61.5% effective against the same germs. As for amphotericin B, its efficacy was greater against *Candida sp.* (76.9%) compared to *C. parapsilosis* (58.1%). These results are close to those of Sana *et al.* [35], Banik *et al.* [51] and Li *et al.* [45] where the sensitivity of *C. albicans* and non-*albicans* species to the antifungal agents tested was high.

In view of the multiresistance observed in our context and the high prevalence of bloodstream infections (BSIs) obtained during the study period, there is important for medical laboratories and research centers to develop strategies to promote the use of faster and more accurate diagnostic techniques as demonstrated in some studies [9] [13] [17] [55-64] to improve surveillance and monitoring of antimicrobial resistance and the management of patients at risk and those contaminated throughout the country.

5. Conclusion

Bloodstream infections (BSIs) are the leading cause of mortality and morbidity in both developed and developing countries. The results of this study showed that the prevalence of infection is very high in our context with the youngest (< 20 years) being vulnerable. Despite the multiresistance observed for most of the families of antibiotics tested, this study revealed that cephalosporins, aminoglycosides, peptides and quinolones are the most effective against most of the bacteria responsible for the infection. The same finding of efficacy was also observed for the antifungals tested. In light of these results, it is nevertheless important to extend the surveillance and control of multiresistance to antibiotics in the context of bloodstream infections in order to considerably reduce the prevalence of infection and improve the management of those at risk, that is to say the youngest people.

List of Abbreviations

BSIs	bloodstream infections
CA-BSIs	community acquired bloodstream infections
CLSI	Clinical Laboratory Standard Institute
CO-BSIs	Community onset bloodstream infections
CoNS	Coagulase negative Staphylococci
CPC	Centre Pasteur of Cameroon
ESBL	extended spectrum beta-lactamase
GNB	Gram negative bacteria
GPB	Gram positive bacteria
HIV	Human immunodeficiency virus
MDR	multidrug-resistant
MRSA	meticillin resistant Staphylococcus aureus
ST	sequence type
UTI	urinary tract infection
WHO	World Health Organisation

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Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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