Ecology of Bloodstream Infections and Temporal Trends of Their Antibiograms with Respect to Source and Duration of Incubation: A 5-Year Retrospective Observational Analysis

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Abstract

Purpose Blood is one of the most important connective tissues of human body. Bloodstream infection can range from inapparent bacteremia till fulminant septic shock with high mortality. Presence of microbes in blood whether continuously, intermittently, or transiently is a grave risk to every organ of body. Culture of blood is a vital tool to diagnose such infections. Drug susceptibility patterns help in rationalizing therapy.

Objective The aim of the study is to perform bacteriological analysis and assess drug sensitivity patterns of blood culture isolates and compare in light of other associated variables.

Design Retrospective observational study was conducted from January 2009 to December 2013 at a tertiary care hospital at Shillong, India. Blood samples were collected with aseptic guidelines and cultured for 7 days. Growths were identified by standard biochemical tests and subjected to sensitivity testing according to Modified Kirby Bauer disk diffusion method. Data for source of blood collection and duration of incubation were noted and compared.

Results A total of 658 (11.2%) pathogens were isolated from 5,867 bacteremia-suspected patient blood specimens. Contamination was observed at the rate of 1.21%. Gram-negative organisms were the predominant pathogens recovered, Klebsiella pneumoniae being the most common. No significant difference was observed between the number of organisms isolated within or beyond 48 hours. Acinetobacter baumannii and K. pneumoniae have significantly higher chances (p < 0.05) of isolation from central line catheters compared with peripheral venipuncture.

Conclusion Successful treatment of sepsis depends on early diagnosis and proper antimicrobial therapy. Local knowledge of bacteriological profile and antimicrobial sensitivity patterns helps rationalize empiric treatment strategies.

Introduction

Blood is in the truest sense the elixir of life. It contains a part of the extracellular fluid along with a wide variety of other constituents which are indispensable for proper functioning and survival of human life. From providing nutrients, limiting pathogens, perfusing and ventilating organs, clotting wounds, removal of toxins and chemicals, and dissemination of hormones and drugs throughout the body it performs a pivotal role in body defense and survival. Presence of organisms in blood can give rise to different clinical scenarios. Clinical presentation ranges from benign transient bacteremia with

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Any growth
► Supplementary is a vital tool for the detection of BSI and is the gold standard hence prompt detection of such infections is a critical role in managing BSI intermittently, or transiently is a grave risk to every organ of the body. Early diagnosis plays a crucial role in managing BSI and when turbidity was noticed. Specimens were discarded after 7 days of unsuccessful aerobic incubation. Any growth obtained was processed and identified by Gram staining, colony morphology, and standard biochemical tests. Antibiotic susceptibility testing was done according to Kirby Bauer disk diffusion method and interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Positive growths were further critically analyzed based on the criteria to be agents of bacteremia, fungemia, and contaminants. The data were manually compiled and analyzed critically for the study. The following strains were used as quality control strains:

1. Staphylococcus aureus (ATCC 25923)
2. Escherichia coli (ATCC 25922)
3. Pseudomonas aeruginosa (ATCC 27853)

Results

The present study involves 5,867 continuous samples received from different wards and intensive care units (ICUs) of the hospital. Among them, 740 isolates showed positive aerobic bacterial growth and 669 (11.40%) of them were recognized pathogens. However, blood bank surveillance revealed 11 pathogens and 17 contaminants. Finally, 658 (11.2%) isolates were recovered from patients as incriminating microorganisms responsible for bacteremia/fungemia. More males suffered from bacteremia than females with a gender ratio skewed at 1.4:1. The mean age of patients was 33.67 ± 23 years (range 0–85 years). Bulk of the specimens were sent from Medicine, Pediatric wards apart from critical care units. Data including the most common clinical syndromes leading to bacteremia/fungemia and the corresponding distribution of the microbial agents responsible are depicted in Table 1. Cerebrovascular accidents and their subsequent complications were the leading cause for BSIs. Contamination in blood culture was documented in 71 (1.21%) isolates in the present study. Most of them were from blood bank and pediatric ICU. A detailed analysis of contaminants obtained from different sections of hospital is presented in Table 2. Among 658 isolates recovered from patients, the spectrum of microbes included 436 (66.3%) gram-negative bacilli (GNB), 195 (29.6%) gram-positive cocci (GPC), 15 gram-negative cocci, 1 gram-positive bacilli,

Materials and Methods

The present study is a 5-year retrospective observational analysis of blood culture isolates received in the Department of Microbiology of the hospital from January 2009 to December 2013. Necessary Ethics Committee Approval was obtained for the study.

Sample Collection

Blood specimens were obtained at bedside either by a trained phlebotomist or by nursing staff from wards and critical care units. The skin was disinfected with 2% chlorhexidine. Approximately 5 to 10 mL of blood was collected from adult patients, 1 to 5 mL from pediatric patients, and 1 to 2 mL from neonates. The antecubital and median cubital fossa were the preferred sampling sites using a needle and syringe. The blood samples from the central vein catheters were obtained from needleless caps that have been disinfected with 70% isopropyl alcohol, allowed to dry, and wiped with sterile gauze prior to obtaining the sample.

Sample Processing

Blood for culture was collected from 5,867 clinically suspected bacteremia cases under strict aseptic precautions. They were inoculated into conventional blood culture bottles containing Brain Heart Infusion broth (1:10 dilution). These were incubated aerobically at 37°C, observed for turbidity every morning, and manually agitated for aeration for 7 complete days. Regular blind subcultures were done at the completion of day 2 and day 7 of aerobic incubation. Subcultures were done on MacConkey agar, 5% Sheep blood agar, and chocolate agar as and when turbidity was noticed. Presence of microbes in blood whether continuously, intermittently, or transiently is a grave risk to every organ of the body. Early diagnosis plays a crucial role in managing BSI and hence prompt detection of such infections is a critical role in clinical microbiology laboratories. Blood culture is a vital tool for the detection of BSI and is the gold standard for bacteremia detection. Initial antimicrobial empirical therapy being very imperative in BSI, must be based on the knowledge of the bacterial profile and their sensitivity patterns. Irrational use of drugs leads to an increase of multi-drug-resistant bugs and thus worsens the management of the infections. Prevalence and susceptibility patterns of microorganisms vary according to the geography and use of antibiotics in different health care settings. There is paucity of similar reports with regard to disease burden from Northeast India, and more so from Meghalaya. This region is unique with respect to its ethnicity, geographical location, topography, climatic condition unlike the rest of the country. The current study intends to report the prevalence, bacteriological analysis of microorganisms, and antimicrobial susceptibility profiles of blood culture isolates and other auxiliary variables in a tertiary health care center in Northeast India.
Table 1  Most common clinical syndromes with incriminating microbes’ distribution

| Sl. no. | Name of initial clinical diagnosis/syndrome | Microbes isolated (n =?) | Staphylococcus spp. | Enterococcus spp. | Klebsiella spp. | Escherichia coli | Pseudomonas spp. | Acinetobacter spp. | Enterobacter spp. | Nonfermenting GNB | Neisseria meningitidis | Salmonella spp. | Others |
|---------|-------------------------------------------|-------------------------|----------------------|-------------------|----------------|----------------|----------------|-------------------|----------------|----------------|-----------------------|----------------|--------|
| 1       | Severe pneumonia                          | 12                      | 4                    | 2                 | 2              | 2              | 2              |                   | 2              | 1              | 1                     |                 | 1      |
| 2       | DM with complications                     | 21                      | 2                    | 1                 | 6              | 7              | 1              | 2                 | 1              | 1              |                       |                 |        |
| 3       | Tuberculous meningitis                    | 15                      | 3                    | 5                 | 1              | 4              | 2              |                   |                 |                |                       |                 |        |
| 4       | Bacteremia and sepsis                     | 14                      | 5                    | 1                 | 3              | 2              | 2              | 1                 |                 |                |                       |                 |        |
| 5       | Seizures and epilepsy                     | 08                      | 3                    | 3                 | 1              | 1              | 1              |                   |                 |                |                       |                 |        |
| 6       | Rheumatic disease with complications      | 14                      | 5                    | 3                 | 1              | 1              | 2              | 1                 |                 | 1              |                       |                 |        |
| 7       | Prematurity                               | 9                       | 2                    | 2                 | 3              | 1              | 1              |                   |                 |                |                       |                 |        |
| 8       | Postoperative infection (general surgical) | 27                      | 4                    | 3                 | 6              | 8              | 3              | 2                 |                 | 1              |                       |                 |        |
| 9       | Post exploratory laparotomy               | 23                      | 2                    | 1                 | 4              | 9              | 6              |                   |                 |                |                       |                 |        |
| 10      | Meningitis and meningoencephalitis        | 28                      | 4                    | 1                 | 2              | 1              | 1              | 1                 | 1              | 13             | 2                     |                 |        |
| 11      | Intracranial hemorrhage                   | 16                      | 1                    | 11                | 1              | 3              |                 |                   |                 |                |                       |                 |        |
| 12      | Hepatic encephalopathy                    | 8                       |                      | 1                 | 1              | 3              | 1              |                   |                 |                |                       |                 | 2      |
| 13      | CKD with complications                    | 26                      | 1                    | 8                 | 4              | 3              | 10             |                   |                 |                |                       |                 |        |
| 14      | Acute pancreatitis                        | 10                      | 2                    | 5                 | 2              |                |                |                   |                 |                |                       |                 |        |
| 15      | CVA with complications                    | 49                      | 3                    | 1                 | 18             | 5              | 15             | 3                 | 1              |                |                       |                 |        |
| 16      | Enteric fever                             | 6                       |                      | 1                 |                |                |                |                   |                 |                |                       |                 | 4      |
| 17      | COPD with complications                   | 8                       | 2                    | 1                 |                |                |                |                   |                 |                |                       |                 | 1      |
| 18      | Fever                                    | 11                      | 3                    | 1                 | 2              |                |                |                   |                 |                |                       |                 | 4      |

(Continued)
Table 1 (continued)

| Sl. | Microbes Isolated | Name of Initial clinical symptom | No. of cases (n=7) | GPCI | Colonised catheters with blood cultures | S. aureus | Enterococcus spp. | K. pneumoniae | P. aeruginosa | E. coli | S. flexneri | S. paratyphi | H. influenzae | S. pneumoniae | S. pyogenes |
|-----|-------------------|--------------------------------|-------------------|------|----------------------------------------|---------|------------------|-------------|-------------|--------|------------|-------------|--------------|--------------|-------------|
| 19  | Fever under 2 days | C. difficile | 13 | 4 | 2 | 4 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 20  | Uncertain evolution | 22 | 5 | 2 | 7 | 1 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 21  | CHD with CCF diagnosis | 8 | 4 | 1 | 1 | 1 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 22  | COPD with autonomic neuropathy | 8 | 1 | 1 | 1 | 1 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 23  | Hypertensive disorders with complications | 13 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

Abbreviations: GPCI, Gram-positive cocci; CHD, chronic heart diseases; CCF, chronic inflammatory demyelinating polyneuropathy; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM, diabetes mellitus; GNB, gram-negative Bacilli.

and 11 yeasts. Isolation of GNBs was significantly higher ($p < 0.001$) than other groups of organisms. Within GNBs, *Klebsiella pneumoniae* (28.67%) was the dominant isolate obtained followed by *Acinetobacter baumannii* (22.47%) and *Pseudomonas aeruginosa* (14.45%). Eleven isolates of *Salmonella* spp. and one isolate of *Hemophilus influenzae* were also recovered. As a group, *Enterobacteriaceae* comprised half of all GNBs and 32.67% of total pathogens recovered. Among GPCs isolated, *S. aureus* (65.6%) was the dominant organism followed by *Enterococcus* spp. (15.38%) and *Streptococcus* spp. (11.8%). One-third of *Enterococcus* spp. isolates carried high-level aminoglycoside resistance (HLAR) genes. *Streptococcus pneumoniae* was recovered from seven bacteraemic patients. Of them, five were children younger than 9 years and two elderly older than 50 years. They were most likely severe cases of pneumococcal pneumonia causing bacteremia. Fifteen isolates of *Neisseria meningitidis* were recovered from the study. *Neisseria meningitidis* is a dreaded organism considering the capability of this organism to rapidly deteriorate relatively benign bacteremia into fulminant bacteremia and septic shock. Worth mentioning here is that all these cases were recovered during an outbreak between November 2008 and April 2009. Fungemia confirmed in 11 cases were mostly *Candida* spp. A single case of bacteremia by *Listeria monocytogenes* was also detected in a 2-year-old child who presented with acute gastroenteritis. Comparison of isolation rates of organisms on different days of incubation shows that chances of isolation of microbes within the second day of incubation was significantly ($p < 0.001$) higher than other days. The distribution of different isolates and groups recovered with each passing day of incubation is presented in Table 3. Significant isolation ($n = 242$, 36.7%) of organisms was obtained subsequent to turbidity detection on the second day. This was followed by higher detection of organisms on the third day ($n = 115$) and first day ($n = 89$) of incubation. A total of 331 isolates were recovered after detecting turbidity within the first 48 hours of aerobic incubation compared with 327 isolates of organisms which were recovered when incubation was continued beyond 48 hours till 7 days. Interestingly, both *K. pneumoniae* and *Escherichia coli* were consistently isolated better in significant proportions ($p < 0.001$) within the first 48 hours. Almost 73.8 and 80% isolates of *K. pneumoniae* and *E. coli*, respectively were detected within initial 48 hours. Concurrently, organisms which have significantly higher chances of recovery after initial 48 hours include *Candida* spp. ($p = 0.006$), *N. meningitidis* ($p = 0.017$), *Salmonella paratyphi* ($p = 0.044$), methicillin-resistant *S. aureus* (MRSA; $p < 0.001$), and methicillin-sensitive *S. aureus* (MSSA, $p = 0.024$). However, there was no significant difference between number of organisms isolated within or beyond 48 hours till 7 days. A comprehensive distribution frequency table shows different microbes with their growth patterns at 48 hours and at 7 days (Table 4). A comparison of data about the source of blood collection shows that *A. baumannii* and *K. pneumoniae* have significantly higher chances ($p < 0.05$) of isolation from central line catheters compared with peripheral venipuncture, while
chances of recovery of isolates from peripheral venipuncture were observed to be significantly higher for *Candida spp.*, *Enterococcus* (HLAR) spp., *Salmonella typhi*, *S. aureus*, *S. pneumoniae*, and other α and β hemolytic *Streptococcus* spp. A description about the same attribute is depicted in Table 5. The antibiotic susceptibility patterns for GPCs and GNBs were interpreted in accordance to prevalent CLSI guidelines4 and are represented in Tables 6 and 7, respectively.

Beta lactams proved least effective for GPCs with sensitivity lowest in penicillin (29.6%), ceftriaxone (45.6%), and cephalixin (52.6%). Erythromycin (31.7%) and rifampicin (48.6%) were largely ineffective. Relative sensitivity was highest for vancomycin (96.5%) and linezolid (90.2%). Even broad-spectrum antibiotics like chloramphenicol (78.5%) and tetracycline (74.8%) had good sensitivity against GPCs, especially MRSA. MSSA isolates uniformly showed very high sensitivities of >85% to ampicillin, gentamicin, amikacin, tetracycline, chloramphenicol, levofloxacin, and cefotaxime. *Streptococcus pneumoniae* showed an incredibly good sensitivity to amoxicillin (100%), cefepime (100%), and penicillin (80%).

*Neisseria meningitidis* isolates showed high sensitivity to penicillin (81.8%), azithromycin (75%), and ceftriaxone (66.67%). Interestingly, ciprofloxacin (41.67%) was only moderately effective. This is important because ciprofloxacin was the antimicrobial initially used to control the outbreak and also for the prophylaxis of contacts.

For GNBs, carbapenems were the most effective drugs (approximately >85% sensitivity). Cefoperazone-sulbactam (CFS, 83.1%) was the only other drug with sensitivity ≥80%. Quinolones were much less effective. Injectables like gentamicin (58%) and amikacin (63%) showed moderate sensitivity. Cephalosporins were mostly ineffective with sensitivities as low as 10%. *K. pneumoniae* and *E. coli* were highly susceptible to carbapenems (≥95% sensitivity) and CFS. *E. coli* additionally had better susceptibility (≥85%) against aminoglycosides too. Quinolones were moderately effective for *Klebsiella spp.* (60–75% sensitivity) but serve as very poor drugs to treat *E. coli* (15–20% sensitivity) BSIs. *A. baumannii* was most sensitive to carbapenems, CFS, moderately sensitive to quinolones, gentamicin, piperacillin–tazobactam. However, *Acinetobacter lwofii* documented better sensitivity to aminoglycosides and quinolones compared with carbapenems. *P. aeruginosa* isolated in 14.4% BSIs, was better managed with imipenem, CFS (>80% sensitivity), piperacillin–tazobactam, and levofloxacin, whereas typical antipseudomonal drugs like cefoperazone and ceftazidime were largely ineffective. Nonfermenting GNBs (other than *Acinetobacter* and *Pseudomonas spp.*) were highly susceptible to quinolones, meropenem, CFS, piperacillin–tazobactam, and chloramphenicol. Imipenem and gentamicin were drugs which were moderately sensitive

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**Table 2** Details of samples, pathogens, and contaminants from different wards

| Department               | Total samples | Negative culture samples | Organisms isolated (%) | Pathogen yield (%) | Contamination (%) |
|--------------------------|---------------|--------------------------|------------------------|-------------------|-------------------|
| Blood bank               | 181           | 153                      | 28                     | 15.47             | 11                | 6.08              | 17                | 9.39              |
| Cardiology               | 326           | 315                      | 11                     | 3.37              | 10                | 3.07              | 1                 | 0.31              |
| Medicine                 | 1,236         | 1,162                    | 74                     | 5.99              | 64                | 5.18              | 10                | 0.81              |
| CTVS                     | 147           | 127                      | 20                     | 13.61             | 19                | 12.93             | 1                 | 0.68              |
| Dialysis unit            | 8             | 6                        | 2                      | 25.00             | 2                 | 25.00             | 0                 | 0.00              |
| Otolaryngology           | 16            | 16                       | 0                      | 0.00              | 0                 | 0.00              | 0                 | 0.00              |
| General surgery          | 40            | 38                       | 2                      | 5.00              | 1                 | 2.50              | 1                 | 2.50              |
| Coronary care unit       | 172           | 155                      | 17                     | 9.88              | 17                | 9.88              | 0                 | 0.00              |
| ICU                      | 1,170         | 800                      | 370                    | 31.62             | 362               | 30.94             | 8                 | 0.68              |
| Neurology                | 60            | 59                       | 1                      | 1.67              | 1                 | 1.67              | 0                 | 0.00              |
| Obstetrics and gynecology| 143           | 134                      | 9                      | 6.29              | 8                 | 5.59              | 1                 | 0.70              |
| Oncology                 | 42            | 42                       | 0                      | 0.00              | 0                 | 0.00              | 0                 | 0.00              |
| Ophthalmology            | 2             | 1                        | 1                      | 50.00             | 0                 | 0.00              | 1                 | 50.0              |
| Orthopedics              | 45            | 39                       | 6                      | 13.33             | 5                 | 11.11             | 1                 | 2.22              |
| Pediatrics               | 911           | 836                      | 75                     | 8.23              | 65                | 7.14              | 10                | 1.10              |
| Pediatric ICU            | 1,239         | 1,122                    | 117                    | 9.44              | 98                | 7.91              | 19                | 1.53              |
| Private ward             | 84            | 79                       | 5                      | 5.95              | 4                 | 4.76              | 1                 | 1.19              |
| Urology                  | 45            | 43                       | 2                      | 4.44              | 2                 | 4.44              | 0                 | 0.00              |
| **Total**                | 5,867         | 5,127                    | 740                    | 12.61             | 669               | 11.40             | 71                | 1.21              |

**Abbreviations:** CTVS, cardiothoracic and vascular surgery; ICU, intensive care unit.
to these organisms. **Morganella, Salmonella,** and **Hemophilus spp.** isolates recovered were completely susceptible to usual drugs tested and no major antimicrobial resistance trends were observed in them.

### Discussion

BSI constitutes one of the major causes of morbidity and mortality. Definitive diagnosis is established by bacteriologic culture of blood samples to identify organisms and provide antimicrobial susceptibility. Numerous analyses have concluded that early treatment of bacteremic patients with an appropriate antimicrobial drug improves survival. There exists a strong relationship between delay in effective initiation of therapy and in-hospital mortality of septic shock. Each hour of delay in therapy initiation is associated with an average decrease in survival of 8%. Defining pathogen distribution and drug resistance patterns provides basis for empirical as well as definitive therapy. This present study is an attempt to analyze the bacterial

| Gram-positive cocci | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Total |
|---------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| *Staphylococcus aureus* (MSSA) | 5 | 20 | 13 | 12 | 4 | 7 | 6 | 67 |
| *Staphylococcus aureus* (MRSA) | 4 | 7 | 17 | 13 | 9 | 8 | 3 | 61 |
| CoNS | 0 | 3 | 2 | 1 | 0 | 1 | 0 | 7 |
| Enterococcus spp. | 3 | 9 | 4 | 0 | 0 | 3 | 1 | 20 |
| Enterococcus spp. (HLAR) | 2 | 4 | 0 | 1 | 1 | 0 | 2 | 10 |
| α-hemolytic Streptococcus spp. | 6 | 4 | 3 | 4 | 0 | 1 | 0 | 18 |
| β-hemolytic Streptococcus spp. | 0 | 2 | 2 | 0 | 0 | 0 | 1 | 5 |
| *Streptococcus pneumoniae* | 0 | 4 | 1 | 2 | 0 | 0 | 0 | 7 |
| Total | | | | | | | | 195 |

| Gram-negative bacilli | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Total |
|-----------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| *Escherichia coli* | 11 | 17 | 4 | 1 | 1 | 1 | 0 | 35 |
| *Klebsiella oxytoca* | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 5 |
| *Klebsiella pneumoniae* | 29 | 63 | 13 | 5 | 9 | 1 | 5 | 125 |
| Nonfermenter GNB | 3 | 11 | 1 | 6 | 6 | 4 | 4 | 35 |
| *Acinetobacter baumannii* | 14 | 39 | 12 | 12 | 9 | 2 | 10 | 98 |
| *Acinetobacter lwoffii* | 1 | 8 | 3 | 0 | 5 | 1 | 4 | 22 |
| Proteus spp. | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 3 |
| Proteus mirabilis | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| *Morganella morganii* | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 2 |
| Enterobacter spp. | 3 | 10 | 2 | 0 | 1 | 5 | 4 | 25 |
| *Citrobacter freundii* | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 3 |
| *Citrobacter diversus* | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 4 |
| *Pseudomonas spp.* | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 2 |
| *Pseudomonas aeruginosa* | 3 | 26 | 16 | 10 | 1 | 4 | 3 | 63 |
| *Salmonella paratyphi* | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 4 |
| *Salmonella enteritidis* | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| *Salmonella typhi* | 0 | 2 | 1 | 0 | 0 | 1 | 2 | 6 |
| *Hemophilus influenzae* | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Total | | | | | | | | 436 |

| Others | GRAND TOTAL |
|--------|--------------|
| *Neisseria meningitidis* | 1 | 2 | 8 | 0 | 1 | 1 | 2 | 15 |
| *Listeria monocytogenes* | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| *Candida spp.* | 0 | 1 | 4 | 0 | 4 | 2 | 0 | 11 |
| | **89** | **242** | **115** | **67** | **53** | **44** | **48** | **658** |

Abbreviations: CoNS, coagulase negative *Staphylococcus* spp.; GNB, gram-negative bacilli; HLAR, high-level aminoglycoside resistance; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*. 
profile of blood culture isolates, assess antimicrobial trends, correlate bacteremic source and their impact, and discuss other variables which may help us devise the best ways of managing BSIs.

This is a 5-year retrospective analysis of 5,867 blood samples received from clinically suspected bacteremia patients. A total of 658 recognized pathogens were recovered from 637 specimens. A total of 97% isolates had monomicrobial growths. The rate of isolation for blood culture pathogens was observed at 11.2%. This is significant considering it is a new tertiary level 450-bedded hospital apart from the fact that the laboratory uses conventional blood culture bottles with no provision for continuous monitoring of culture bottles. Besides, this rate of isolation is in consonance with many studies from India\textsuperscript{17-22} and abroad\textsuperscript{23-25}.

Although the mean age of bacteremic patients in the present study was 33.7 years, the highest number of cases of sepsis and shock were observed in children younger than 5 years age group as well as adults from 21 to 40 years age bracket. After the age of 40 years, the incidence of bacteremia cases shows a steady decline with every passing decade. Neonates, infants, and young children are particularly vulnerable to BSI owing to numerous risk factors like premature rupture of membrane, prolonged rupture, prematurity, recurrent urinary tract infection, poor maternal nutrition, low birthweight, birth asphyxia, congenital anomalies, and nascent/weak host immunity.\textsuperscript{10}

Almost 31% of all medical ICU patients suspected with bacteremia were confirmed by culture. This is understood as patients admitted in ICU are usually already severely ill who are put under continued and enhanced vigilant care. Since

### Table 4

| Pathogen                        | N   | %     | N   | %     | Z-Stat | p-Value |
|----------------------------------|-----|-------|-----|-------|--------|---------|
| Acinetobacter baumannii         | 53  | 16.01%| 45  | 13.76%| 0.81   | 0.417   |
| Acinetobacter hofii             | 9   | 2.72% | 13  | 3.98% | -0.9   | 0.37    |
| Candida spp.                    | 1   | 0.30% | 10  | 3.06% | -2.76  | 0.006   |
| Citrobacter spp.                | 4   | 1.21% | 3   | 0.92% | 0.36   | 0.716   |
| CoNS                            | 3   | 0.91% | 4   | 1.22% | -0.4   | 0.692   |
| Enterobacter spp.               | 13  | 3.93% | 12  | 3.67% | 0.17   | 0.863   |
| Enterococcus spp.               | 12  | 3.63% | 8   | 2.45% | 0.88   | 0.378   |
| Enterococcus spp. (HLAR)        | 6   | 1.81% | 4   | 1.22% | 0.62   | 0.536   |
| Escherichia coli                | 28  | 8.46% | 7   | 2.14% | 3.66   | <0.001  |
| Hemophilus influenzae           | 1   | 0.30% | 0   | 0.00% | -1     | 0.317   |
| Klebsiella oxytoca              | 4   | 1.21% | 1   | 0.31% | 1.34   | 0.18    |
| Klebsiella pneumoniae           | 92  | 27.79%| 33  | 10.09%| 5.95   | <0.001  |
| Listeria monocytogenes          | 0   | 0.00% | 1   | 0.31% | -1     | 0.317   |
| Morganella morganii             | 2   | 0.60% | 0   | 0.00% | 1.42   | 0.156   |
| Neisseria meningitidis          | 3   | 0.91% | 12  | 3.67% | -2.38  | 0.017   |
| Nonfermenter GNB                | 14  | 4.23% | 21  | 6.42% | 1.25   | 0.21    |
| Proteus spp.                    | 2   | 0.60% | 3   | 0.92% | -0.46  | 0.644   |
| Pseudomonas aeruginosa          | 29  | 8.76% | 34  | 10.40%| -0.71  | 0.476   |
| Pseudomonas spp.                | 0   | 0.00% | 2   | 0.61% | -1.42  | 0.156   |
| Salmonella enteritidis          | 1   | 0.30% | 0   | 0.00% | 1      | 0.317   |
| Salmonella paratyphi            | 0   | 0.00% | 4   | 1.22% | -2.01  | 0.044   |
| Salmonella Typhi                | 2   | 0.60% | 4   | 1.22% | -0.83  | 0.404   |
| Staphylococcus aureus (MRSA)    | 11  | 3.32% | 50  | 15.29%| -5.39  | <0.001  |
| Staphylococcus aureus (MSSA)    | 25  | 7.55% | 42  | 12.84%| -2.25  | 0.024   |
| Streptococcus pneumoniae        | 4   | 1.21% | 3   | 0.92% | 0.36   | 0.716   |
| α-hemolytic Streptococcus spp.  | 10  | 3.02% | 8   | 2.45% | 0.45   | 0.651   |
| β-hemolytic Streptococcus spp.  | 2   | 0.60% | 3   | 0.92% | -0.46  | 0.644   |
| **Total**                       | **331** | **100.00%** | **327** | **100.00%** | **658** |
they are better equipped to handle such serious infections, critical patients are referred to ICUs more frequently from other departments which explains the highest positivity yield of blood culture specimens received from medical ICU.

The rate of contamination observed (1.21%) is below the target level suggested by Hall and Lyman. This correlates well with other studies by Archibald et al. and Weinstein. These included mainly isolates of Bacillus spp., Corynebacterium spp., and Micrococcus spp.

Among 658 pathogens isolated, GNB were significantly the predominant organisms. This corresponds to findings documented by other similar studies. Klebsiella spp. as a dominant microbe causing BSIs was also reported by Roy et al. and Tariq. Within GPCs, S. aureus (65.6%) was the predominant pathogenic organism isolated. Pre-eminence of S. aureus as a bloodstream pathogen has been documented by numerous similar studies. If a comparison of methicillin sensitivity is attempted among S. aureus strains, 52.34% were MSSA and rest were MRSA. MRSA are notorious since these are resistant to action of a broad group of β-lactam antibiotics, which cannot be used for therapy. One-third (10/30) of Enterococcus

| Table 5 Comparative data about blood stream infections from central line vs. peripheral lines* |
|-----------------------------------------------|
| Line | Total | Significance test |
|------|-------|-------------------|
|      | Central | Peripheral | % | % | Z-Stat | p-Value |
| Acinetobacter baumannii | 26 | 27.96% | 59 | 14.94% | 85 | 2.6100 | 0.0090 |
| Acinetobacter lwoffi | 3 | 3.23% | 12 | 3.04% | 15 | 0.0900 | 0.9260 |
| Candida spp. | 0 | 0.00% | 5 | 1.27% | 5 | -2.2500 | 0.0240 |
| Citrobacter spp. | 0 | 0.00% | 2 | 0.51% | 2 | -1.4200 | 0.1560 |
| CoNS | 1 | 1.08% | 3 | 0.76% | 4 | 0.2700 | 0.7850 |
| Enterobacter spp. | 3 | 3.23% | 16 | 4.05% | 19 | -0.4000 | 0.692 |
| Enterococcus spp. | 3 | 3.23% | 12 | 3.04% | 15 | 0.0900 | 0.9260 |
| Enterococcus spp. (HLAR) | 0 | 0.00% | 6 | 1.52% | 6 | -2.4700 | 0.0140 |
| Escherichia coli | 3 | 3.23% | 23 | 5.82% | 26 | -1.1900 | 0.2330 |
| Hemophilus influenzae | 0 | 0.00% | 1 | 0.25% | 1 | -1.0000 | 0.3170 |
| Klebsiella oxytoca | 1 | 1.08% | 2 | 0.51% | 3 | 0.5000 | 0.4700 |
| Klebsiella pneumoniae | 31 | 33.33% | 68 | 17.22% | 99 | 3.0700 | 0.0020 |
| Listeria monocytogenes | 0 | 0.00% | 1 | 0.25% | 1 | -1.0000 | 0.3170 |
| Morganella morganii | 1 | 1.08% | 1 | 0.25% | 2 | 0.7500 | 0.4540 |
| Neisseria meningitidis | 0 | 0.00% | 1 | 0.25% | 1 | -1.0000 | 0.3170 |
| Nonfermenting gram-negative Bacilli | 4 | 4.30% | 29 | 7.34% | 33 | -1.2300 | 0.2200 |
| Proteus spp. | 2 | 2.15% | 3 | 0.76% | 5 | 0.8900 | 0.3750 |
| Pseudomonas aeruginosa | 11 | 11.83% | 39 | 9.87% | 50 | 0.5300 | 0.5940 |
| Pseudomonas spp. | 0 | 0.00% | 0 | 0.00% | 0 | NA |
| Salmonella enteritidis | 0 | 0.00% | 1 | 0.25% | 1 | -1.0000 | 0.3170 |
| Salmonella paratyphi | 0 | 0.00% | 3 | 0.76% | 3 | -1.7400 | 0.0820 |
| Salmonella typhi | 0 | 0.00% | 4 | 1.01% | 4 | -2.0100 | 0.0440 |
| Staphylococcus aureus (MRSA) | 2 | 2.15% | 38 | 9.62% | 40 | -3.5400 | < 0.001 |
| Staphylococcus aureus (MSSA) | 2 | 2.15% | 45 | 11.39% | 47 | -4.2100 | < 0.001 |
| Streptococcus pneumoniae | 0 | 0.00% | 5 | 1.27% | 5 | -2.2500 | 0.0240 |
| α-Hemolytic Streptococcus spp. | 0 | 0.00% | 11 | 2.78% | 11 | -3.3600 | 0.0010 |
| β-Hemolytic Streptococcus spp. | 0 | 0.00% | 5 | 1.27% | 5 | -2.2500 | 0.0240 |

Abbreviations: CoNS, coagulase negative Staphylococcus spp.; HLAR, high-level aminoglycoside resistance; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus.

*Data for 2011 to 2013 only.
spp. isolates carried genes for HLAR, where a combination of β-lactams and aminoglycosides may not work in vivo for therapy even though they may have been sensitive in vitro. Coagulase negative Staphylococcus (CoNS), long considered as contaminants in 1970s and 1980s are nowadays considered to be agents capable of causing bacteremia. They are mostly incriminated as nosocomial pathogens specifically in catheter-related BSI. In fact, two studies\textsuperscript{17,28} reported CoNS as the most common isolate causing BSIs in ICU patients. Seven such isolates of CoNS were recovered in the present study which fulfilled the criteria for sepsis.

All patients with fungemia were critical and under observation in different ICUs. Risk factors for fungemia include prolonged hospital stay, hyper alimentation, previous broad-spectrum antimicrobial therapy, and ulcerations in gastrointestinal mucosa. Prognosis in fungemia patients is relatively poor.\textsuperscript{29}

Frequency of isolation on different days of incubation within the 7-day incubation period reveals interesting trends. Most of the prominent isolates had a peak of detection on the second day of incubation which gradually tapered within the next 2 days. However, there was no significant difference observed between organisms isolated within the first 48 hours or beyond initial 48 hours.

An attempt was made to evaluate any correlation between the source of blood collection and the frequency of organisms isolated. The data for this information were available roughly for approximately 3 years (2011–2013) only. Chances of recovery of positive blood culture isolates from central line catheters were significantly higher in A. baumannii ($p<0.0029$) and K. pneumoniae ($p<0.002$). This is easily comprehensible since central venous catheters are kept in situ for longer durations compared with peripherally inserted catheters. These organisms are known to produce biofilm which improves their persistence within intravascular devices. Biofilm formation also imparts them the ability to reduce their metabolism rate, prevent antibiotic entry, and promote transfer of resistance plasmids.

### Table 6 Drug sensitivity profile of gram-positive strains

| Drug         | Overall GPC | Enterococcus spp. | Enterococcus spp. (HLAR) | MRSA | MSSA | Streptococcus pneumoniae | CoNS | α-Hemolytic Streptococcus spp. | Neisseria meningitidis |
|--------------|-------------|-------------------|--------------------------|------|-----|-------------------------|------|-----------------------------|-----------------------|
| Imipenem     | 85.7        | 90.9              | 60.0                     |      |     |                         |      |                             |                       |
| Ciprofloxacin| 57.3        | 58.3              | 0.0                      | 39.6 | 76.3| 50.0                    | 100.0| 41.7                        |                       |
| Penicillin   | 29.6        | 35.7              | 100.0                    | 10.3 | 100.0| 80.0                    | 33.3 | 77.8                        | 81.8                  |
| Ampicillin   | 71.4        | 68.4              | 50.0                     |      |     |                         |      |                             |                       |
| Vancomycin   | 96.5        | 100.0             | 87.5                     | 96.3 | 100.0| 100.0                   | 100.0| 100.0                       |                       |
| Linezolid    | 90.2        | 90.0              | 100.0                    | 96.3 |     |                         |      |                             |                       |
| Gentamicin   | 79.8        | 86.7              | 0.0                      | 65.3 | 97.9| 80.0                    | 80.0 |                             |                       |
| Tetracycline | 74.8        | 42.9              | 20.0                     | 83.3 | 87.2| 50.0                    | 25.0 | 100.0                       |                       |
| Amikacin     | 68.9        | 0.0               | 0.0                      | 85.7 | 100.0|                         |      |                             |                       |
| Levofloxacin | 33.3        | 0.0               | 0.0                      | 60.0 | 91.3| 50.0                    | 100.0|                             |                       |
| Cefotaxime   | 67.8        | 100.0             | 0.0                      | 23.1 | 90.0| 75.0                    | 83.3 | 83.3                        |                       |
| Chloramphenicol | 78.5      | 50.0              | 70.6                     | 88.5 | 60.0| 50.0                    | 100.0| 50.0                        |                       |
| Ofloxacin    | 61.4        |                  | 46.8                     | 86.1 |     |                         |      |                             |                       |
| Netilmicin   | 85.9        |                  | 81.3                     | 97.1 |     |                         |      |                             |                       |
| Rifampicin   | 48.6        |                  | 33.3                     | 0.0  | 0.0 | 100.0                   | 50.0 |                             |                       |
| Cephalexin   | 52.6        |                  | 10.5                     | 100.0|     |                         |      |                             |                       |
| Clindamycin  |            |                  | 50.0                     |      |     |                         |      |                             |                       |
| Erythromycin | 31.7        |                  | 7.9                      | 47.1 | 40.0| 100.0                   |      |                             |                       |
| Ceftriaxone  | 45.3        |                  | 9.7                      | 73.5 | 50.0| 50.0                    | 66.7 |                             |                       |
| Cefepime     | 0.0         |                  | 75.0                     | 100.0|     |                         |      |                             |                       |
| Azithromycin |            |                  | 75.0                     |      |     |                         |      |                             |                       |
| Amoxicillin  |            |                  | 100.0                    | 100.0|     |                         |      |                             |                       |
| Norfloxacin  |            |                  | 100.0                    |      |     |                         |      |                             |                       |

Abbreviations: CoNS, coagulase negative Staphylococcus spp.; GPC, gram-positive Cocci; HLAR, high-level aminoglycoside resistance; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus.
| Organism                      | Ceftriaxone | Ceftazidime | Cefoperazone | Piperacillin-tazobactam | Imipenem | Meropenem | Levofloxacin | Ciprofloxacin | Ofloxacin | Ampicillin | Gentamicin | Amikacin | Chloramphenicol | Colistin | Cefepime | Overall GNB |
|------------------------------|-------------|-------------|--------------|--------------------------|-----------|-----------|--------------|---------------|------------|------------|------------|-----------|-----------------|----------|----------|-------------|
| Overall GNB                  | 23.8        | 19.2        | 83.1         | 30.7                     | 96.6      | 86.9      | 46.6         | 59.3          | 50.0      | 63.0       | 63.0      | 60.0     | 60.0             | 60.0     | 60.0     | 60.0        |
| **Acinetobacter baumannii**  | 19.6        | 12.6        | 35.3         | 78.4                     | 100.0     | 65.7      | 58.6         | 60.8          | 64.9      | 43.8       | 43.8      | 40.5     | 40.5             | 40.5     | 40.5     | 40.5        |
| **Acinetobacter lwoffii**    | 20.0        | 23.5        | 66.7         | 100.0                    | 25.0      | 66.2      | 68.2         | 69.3          | 29.3      | 25.0       | 25.0      | 22.5     | 22.5             | 22.5     | 22.5     | 22.5        |
| **Escherichia coli**         | 20.0        | 21.9        | 92.0         | 0.0                      | 14.4      | 97.4      | 73.8         | 66.7          | 66.7      | 66.7       | 66.7      | 66.7     | 39.3             | 39.3     | 39.3     | 39.3        |
| **Klebsiella pneumoniae**    | 10.6        | 11.8        | 73.8         | 100.0                    | 11.8      | 73.8      | 98.4         | 92.8          | 79.3      | 79.3       | 79.3      | 79.3     | 79.3             | 79.3     | 79.3     | 79.3        |
| **Klebsiella oxytoca**       | 0.0         | 0.0         | 100.0        | 0.0                      | 0.0       | 0.0       | 66.7         | 75.0          | 75.0      | 75.0       | 75.0      | 75.0     | 50.0             | 50.0     | 50.0     | 50.0        |
| **Pseudomonas aeruginosa**   | 23.3        | 26.8        | 80.8         | 80.8                     | 50.0      | 52.8      | 66.9         | 83.9          | 0.0       | 0.0        | 0.0       | 0.0      | 0.0              | 0.0      | 0.0      | 0.0          |
| **Citrobacter freundii**     | 21.3        | 26.8        | 80.8         | 80.8                     | 50.0      | 52.8      | 66.9         | 83.9          | 0.0       | 0.0        | 0.0       | 0.0      | 0.0              | 0.0      | 0.0      | 0.0          |
| **Proteus mirabilis**        | 31.0        | 26.6        | 100.0        | 100.0                    | 25.0      | 72.0      | 96.0         | 96.0          | 96.0      | 96.0       | 96.0      | 96.0     | 96.0             | 96.0     | 96.0     | 96.0        |
| **Citrobacter koseri**       | 30.0        | 26.6        | 100.0        | 100.0                    | 25.0      | 72.0      | 96.0         | 96.0          | 96.0      | 96.0       | 96.0      | 96.0     | 96.0             | 96.0     | 96.0     | 96.0        |
| **Proteus vulgaris**         | 31.0        | 26.6        | 100.0        | 100.0                    | 25.0      | 72.0      | 96.0         | 96.0          | 96.0      | 96.0       | 96.0      | 96.0     | 96.0             | 96.0     | 96.0     | 96.0        |
| **Proteus morganii**         | 0.0         | 0.0         | 100.0        | 100.0                    | 0.0       | 0.0       | 66.7         | 75.0          | 75.0      | 75.0       | 75.0      | 75.0     | 50.0             | 50.0     | 50.0     | 50.0        |
| **Escherichia coli**         | 100.0       | 100.0       | 100.0        | 100.0                    | 100.0     | 100.0     | 100.0        | 100.0         | 100.0     | 100.0      | 100.0     | 100.0    | 100.0            | 100.0    | 100.0    | 100.0       |
Such foci of bacteria can lead to sustained bacteremia if not dislodged in time, or catheter being removed. Contamination rates were similar for both sources of blood collection at approximately 1%. A study by Beutz et al\textsuperscript{30} claims sensitivity of 92.5 and 95.9% for blood cultures drawn from central vein catheters and peripheral venipuncture, respectively. Even though the negative predictive values of both sources of blood collection was > 95%, positive predictive values of blood cultures were low at 58.3 and 66.7%, respectively.

Beta lactam drugs are rapidly becoming ineffective for treating BSIs because of its indiscriminate and non-judicious usage. Vancomycin, linezolid, aminoglycosides, and broad-spectrum drugs like chloramphenicol and tetracycline are the most reliable treatment options for GPCs, whereas carbapenems, CFS, aminoglycosides, and quinolones are remaining treatment options for GNBs. Aminoglycosides are good options for \textit{E. coli} but not \textit{K. pneumoniae} BSIs, while the opposite is true for quinolones. Cephalosporins and typical antipseudomonal drugs failed terribly in controlling concerning BSIs. Hence rationalized drug therapy is the call of the hour and therefore, studies of this type are quite warranted. De-escalation of high-end antimicrobials once actual sensitivity pattern is known contributes to reduction of antimicrobial pressure. Poor infection control practices and inappropriate use of antibiotics are main driving forces for the spread of resistant organisms. Aggressive measures like routine surveillance cultures to identify and isolate carriers, control of environmental sources, antibiotic restriction, antibiotic recycling, recommending combination therapy, implementing proper aseptic techniques, performing hand hygiene, maintaining robust infection control practices, and periodical assessment of antimicrobial policy will go a long way in preventing emergence of resistant organisms.

\section*{Conclusion}
Successful treatment of sepsis cases hinges on early diagnosis and proper antimicrobial therapy. The choice of antibiotics is based upon local knowledge of bacteriological profile and antimicrobial sensitivity patterns. The serious nature of the BSIs underscores the importance of periodic epidemiological surveillance studies such as the current one to provide useful insights for rational policy development and management of similar infections.

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