ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ALARMING INCREASE IN DRUG RESISTANCE AMONGST THE BACTERIAL AND FUNGAL ISOLATES OF BLOOD CULTURE IN A TERTIARY CARE CENTRE OF NORTH INDIA : TIME TO SWITCH FOR ANTIBIOTIC HOLIDAY

Microbiology

Nidhi Negi MD Microbiology, Department of Microbiology SGRRIM&HS Patel Nagar Dehradun Uttrakhand.

Bipin Chandra pokhriyal MD student, Department of Microbiology SGRRIM&HS Patel Nagar Dehradun Uttrakhand.

Iva chandola* MD Microbiology, Department of Microbiology SGRRIM&HS Patel Nagar Dehradun Uttrakhand. *Corresponding Author

V. K. Kataria MD Microbiology, Professor &Head, Department of Microbiology SGRRIM&HS Patel Nagar Dehradun Uttrakhand

ABSTRACT

Background: Bloodstream infections (BSI) are an important cause of morbidity and mortality both in developed and developing part of world. They constitute an important part of health care associated infections and require adequate and early antimicrobial therapy even before the blood culture reports are available in laboratory. Therefore it has become mandatory to analyse the prevalent microorganisms responsible for blood stream infections as well as the pattern of antimicrobial drug resistance.

Methods: A total of 3931 blood culture samples were included in the study & tested for their positivity by bac T alert 3d system and antimicrobial susceptibility by VITEK 2.

Results: A total of 520 blood culture samples came out to be positive. Isolates consisted of Escherichia coli (21%) , Candida spp (18%), Acinetobacter baumanii (16%), Salmonella Typhi (13%), Klebsiella pneumoniae (12%), Pseudomonas aeruginosa (9%), Enterococcus spp (7%) and Staphylococcus aureus (4%). Antibacterial as well as antifungal susceptibility pattern was analysed for bacterial and fungal isolates respectively.

Conclusion: there is increasing prevalence of Gram negative bacteremia in hospital settings. Inspite of the advances in antimicrobial therapy, the drug resistance is prevailing rampantly especially for the polypeptide group of drugs like colistin.

KEYWORDS

bloodstream infections (BSI), *Escherichia coli,* drug resistance

INTRODUCTION :

Bloodstream infections (BSI) constitute a major part of infectious disease morbidity and mortality worldwide. Since positive blood culture is a must to establish the cause for the presence of infections, there are a number of criteria which must be looked upon for establishment of this entity. Hospital-onset bloodstream infections are those bloodstream infections which are first identified (culture drawn) >48 h after hospital admission and within 48 h following hospital discharge.[1]

Community-onset BSIs are those bloodstream infections that occur in out patients or are first identified < 48 h after admission to hospital, and they may be subclassified further as health care associated, when they occur in patients with significant prior health care exposure, or community associated, in other cases.[2]

The most common causes of community-onset BSI include *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*. Antimicrobial-resistant organisms, including methicillin-resistant *Staphylococcus aureus* and extended-spectrum-lactamase/metallo-lactamase/carbapenemase-producing *Enterobacteriaceae*, have emerged as important etiologies of community-onset BSI. [3]

Earlier blood stream infection due to resistant microorganisms was more common among patients admitted to intensive care units [4,5]. Although in past few years there is emergence of multi drug resistant organisms arising in the community as well. Examples include community-onset MRSA [6,7] and ESBL [8], metallo β lactamase, and other carbapenemase producing *Enterobacteriaceae* . [9]

MATERIAL METHODS

This study was carried out prospectively for a period of one year ranging from June 2017 to May 2018, from the blood culture samples of patients admitted in different wards and ICUs of Sri Guru Ram Rai Institute of Medical and Health Sciences Dehradun. The study was carried out using automated blood culture (bac T alert 3D) system and drug susceptibility testing (Vitek II) in the clinical microbiology laboratory located in central laboratory of hospital. A total of 3931 blood culture samples were included in the study & tested for their positivity.

Sample collection

Samples were collected by nurses from the patients after disinfection of vein puncture site with 70% alcohol. Subject included in the present study were diagnosed as a case of one of the following; meningitis, bacterial pneumonia, urinary tract infection, pyogenic infection, bacteremia/septicemia or diarrheal diseases.

A paired set of blood culture was done for pediatrics as well as adults. 2-3ml of blood was inoculated in 30ml BacT/Alert blood culture bottle for paediatrics and 4-5ml blood was inoculated in 30ml BacT/Alert blood culture bottle for adults. These bottles were incubated in BacT/Alert automated system. The bottles which showed positive signal for growth were removed from the automated system and subculture was done on blood agar and MacConkey's agar. Smears from the colony of different agar plates were prepared and stained with Gram stain to identify the growth (i.e. Gram positive or Gram negative bacteria). Then the growth of the bacteria was run on VITEK II automated system for identification of the organism and Antibiotic Sensitivity. If there is no growth of bacteria within five days of inoculation of blood sample into BacT/Alert blood culture bottle then the sample is considered to be negative.

RESULTS

Table 1: Bacteria and yeast isolated from blood culture samples (n=520)

Isolate	Positive (%)
Escherichia coli	(108/520) 21%
Candida species	(82/520) 16%
Acinetobacter baumanii	(82/520) 16%
Salmonella species	(67/520) 13%
Klebsiella pneumoniae	(52 /520) 10%
Pseudomonas aeruginosa	(50/520) 9%
Staphylococcus aureus	(26/520) 5%
Enterococcus faecalis	(21/520) 4%
Enterobacter aerogenes	(21/520) 4%
Coagulase negative Staphylococcus	(11/520) 2%

As per table 1, the most common isolate obtained in the present study is *E.coli* (21%), followed by *Candida* spp (16%) & *Acinetobacter baumanii* (16%). Least common isolates were *Staphylococcus aureus*

(4%), Enterobacter aerogenes (4%) and Coagulase negative Staphylococcus (2%).

Table 2a: Age wise & Sex wise distribution of positive and negative blood cultures

Parameter	Blood culture results n=3931		
	Positive	Negative	Total
Male	325 (8.2%)	1876 (47.7%)	2201
Female	195 (4.9%)	1530 (38.9%)	1725
Age	Blood culture results		
<5 yrs	242 (6.1%)	1256 (31.9%)	1498
5-20yrs	116 (2.9%)	1027 (26.1%)	1143
>20yrs	162 (4.1%)	1123 (28.5%)	1285

According to table 2, the percentage of positivity was more in males (8.2%) as compared to females (4.9%). When considering age wise the maximum positivity was seen in age group < 5yrs (6.1%) followed by age group >20yrs (4.1%).

Table 2b : Ward wise distribution of sample

Name of ward/location	Percentage of total sample received
NICU+PICU	34%
SICU	17%
MEDICINE	16%
MICU &MHDU	14%
PEDIATRICS	13%
OBSTETRICS & GYNAE	4%
SURGERY	2%

As per table 2b, majority of sample which we received was from NICU &PICU (34%).

Table 3: Antimicrobial Susceptibility of Gram negative bacilli.

Name of organism	Ciprofloxacin	Cotrimoxazole	Amikacin	Imipenem	Meropenem	Pip taz	Cefuroxime	Cef.axetil	cefepime	colistin	ceftriaxone
Escherichia Coli	30%	25%	57%	85%	85%	75%	44%	44%	60%	83%	45%
Klebsiella pneumoniae	14%	22%	32%	39%	39%	29%	20%	20%	46%	95%	22%
Acinetobacter baumanii	29%	44%	40%	41%	40%	18%	44%	44%	-	98%	47%
Pseudomonas aeruginosa	48%	61%	30%	46%	66%	39%	14%	14%	57%	65%	50%
Salmonella Typhi	73%	97%	-	98	98%	99%	94%	94%	94%	99%	99%

According to table 3, majority of the isolates of *E.coli* were sensitive to imipenem and meropenem (85%) and piperacillin tazobactam (75%). The resistance to polypeptide group of drugs has also started appearing, only 83% of the isolates were sensitive for it, followed by decreased sensitivity to cephalosporins ranging from 44% to 60%. For aminoglycoside group of drugs i.e amikacin it was (57%) and least susceptibility was seen for ciprofloxacin (30%) and cotrimoxazole (25%) .

When looking at antimicrobial susceptibility pattern of another member of family Enterobacteriaceae i.e *Klebsiella pneumoniae*, larger percentage of susceptibity is seen for colistin (95%) only. Decreasing susceptibility pattern was seen for rest of other classes of drugs . For cefepime it was 46%, for carbapenem group of drugs like Imipenem and meropenem it was (39%). Lowest susceptibility rates were seen for amikacin (32%), piperacillin– tazobactam (29%), ceftriaxone and cotrimoxazole (22%), cefuroxime (20%) and ciprofloxacin (14%).

Talking about the drug susceptibility pattern of nonfermenters, for *Acinetobacter baumanii* maximum susceptibility was seen for colistin (98%), followed by ceftriaxone (47%), cefuroxime and cotrimoxazole (44%), Imipenem (41%), meropenem and amikacin (40%). Least susceptibility was noted for ciprofloxacin (29%).

For *Pseudomonas aeruginosa*, maximum susceptibility was seen for colistin (67%) which shows increasing resistance towards polypeptide group of drugs, followed by meropenem (66%), cotrimoxazole (61%), cefepime (57%), ceftriaxone (50%), Imipenem (46%), amikacin (29%), ciprofloxacin (29%). Least susceptibility was noted for cefuroxime (14%).

In the present study majority isolates of *Salmonella* Typhi were susceptible for ceftriaxone & piperacillin –tazobactam (99%), followed by carbapenem group of drugs (98%), cotrimoxazole (97%), cefuroxime (94%) and ciprofloxacin (73%).

Table 4: Antifungal Susceptibility of yeast isolated from blood culture.

Name of Antimicrobial	Candida species (Sensitivity in percentage)
Caspofungin	95%
Voriconazole	95%
Micafungin	95%
Amphotericin B	90%
Flucytosine	90%

As per table 4 the maximum percentage of sensitivity was seen for Caspofungin, Voriconazole & micafungin (95%).

Table5: Antimicrobial Susceptibility of Gram positive cocci isolated from blood culture.

Name of antibiotic	Name of Gram positive organism		
	Staphylococcus aureus	*CoNS	Enterococcus faecalis
Benzyl penicillin	0%	06%	0%
Ciprofloxacin	55%	40%	20%
Methicillin	60%	50%	-
Linezolid	92%	99%	92%
Vancomycin	85%	100%	100%
Erythromycin	25%	56%	08%
Clindamycin	45%	50%	-
Tigecycline	99%	95%	100%

*coagulase negative *Staphylococcus*

According to table 5, majority isolates of *Staphylococcus aureus* were susceptible for tigecycline (99%), Linezolid (92%) and vancomycin (85%). For CoNS, all isolates were susceptible for vancomycin (100%) and majority were susceptible for tigecycline (99%). For *Enterococcus faecalis* all isolates were susceptible for vancomycin and tigecycline (100%).

DISCUSSION :

A total of 3931 blood culture samples were included in the study out of which 520 blood culture samples came out to be positive (13.23%) which is higher than the studies conducted by Gohel et al from Gujrat (9.2%), Mehta et al from chandigarh (9%) but lower than katyal et al (24.86%), Wasihun et al (28%). The varying rates of positivity may be due to different environmental regions as well as different type of antimicrobials drugs given.

Moreover as ours is a tertiary care hospital the patients usually come after referral from primary and secondary care hospitals, private nursing homes where patients have already received antimicrobial drugs. Also sometimes when the patient's condition is critical at the time of admission patient so antimicrobial drugs are given at the time of admission before blood culture is taken.

Percentage of total sample which we received in our hospital was more from children age < 5yrs of age group and relatively higher in males as compared to females, which matches with the study conducted by

Saleem et al from Puducherry in 2016.

The incidence of Gram negative organisms in our study was higher as compared to Gram positive organisms which is similar to other studies conducted in India [13,15,16,17] but not supported by studies done at some places [10,12]. Majority of the iolates in our study were multidrug resistant as comapared to other studies as well. [12]

Predominant isolate obtained in our study was *E.coli* (21%) as reported in other studies also (15,16) while in some studies *Acinetobacter* was the most common isolate [13,17], some have reported *Staphylocooci* as the predominant isolate. [10,12] In some studies *Pseudomonas* has been reported as the most common isolate followed by *E.coli* (18). Higher prevalence of *E.coli* followed by *Candida* species & *Acinetobacter baumanii* in our hospital settings can be attributed to the fact that majority of sample which we received was from ICU settings especially NICU and PICU as supported by other studies also. [20,21]

Amongst the Enterobacteriaceae isolates a good antimicrobial susceptibility was shown against colistin & carbapenems which is comparable to studies done by swamy MA et al. increasing resistance against beta lactam group of drugs, flouroquinolones and cotrimoxazole may be due to their irrational and empirical use in many infections as noted by other workers also. [12, 19]

Amongst the Gram positive isolates Staphylococcus aureus was the most common isolate and Tigecycline, vancomycin and linezolid were the most effective drugs for Gram positive supported by other studies also. [14,23] For candida species the most effective drugs were caspofungin, voriconazole and micafungin as proved by other studies also. [24]

CONCLUSION

The present study represents the distribution of bacterial and fungal isolates from a tertiary care centre of North India, which has got a great role in management of patients as well as starting therapy empirically when the condition is critical. As the drugs left in pipeline are only a few, authors recommend that strict hospital antibiotic policy should be prepared and implemented and irrational use of drugs in name of empirical treatment should be stopped.

REFERENCES :

1. Filice GA,Van Etta LL, Darby CP, Fraser DW. Bacteremia in Charleston County, South Carolina. Am. J. Epidemiol. 1986; 123:128-136.
2. Morin CA, Hadler JL. Population-based incidence and characteristics of community-onset Staphylococcus aureus infections with bacteremia in 4 metropolitan Connecticut areas, 1998. J. Infect. Dis. 2001; 184(8):1029-34.
3. Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, et al. Health care-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections.Ann.Intern.Med.2002; 137(10):791-97.
4. Tabah A, Koulenti D, Laupland K, Misset B, Valles J, Bruzzi de Carvalho F, et al. Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study. Intensive Care Med.2012; 38(12):1930-45.
5. Timsit JF, Laupland KB. Update on bloodstream infections in ICUs. Curr. Opin. Crit. Care. 2012; 18(5):479- 86.
6. Chuang YY, Huang YC. Molecular epidemiology of community associated meticillin-resistant Staphylococcus aureus in Asia. Lancet Infect. Dis. 2013; 13(8):698-708.
7. David MZ, Daum RS. Community-associated methicillinresistant Staphylococcus aureus: epidemiology and clinical consequences of an emerging epidemic. Clin. Microbiol Rev. 2010; 23(3):616-87.
8. Pitout JD, Laupland KB. Extended-spectrum beta-lactamase producing Enterobacteriaceae: an emerging public-health concern. Lancet Infect. Dis. 2008; 8(3):159-66.
9. Nordmann P. Carbapenemase-producing Enterobacteriaceae: overview of a major public health challenge. Med. Mal. Infect. 2014: 44(2):51-56.
10. Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological Profile and Drug Resistance Patterns of Blood Culture Isolates in a Tertiary Care Nephrourology Teaching Institute. Biomed Res Int. 2014; 2014:1-5.
11. Mehta M, Dutta P, Gupta V. Antimicrobial Susceptibility Pattern of Blood Isolates from a Teaching Hospital in North India. Jpn. J. Infect. Dis. 2005; 58:174-76.
12. Katyal A, Singh D, Sharama M, Chaudharu U. Bacteriological Profile and Antibiogram of Aerobic Blood Culture Isolates from Intensive Care Units in a Teaching Tertiary Care Hospital. J Health Sci Res. 2018; 9(1):6-10.
13. 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; 4:1-7.
14. Saleem M, Gopal R, Mangaiyarkarsi1 T, Sunil S, Krishnapriya J and Nagma R. Profile of Bacterial Isolates from Blood Cultures and their Antimicrobial Susceptibility Pattern Int.J.Curr.Microbiol.App.Sci 2016; 5(11): 86-91.
15. Uslan DZ, Crane SJ, Steckelberg JM, Cockerill FR, Sauver JL, Wilson WR, et al. Age- and sex-associated trends in bloodstream infection: a population-based study in Olmsted County, Minnesota. Arch Intern Med. 2007; 167(8): 834-39.
16. Valles J, Rello J, Ochagavia A, Garnacho J, Alcala MA. Community-acquired bloodstream infection in critically ill adult patients: impact of shock and inappropriate antibiotic therapy on survival. Chest. 2003; 123(5):1615-24.
17. Barati M, Taher MT, Abasi R, Zadeh MM, Barati M, Shamshiri AR. Bacteriological profile and antimicrobial resistance of blood culture isolates. Iranian Journal of Clinical Infectious Diseases.2009; 4(2):87-95.
18. Kholoujini M, Karami P, Khaledi A, Neshani A, Matin P, Alikhani MY. Identification of Pathogenic Bacteria in Blood Cultures and Susceptibility Testing of Isolates with Various Antibiotics. Avicenna J Clin Microb Infec. 2016; 3(3):1-5.
19. Swamy MA, Golia S, Varania N. Spectrum of aerobic bacteria and their antimicrobial pattern in blood stream infections of hospitalised patients: a retrospective study.Int.J.Res.Med.Sci.2018;oct;6(10):3298-3302
21 Chang MR, Correia FP, Costa LC, Xavier PC, Palhares DB, Taira DL, et al. Candida bloodstream infection: data from a teaching hospital in Mato Grosso do Sul, Brazil. Rev Inst Med Trop Sao Paulo. 2008; 50(5):265-8.
22. Akeme Yamamoto AC, de Paula CR, Dias LB, Tadano T, Martins ER, Amadio JV, et al. Epidemiological and clinical characteristics of nosocomial candidiasis in university hospitals in Cuiabá--Mato Grosso, Brazil. Rev Iberoam Micol. 2012; 29(3):164-8
23 Meenakshi Kante, P. Uma, Maria Sindhura John and M. Prasad Naidu. 2014. Bacterial profile of blood stream infections and antibiotic susceptibility pattern of isolates. Int. J. Curr. Microbiol. App. Sci., 3(12): 222-233.
24 Epidemiology and antifungal susceptibility of Candida species in a tertiary care hospital, Kolkata, India Bhattacharjee P* NH-Rabindranath Tagore International Institute of Cardiac Sciences 124, E. M. Bypass, Mukundapur, Kolkata,700099-West Bengal, India