Susceptibility Pattern of Pathogens Causing Blood Stream Infections in a Tertiary Care Hospital: A Two-year Retrospective Study from Southern Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author BEE conceptualized study, designed the study and wrote the initial manuscript. Authors UEE, AAI and EAO carried out content editing, proofreading of manuscript and edited grammar. Author BEM wrote the methodology. Author SEE interpreted data and reviewed manuscript and author BAA did literature review and wrote the introduction. All authors read and approved the final manuscript.

ABSTRACT

Aim: Bloodstream infections are a major cause of morbidity and mortality worldwide. The prevalence of causative microorganisms varies from one geographical region to another. This study was aimed at determining the etiological agents prevalent in our environment and their susceptibility profile.

Study design: This is a retrospective study carried out at the University of Calabar Teaching Hospital, Calabar, Nigeria.

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2. MATERIALS AND METHODS

Methodology: Blood culture results of patients documented over a two-year period were retrieved and analyzed. Blood culture positive isolates were detected using conventional method and Oxoid signal blood culture systems. Antimicrobial sensitivity tests were carried out by Kirby-Bauer disc diffusion method. Methicillin resistance in *Staphylococcus aureus* and coagulase negative *Staphylococcus species* (CoNS) was detected by disk diffusion method using 30 µg cefoxitin disk. ESBL production was detected by phenotypic confirmatory disc diffusion test (PCDDT) and the double disc synergy test (DDST).

Results: A total of 413 blood culture antimicrobial susceptibility test results were analyzed, of which 116 (28.09%) were identified as culture positive. Sixty-nine (59%) of the positive isolates were from female patients. Out of 116 positive cultures, 58.62% (68/116) were Gram positive organisms, 40.52% (47/116) were Gram negative organisms, non *albicans* *Candida* accounted for 0.86% (1/116). *Staphylococcus aureus* (n=41, 35.3%) was the predominant isolate and showed high sensitivity to levofloxacin (100%), Linezolid (100%) and Amikacin (100%). Twelve isolates of *S. aureus* were methicillin resistant, while 1 isolate was inducible clindamycin resistant. Of the 116 isolates identified in this study, forty-three (43) were multidrug resistant with highest number of multidrug resistant isolates from *Staphylococcus aureus* (n=20). 21.28% (n=10) of the Gram-negative isolates were positive for extended spectrum beta lactamases.

Conclusion: A high rate of antimicrobial resistance is observed among microorganisms causing blood stream infections. This emphasizes the need for antimicrobial sensitivity testing in the management of blood stream infections.

**Keywords:** Infections; septicemia; susceptibility; mortality.

1. INTRODUCTION

Blood stream infections (BSIs) are the leading cause of morbidity and mortality in Sub-Saharan Africa especially in immune-compromised patients, yet few facilities have been able to maintain surveillance [1,2]. Globally, Blood stream infection affects about 30 million people and accounts for 6 million deaths, with 3 million new born and 1.2 million children suffering from sepsis annually [1]. Advances in medicine, increasing use of invasive devices, prolonged hospital stay, immunosuppressive therapy, neutropenia, and organ transplantation are some of the risk factors associated with blood stream infections [2,3]. Our study was aimed at determining the microbial etiology of BSIs in our locality and their susceptibility profile.

2. MATERIALS AND METHODS

This is a retrospective study, conducted at the University of Calabar Teaching Hospital Calabar, Nigeria. Study population comprised all patients who were investigated for septicemia from July, 2018 to June, 2020. Blood culture results of patients were retrieved and analyzed. Details on the history of prior antibiotic therapy before blood culture could not be ascertained.

Processing of blood samples was done using the conventional method and the Oxoid signal blood culture system. Using the conventional method, blood samples were collected in brain heart infusion broths, in a ratio of 1:10 for both paediatrics and adult patients under strict aseptic conditions and thereafter continuously incubated aerobically at 37°C. A blind subculture was done after 18–24 h of incubation on MacConkey agar or Cysteine lactose electrolyte deficient agar and 5% sheep blood agar irrespective of the degree or level of turbidity [4,5]. The bottles were taken out and visually observed for turbidity every morning and subcultures were done for bottles that showed turbidity. The bottles that were negative for turbidity were incubated for additional 7 days, after which another blind subculture was done before reporting them as negative. Blood samples inoculated in Oxoid signal bottles that showed positive results were subcultured on MacConkey agar or Cysteine lactose electrolyte deficient agar and 5% sheep blood agar, while those with negative results were discarded after 7 days of incubation. Culture isolates were identified by Gram staining, colony morphology and standard biochemical tests. Kirby-Bauer disc diffusion method on Mueller-Hinton agar plates was used to determine the antibiotic susceptibility pattern of the isolated organisms and interpreted either as ‘Sensitive’ or ‘Resistant’ or ‘Intermediate’ based on the Clinical Laboratory Standard Institute (CLSI), guidelines, 29th edition [4]. Antibiotics against which sensitivity was tested in this study included amoxicillin-clavulanate, cefoxitin, ceftriaxone, cefuroxime, ceftazidime, cefixime,
ciprofloxacin, levofloxacin, piperacillin/tazobactam and gentamicin. Isolates showing resistance to Cefpodoxime (10µg) or Ceftazidime(30µg) or Aztreonam(30µg) or Cefotaxime(30µg) or Ceftriaxone(µg) were phenotypically tested for the production of extended spectrum beta-lactamase (ESBL) as per CLSI guidelines [6,7]. All strains of *Staphylococcus aureus* and CoNS were tested for methicillin resistance using cefoxitin disc. Interpretation was done following the CLSI guidelines [6]. All strains of *Staphylococcus aureus* that were resistant to erythromycin, but intermediate or susceptible to clindamycin were tested for inducible clindamycin resistance as per CLSI guidelines [6].

### 3. RESULTS

A total of 413 blood culture antimicrobial susceptibility test results were analyzed, out of which 116 (28.09%) were positive for growth of microorganisms. Of the 116, 69 (59%) belonged to females. The maximum number of positive blood culture (n=74) was from age group < 1 year old, while the minimum number of positive blood culture (n=6) was from age group >60 years (Table 1).

#### Table 1. Age distribution of patients with blood stream infections

| Age group (years) | Number of isolates | Percentages |
|-------------------|--------------------|-------------|
| < 1 year          | 74                 | 63.79       |
| < 20              | 16                 | 13.79       |
| 20-60             | 20                 | 17.24       |
| >60               | 6                  | 5.17        |
| Total             | 116                | 100         |

A single organism was reported for each blood culture antimicrobial susceptibility test result giving a total of 116 microorganisms. *Staphylococcus aureus* (n=41, 35.3%) was the predominant isolate. Of the 41 S. aureus isolates, 12 (29.27%) were methicillin resistant, 1 (2.44%) was inducible clindamycin resistant. Of the 5 coagulase negative *Staphylococcal spp.*, 1 was methicillin resistant. The summary of isolates identified and their frequencies is shown in Table 2.

#### Table 2. Summary of blood culture isolates and their frequencies

| Isolates                  | Number | Percentage |
|---------------------------|--------|------------|
| *Acinetobacter baumanii*  | 3      | 2.6        |
| CoNS                      | 5      | 4.3        |
| *Enterococcus spp.*       | 15     | 12.9       |
| *Escherichia coli*        | 9      | 7.8        |
| *Klebsiella oxytoca*      | 2      | 1.7        |
| *Klebsiella pneumoniae*   | 3      | 2.6        |
| *Morganella morganii*     | 9      | 7.8        |
| *Non albicans candida*    | 1      | 0.9        |
| *Proteus mirabilis*       | 2      | 1.7        |
| *Proteus vulgaris*        | 2      | 1.7        |
| *Providencia alcalifaciens* | 4  | 3.4        |
| *Providencia rettgeri*    | 5      | 4.3        |
| *Providencia stuartii*    | 5      | 4.3        |
| *Pseudomonas aeruginosa*  | 1      | 0.9        |
| *Salmonella spp.*         | 1      | 0.9        |
| *Staphylococcus aureus*   | 41     | 35.3       |
| *Streptococcus pneumoniae*| 7      | 6.0        |
| *Tatumella ptyseos*       | 1      | 0.9        |
| Total                     | 116    | 100        |

CoNS, Coagulase negative *Staphylococcus* spp.
Table 3. Antibiotic susceptibility of gram-positive isolates

| Antibiotics  | Isolates | S. aureus | CoNS | MRSA | E. spp. | S. pneumoniae |
|--------------|----------|-----------|------|------|---------|---------------|
| Levofloxacin | 2(100)   | NT        | 5(20)| 2(0) | NT      |               |
| Ciprofloxacin| 23(73.9) | 5(0)      | 11(36.4)| 10(50)| 6(50)   |               |
| Gentamicin   | 22(45.5) | 4(25)     | 11(27.2)| 7(57.1)| 5(0)    |               |
| Amikacin     | 2(100)   | 1(100)    | 6(50) | NT   | NT      |               |
| Erythromycin | 12(16.7) | 3(0)      | 8(37.5)| 1(100)| 5(40)   |               |
| Azithromycin | 5(20)    | 1(0)      | 2(100)| 5(20) | 2(100)  |               |
| Linezolid    | 6(100)   | NT        | 1(100)| 6(100)| 1(100)  |               |
| Vancomycin   | 5(40)    | NT        | 3(0) | NT   | NT      |               |

CoNS, Coagulase negative Staphylococcus species; MRSA, Methicillin resistant S. aureus; NT, Not tested; T=Total tested, %S= percentage of sensitivity

Table 4. Antibiotic susceptibility of gram-negative isolates

| Ant. Isolates | A. Baumanii | E. coli | K. spp. | M. morganii | Proteus spp. | Providencia spp. | P. aeruginosa |
|--------------|-------------|---------|---------|-------------|--------------|------------------|--------------|
| CRO          | 3(0)        | 9(55.6)| 5(40)  | 9(11.1)     | 4(50)        | 14(28.57)        | NT           |
| CXM          | NT          | 9(44.4)| 5(40)  | 9(22.2)     | 4(25)        | 14(7.1)         | NT           |
| CAZ          | 3(0)        | 9(55.6)| 5(40)  | 9(11.1)     | 4(50)        | 14(21.4)        | 1(100)       |
| CN           | 3(66.7)     | 9(33.3)| 5(60)  | 9(11.1)     | 4(25)        | 14(28.6)        | 1(100)       |
| AK           | 2(50)       | NT     | 2(100) | NT          | NT           | NT               | NT           |
| LEV          | 1(100)      | 1(100)| 2(0)   | NT          | NT           | NT               | NT           |
| CIP          | 3(66.7)     | 8(62.5)| 3(66.7)| 9(77.7)     | 3(66.7)      | 13(69.2)        | 1(100)       |
| AMC          | NT          | 6(33.3)| 4(0)   | 4(50)       | 3(33.3)      | 9(22.2)         | NT           |
| IMP          | 1(100)      | NT     | 5(60)  | NT          | NT           | NT               | NT           |
| CFM          | 2(50)       | NT     | 4(75)  | 1(0)        | NT           | NT               | NT           |
| CFX          | NT          | 4(50)  | 1(0)   | 5(20)       | NT           | 7(42.9)         | NT           |
| PTZ          | 1(0)        | NT     | NT     | 3(0)        | 2(50)        | 1(0)            | NT           |

CRO, Ceftriaxone; CXM, Cefuroxime CAZ; CAZ; Cefazidime CN; Gentamicin; AK, Amikacin; LEV, Levofloxacin; CIP, Ciprofloxacin; AMC, Amoxicillin-Clavulanate; IMP, Imipenem; CFM, Cefepime; CFX, Cefixime; PTZ, Piperacillin tazobactam; NT, Not tested; Ant, Antibiotics; T=Total tested, %S= percentage of sensitivity

4. DISCUSSION

The hallmark of BSIs is the presence of viable bacterial or fungal microorganisms in the bloodstream demonstrated by positivity of one or more blood cultures [8]. They are potentially life-threatening infections and a major cause of morbidity and mortality globally [9,10]. Early detection of bloodstream infections with prompt antimicrobial therapy could prevent implantation of microorganisms into vital organs such as brain, lungs, heart or kidneys and eventually improved clinical outcome. Additionally, empirical therapy guided by local susceptibility profile is also crucial for successful management of patients with BSIs [3,11]. There’s a strong relationship between delay in initiation of effective therapy and mortality from bloodstream infections. Each hour delay in commencement of therapy is associated with an average decrease in survival of 8% [12].

The isolation rate of blood culture positive cases in our study was 28.09%. This was similar to previous reports from India and Ethiopia [2,13,14] but however showed variation with other studies [1,12,15-18], as shown in Table 5.

Table 5. Isolation rates from previous studies

| Isolation rate | Location | Reference |
|---------------|----------|-----------|
| 27.7%         | India    | [2]       |
| 27.1%         | India    | [13]      |
| 28%           | Ethiopia | [14]      |
| 14.24%        | India    | [12]      |
| 19.2%         | *India   | [15]      |
| 38.95%        | *Nigeria | [16]      |
| 51.4%         | India    | [17]      |
| 51.4%         | Ghana    | [1]       |
| 33.3%         | *Nigeria | [18]      |
| 31.4%         | Nigeria  | [19]      |

* study population was neonates
Variations in blood culture positive rates may be due to the use of different laboratory diagnostic procedures, different patient populations, underlying disease conditions, hospital types, geographical locations and differences in the infection control policies [10,13]. Furthermore, variation in blood stream infection rates may be attributed to timing and number of blood cultures or difference in blood culture system, sampling volume of blood culture, and medium formulation [10,20].

In this study, women (59%) had high culture positivity compared to men (41%). This was consistent with a study done by Zenebe et al. [21], who reported a higher culture positivity in women, 59.2% than men, 40.8%. However, some studies also report a higher prevalence rate of BSIs in men compared to women [3].

The prevalence of BSIs in our study varied across age groups, with the highest prevalence among infants (63.79%). More paediatric patients (77.59%) were found with BSIs compared to adult patients of 22.41% (Table 1). This was consistent with previous reports from studies done by Jhajhria et. al, Ayobola et. al, and Bichitrnananda et. al [3,22,23], with BSIs prevalence rate of 57.3%, 58.3% and 50% respectively among infants. The high rate of BSIs in infants compared to other age groups may be due to poor skin integrity, immature immune system and frequent participation in activities that may predispose them to infections [20]. Furthermore, drugs are administered to infants mostly by means of intravascular devices which may easily introduce pathogens into their bloodstream [3].

In our study, the frequency of isolation of Gram-positive bacteria (n=68, 58.62%) was more than that of Gram-negative bacteria (n=47, 40.52%), as shown in Table 2. This was in keeping with findings from previous studies done by Kamga et. al, China et. al and Karlowsky et. al [24,25,26]. However, in some studies, the rate of isolation of Gram-positive organisms was lower than that of Gram-negative organisms [27]. These differences may be explained by the variation in the spectrum of causative organisms across geographical regions [2,8].

Among Gram-positive bacteria, Staphylococcus aureus was the most frequently isolated pathogen followed by Enterococcus spp., Streptococcus pneumoniae and CoNS (Table 2). This finding was in accordance with previous studies [28,29]. Some studies however, have reported a higher incidence of CoNS among Gram-positive bacteria causing BSIs [2]. S. aureus remains a leading cause of bacteremia with associated high mortality rates [30,31]. The high incidence of S. aureus bacteremia in this study may be due to risk factors such as the use of prosthetic devices, like central venous catheters, surgically implanted materials, and orthopedic prostheses, which serve as a direct channel into the intravascular space, allowing S. aureus access to the bloodstream [32]. Additionally, the use of intravenous drugs and underlying medical comorbidities such as diabetes, immunosuppressive therapy, and malignancy may also predispose to S. aureus bacteremia [32]. The incidence of MRSA-related bacteremia in our study was 10.34% (12/116). Incidence rates vary significantly from hospital to hospital globally [33,34]. MRSA bacteremia is associated with higher mortality rates, increased morbidity, longer hospital length of stay and health care costs compared with that of methicillin sensitive S. aureus (MSSA) [3,33,34].

Gram positive organisms were uniformly sensitive to Linezolid (100%). S. aureus showed high sensitivity to Levofloxacin (100%), Amikacin (100%) and Linezolid (100%). MRSA was highly sensitive to Linezolid (100%) and Azithromycin (100%), as shown in Table 3. However, the availability of some of these drugs poses a challenge to treatment in many 3rd world countries like Nigeria.

Sensitivity of Gram-negative organisms to tested antibiotics was varied, with most Gram-negative organisms showing sensitivity to Ciprofloxacin, Levofloxacin and Imipenem as shown in Table 4. Of the 47 Gram negative isolates, 10 (21.28%) were positive for extended spectrum beta lactamases (ESBL). Table 6 highlights Gram negative ESBL positive isolates and their respective percentages.

Table 6. ESBL producing isolates

| Isolates                      | Number of ESBL isolates (%) |
|-------------------------------|-------------------------------|
| Acinetobacter baumannii       | 1 (10)                        |
| Escherichia coli              | 3 (30)                        |
| Klebsiella pneumoniae         | 1 (10)                        |
| Morganella morganii           | 2 (20)                        |
| Providencia                   | 1 (10)                        |
| alcalifaciens                 |                              |
| Klebsiella oxytoca            | 1 (10)                        |
| P. rettgerii                  | 1 (10)                        |
| Total                         | 10 (100)                      |
ESBL are enzymes produced by Enterobacteriaceae group of organisms that make them resistant to beta-lactam antibiotics such as penicillin, cephalosporins, and monobactams except for cephamycins and carbapenems. They are plasmid mediated and also confer resistance to other commonly used antimicrobials such as fluoroquinolones, aminoglycosides, and sulphonamides [35,36]. Prolonged hospital stays, use of invasive medical devices (urinary catheters, endotracheal tubes, central venous lines, nasogastric tubes, gastrostomy and jejunostomy tubes, arterial lines) for a prolonged duration, recent surgeries, haemodialysis, decubitus ulcers, poor nutrition and prolonged use of antibiotics are risk factors associated with infection by ESBL producing Gram negative bacteria [35,36]. The incidence of multidrug resistance in this study was 37.07% (43/116) with highest number of MDR isolates from *S. aureus* (n=20). A summary of MDR isolates and their respective percentages is shown in Table 7.

**Table 7. MDR isolates**

| Isolates                | Number of MDR (%) |
|------------------------|-------------------|
| *Acinetobacter baumanii* | 2(4.65)           |
| CoNS                   | 5(11.63)          |
| *Enterococcus spp.*    | 3(6.98)           |
| *Escherichia coli*     | 2(4.65)           |
| *Klebsiella oxytoca*   | 2(4.65)           |
| *M. morganii*          | 1(2.33)           |
| *Providencia*          | 2(4.65)           |
| *alcalifaciens*        |                   |
| *Providencia rettgeri* | 1(2.33)           |
| *Providencia stuartii* | 3(6.98)           |
| *Proteus mirabilis*    | 1(2.33)           |
| *Proteus vulgaris*     | 1(2.33)           |
| *S. aureus*            | 20(46.51)         |
| Total                  | 43(100)           |

CoNS, Coagulase negative Staphylococcus spp.; MDR, multidrug resistant; %, percentage of isolates

5. CONCLUSION

The predominant isolates in this study among the Gram positive and Gram-negative organisms were *S. aureus* and *Escherichia coli* respectively. The Gram-positive organisms were uniformly sensitive to Levofloxacin and Linezolid. Except for *Klebsiella oxytoca*, the Gram-negative organisms tested against Levofloxacin were uniformly sensitive. Levofloxacin should be adopted as a first line antimicrobial for blood stream infections in our environment, considering 100% sensitivity to it among the predominant isolates. This study provides information on the etiology of blood stream infections from our region as well as the antimicrobial susceptibility profile of these microorganisms. It also provides a guide for the management of septiccaemic patients for physicians especially when initiating empirical therapy. Additionally, the high prevalence of antimicrobial resistance seen in this study further emphasizes the need for routine microbial surveillance (gathering data on the prevalence of microorganisms and their susceptibility profile), formulating policies for empirical antimicrobial therapy and compliance with existing guidelines for the use of antimicrobials.

6. LIMITATIONS OF THE STUDY

- Details on the history of prior antibiotic therapy before blood culture could not be ascertained due to incomplete documentation of blood culture request forms.
- We were all unable to compartmentalize data from different departments (surgical out patient departments, medical outpatient department, general outpatient departments and children outpatient department) and hospital wards due to inconsistencies in the blood culture request forms.
- The same challenge also accounts for why we were unable to state the percentage of blood stream infections that were nosocomially acquired.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline patients consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Deku JG, Dakorah MP, Lokpo SY, Orish VN, Ussher FA, Kpene GE, et al. The Epidemiology of Bloodstream Infections and Antimicrobial Susceptibility Patterns: A Nine-Year Retrospective Study at St.
11. Stream Infections and their antibiotic susceptibility profile in a Neonatal intensive care unit of a tertiary care hospital; a current perspective. J Pak Med Assoc. 2019;69(11).

12. Banik A, Bhat SH, Kumar A, Palit A, Snehaa K. Bloodstream infections and trends of antimicrobial sensitivity patterns at Port Blair. J Lab Physicians. 2018;10:332-7.

13. Paul M, Bhatia M, Sasi Rekha U, Ji Omar DB, Gupta P. Microbiological Profile of Blood Stream Infections in Febrile Neutropenic Patients at a Tertiary Care Teaching Hospital in Rishikesh, Uttarakhand. J Lab Physicians. 2020;12:147–153.

14. Wasihun, AG, Wlekidan, LN, Gebremariam, SA, Dejene TA, Welderufael AL, Haile TD, et. al. Bacteriological profile and antimicrobial susceptibility patterns of blood culture isolates among febrile patients in Mekelle Hospital, Northern Ethiopia. Springerplus. 2015;4(1):314.

15. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. J Nat Sc Biol Med.2013;4(2).

16. Omorieg R, Egbe CA, Dirisu J, Ogere HO. Microbiology of neonatal septicemia in a tertiary hospital in Benin City, Nigeria. Biomarkers and Genomic Medicine. 2013; 5:142e146.

17. Ramana KV, Palange P, Rao SD, Vaish R, Rao BM. Performance analysis of blood culture by an automated blood culture system at a tertiary care teaching hospital, in South India. Am J Clin Med Res. 2015;3:455–9.

18. Aziegbemhin SA, Enabulele OI. Prevalence of bacterial bloodstream infections of neonates in Benin City, Nigeria. J Infect Dis Ther. 2016;4:7.

19. Komolafe AO, Adegoke AA. Incidence of bacterial Septicaemia in Ile-Ife Metropolis, Nigeria. Malaysian Journal of Microbiology. 2008;4(2):51–61.

20. Parajuli NP, Parajuli H, Pandit R, Shakya J, RajKhanal P. Evaluating the Trends of Bloodstream Infections among Pediatric and Adult Patients at a Teaching Hospital of Kathmandu, Nepal: Role of Drug Resistant Pathogens. Can J Infect Dis Med Microbiol. 2017;10.

21. Zenebe T, Kannan S, Yilma D, Beyene G. Invasive bacterial pathogens and their antibacterial susceptibility profile in a Neonatal intensive care unit of a tertiary care hospital; a current perspective. J Pak Med Assoc. 2019;69(11).

22. Banik A, Bhat SH, Kumar A, Palit A, Snehaa K. Bloodstream infections and trends of antimicrobial sensitivity patterns at Port Blair. J Lab Physicians. 2018;10:332-7.

23. Paul M, Bhatia M, Sasi Rekha U, Ji Omar DB, Gupta P. Microbiological Profile of Blood Stream Infections in Febrile Neutropenic Patients at a Tertiary Care Teaching Hospital in Rishikesh, Uttarakhand. J Lab Physicians. 2020;12:147–153.

24. Wasihun, AG, Wlekidan, LN, Gebremariam, SA, Dejene TA, Welderufael AL, Haile TD, et. al. Bacteriological profile and antimicrobial susceptibility patterns of blood culture isolates among febrile patients in Mekelle Hospital, Northern Ethiopia. Springerplus. 2015;4(1):314.

25. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. J Nat Sc Biol Med.2013;4(2).

26. Omorieg R, Egbe CA, Dirisu J, Ogere HO. Microbiology of neonatal septicemia in a tertiary hospital in Benin City, Nigeria. Biomarkers and Genomic Medicine. 2013; 5:142e146.

27. Ramana KV, Palange P, Rao SD, Vaish R, Rao BM. Performance analysis of blood culture by an automated blood culture system at a tertiary care teaching hospital, in South India. Am J Clin Med Res. 2015;3:455–9.

28. Aziegbemhin SA, Enabulele OI. Prevalence of bacterial bloodstream infections of neonates in Benin City, Nigeria. J Infect Dis Ther. 2016;4:7.

29. Komolafe AO, Adegoke AA. Incidence of bacterial Septicaemia in Ile-Ife Metropolis, Nigeria. Malaysian Journal of Microbiology. 2008;4(2):51–61.

30. Parajuli NP, Parajuli H, Pandit R, Shakya J, RajKhanal P. Evaluating the Trends of Bloodstream Infections among Pediatric and Adult Patients at a Teaching Hospital of Kathmandu, Nepal: Role of Drug Resistant Pathogens. Can J Infect Dis Med Microbiol. 2017;10.
antibiotic susceptibility patterns in Jimma University Specialized Hospital, Jimma, Southwest Ethiopia. Ethiop J Health Sci. 2011;21:1-8.

22. Ayobola ED, Egbule OS, Omonigho O. Study of Prevalence and Antimicrobial Susceptibility of Blood Culture Bacterial Isolates. Malays. J. Microbiol. 2011;7(2):78-82:23.

23. Bchitrananda swain, Sarita Otta. Blood stream infection in a teaching hospital. Ann. Biol. Res. 2012;3(4):1923-1928.

24. Kamga HLF, Njunda Al, Nde PF, Assob JCN, Nsagha DS, Weledji P. Prevalence of Septicemia and Antibiotic Sensitivity Pattern of Bacterial isolates at the University Teaching Hospital, Yaoundé, Cameroon. Afr J Clin Exper Microbiol. 2011;12(1):2-8.

25. China and V. Gupta. Bacteriological profile and antimicrobial susceptibility pattern of blood isolates from a tertiary care hospital in North India. Inter J Pharm Res Biosci. 2013;2(2):24-35.

26. Karlowsky JA, Jones ME, Draghi DC, Thornsberry C, Sahm DF, Volturo GA. Prevalence and antimicrobial susceptibilities of bacteria isolated from blood cultures of hospitalized patients in the United States in 2002. Ann Clin Microbiol Antimicro. 2004;3:7-7.

27. Mehta M, Pyria D, Varsha G. Antimicrobial susceptibility pattern of blood isolates from a teaching Hospital in north India. Japan J Infec Dis. 2005;58:174-176.

28. Kaistha N, Mehta M, Singla N, Garg R, Chander J. Neonatal septicemia isolates and resistance patterns in a tertiary care hospital of North India. J Infect Dev Ctries. 2009; 4:55-7.

29. Thomer L, Schnewind O, Missiakas D. Pathogenesis of Staphylococcus aureus Bloodstream Infections. Annu Rev Pathol. 2016;11:343–364.

30. Yasmin M, El Hage H, Obeid R, El Haddad H, Zaatour M, Khalil A. Epidemiology of bloodstream infections caused by methicillin-resistant Staphylococcus aureus at a tertiary care hospital in New York. Am. J. Infect. Control. 2016;44:41–6.

31. Carvalho Naves KS, Vaz da Trindade N, Gontijo Filho PP. Methicillin-resistant Staphylococcus aureus bloodstream infection: risk factors and clinical outcome in non-intensive-care units. Rev Soc Bras Med Trop. 2012; 45(2):189-193.

32. Core GR. Staphylococcus aureus Bloodstream Infections: Definitions and Treatment. Clinical Infectious Diseases. 2009; 48: S254–9.

33. Carvalho Naves KS, Vaz da Trindade N, Gontijo Filho PP. Methicillin-resistant Staphylococcus aureus bloodstream infection: risk factors and clinical outcome in non-intensive-care units. Rev Soc Bras Med Trop. 2012; 45(2):189-193.

34. Paterson DL, Bonomo RA. Clin. Microbiol. Rev. 2005;18 (4): 657-686.

35. Rawat D, Nair D. Extended-spectrum β-lactamases in Gram Negative Bacteria. J Glob Infect Dis. 264 2010;2(3):263-74.

36. Jacoby GA. AmpC beta-Lactamases. Clin. Microbiol. Rev. 2009;161–182.