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ETIOLOGICAL AGENTS AND PATTERN OF ANTIMICROBIAL DRUG RESISTANCE IN BLOOD STREAM INFECTIONS IN A TERTIARY CARE TEACHING HOSPITAL OF RURAL GUJARAT.

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Abstract
blood stream infection is a common clinical condition affecting neonates to geriatric patients. Present study was undertaken to identify and characterize different blood pathogens to assess Antimicrobial resistance pattern and to find out factors associated with blood stream infection. *Methods*: - observational study was carried out during January – 2017 to January – 2018 in a tertiary care teaching hospital. Relevant demographic and clinical details were collected. Identification and antimicrobial susceptibility testing of blood pathogen was done by using VITEK2 – compact microbiology systems.*Results:* - In one year duration 156 positive blood sample analysed for bacterial and fungal infection. Blood stream infection were more frequent in males 97(62.17%) and its incidence varied with age. Affecting the elderly and neonates patients more i.e. 48(30.76%). E coli 23(14.7%), S.aureus and K.pneumoniae were similar i.e. 17(10.8%) was the most common pathogen implicated in BSI. Distribution of sample from intensive care units and various wards i.e. E coli 13(15.52%), 10(43.47%). S.aureus 8(47.05%), 9(52.94%), K.pneumoniae 12(70.58%), 5(29.41). Resistance to antimicrobials was common but highly variable in our study.*Interpretation & conclusion*: - E.coli, S.aureus and K.pneumoniae was the most common etiological agent of BSI. Distribution of blood sample from intensive care units was more frequent than various wards.

Key Words: Blood stream infection, antimicrobial resistance, Prevalence.

Introduction

Blood stream infection remains one of the most important causes of morbidity and mortality all over the world. About 200,000 cases of bacteraemia occur annually with mortality rates ranging from 20 – 50 % worldwide. In developing countries like India septicaemia is an important cause of illness and death.[1]

Blood stream infection are one of the main causes of death in hospitalized patients with mortality rates ranging from 30 to 70%.Blood culture is the most important procedure to detect systemic infection due to bacteria a wide range of organisms have been implicated in the etiology of blood stream infection.These include Escherichiacoli, Klebsiellapneumoniae, Pseudomonasaeruginosa, Salmonellatyphi andAcinetobacter spp, among Gram-negative bacteria and Staphylococcusaureus, Coagulase negative Staphylococci (CoNS), Enterococci and alpha hemolyticStreptococciamong Gram-positive bacteria.[2]Blood stream infection is potentially life threatening condition and requires rapid identification with the antibiotic susceptibility pattern of the causative agents in order to facilitate specific antimicrobial therapy.[3]

Due to a number of determinants, not limited to changing patients' demographics, shifts in health care delivery models, and increasing globalization, the epidemiology of bloodstream infection has been changing in recent decades.In addition,antimicrobial-resistant organisms, most notably methicillin-resistant *Staphylooccusaureus* (MRSA) and extended-spectrum β-lactamase (ESBL)/metallo-β-lactamase-producing *Enterobacteriaceae*, have emerged as important etiologies of bloodstream infections. At present there is no specific data available regarding bloodstream infection rates, etiological agents and pattern of antimicrobial drug resistance in patients coming to Shree Krishna Hospital, and prompted us to undertake this study.

Methods

This Observational study was conducted in a 610-beded tertiary care teaching hospital during the period of January 2017 to January 2018 after approval of the Institutional Ethics Committee (IEC). Samples were

received from indoor and outdoor patients with clinical symptoms of Blood stream Infection. Relevant demographic and clinical data of each patient was collected in terms of type of infection, duration of hospital-stay, associated factors and outcome till discharge in a predesigned proforma.

Sample Collection and Processing

The blood culture bottle's were received and accepted in the Laboratory as per the laid down acceptance and rejection criteria. Patient's details were entered in to the Hospital information system and sample was processed immediately once received at the Microbiology Laboratory. Gram staining, and sub culture of blood sample was done as per the standard operating protocols.[4] The isolates were identified by VITEK®2compact fully automated microbiological system (bio Merieux, france) by using GN, GP and YST cards.

Antimicrobial Susceptibility Testing (AST)

Minimum inhibitory concentration (MIC) of the antimicrobials was done with VITEK®2Compact fully automated microbiological system (bio Meriux, France), by using AST-N281, AST-N280, AST-P628, and YST-YS 07 cards. Manual AST using Kirby-Bauer disk diffusion method on Muller-Hinton agar medium (Hi-media Laboratories, Mumbai) was done for those agents not covered in AST cards of VITEK®2system. The results were interpreted according to the clinical laboratory standards institute guidelines.[5]

Reference strains E. coli ATCC 25922, P. aeruginosa ATCC 27853, E.fecalis ATCC 29212, S. aureus ATCC29123 and Candida krusei ATCC 6258 were used as a positive control. The results were analysed using Statistical Package for Social Science (SPSS) version14.0 for Windows.

Result

During the study period a total 156 positive blood culture were found from bacterial / fungal pathogens.
Majority of the patients who had blood stream infection <1.year &>71 years of age. i.e. 24(15.38%) each followed by 22(14.10%) in age group of 51-60 years and 20(12.82%) in age group of 61-70 years.

Majority of samples 97(62.175) were male and 56(37.82%) were female. Among the 156 culture positive patients the major leading blood pathogens were E.coli 14.7% (n=23), K.pneumoniae 10.8% (n=17), S.aureus 10.8% (n=17), E.faecium 10.2% (n=16), S.hemolyticus 7% (n=11) all accounting for around 54% (n=84) of total isolates. Gram negative organism represented 51.28% (n=80) of total blood pathogens fallowed gram positive organism represented 44.23% (n=69) and similar rate of candida species i.e. 4.48% (n=1). (Table-1)
Majority of E.coli were isolated from blood samples received from MICU 8(34.7%) followed by SICU 3(13%) other leading organisms K.pneumoniae and S.aureus were isolated predominantly from NICU (29.4%) and MICU 6(35.2%) respectively.

Resistance of E.coli to ampicillin and ceftriaxone was 95.45% and 90.9% respectively while quinolones was 75% and colistin, tigecycline, amilacin, carbapenems, and nitrofurantain showed low resistance in the range of 0% to 17% K.pneumoniae showed 93.3% and 92.8% resistance ceftazidime and cefotaxime respectively. Resistance for A.bumanii ranged from 0% to 100% and for S.typhi ranged was 100%, 50% and 20% resistant to Nalidixic acid, Ciprofloxacin and Chloramphenicol.(Table-2)

S.aureua (n=17) was susceptible to vancomycin 100% and linezolid 94.11%, Whileresistance for ampicillin and Hl.sterptomycin were 100%.*E.* faecium (n=16) were tested quinolones compound resulted to be equally resistant against E. faeciumranging from 76% to 100%. Resistance to erythromycin, clindamycin, ciprofloxacin, levofloxacin, tetracycline and Nitrofurantoin 100% each. While resistance rate for linezolid and Vancomycin were lower i.e. 12.5% and 25%. S.hemolyticus (n=11) were 100% susceptible to Vancomycin, Tecoplanin and linezolid. (Table-3).

Discussion

The present study describes the bacterial and fungal species isolated in which age and gender of the patients, antimicrobial, resistance, associated clinical condition and outcome of the patient during one year period where 156 positive blood culture samples was collected from indoor and outdoorpatients.

In this study, men had high culture positivity as compared with women i.e. (62.17% male and 37.82% were female) the result was consistent with the study done by Vanitha Rani et.al.[6]Who reported highly culture positivity as 60.2% in male & 36.7% in female. A similar study was done by Kaur and Singh [7]Who reported high culture positivity in 65.22% men. However, Zenebe et.al.[8]Reported more high culture positivity in women, 59.2% than men 40.8%, in their study. The reason for this difference is because of gender bias. Secondly, it may be due to more male new-borns being admitted in NICU as they are more prone to neonatal septicaemia as compared to female newborns.[9]

In this study we found the Frequency of BSI has been reported toage above 71 and below 1 year in both male and female in. 15.38% patients in our study were above 71years and below 1years of age followed by 14.1% in the age group 51-60 and 12.82% were 61-70 years of age. The results were in concordance with the fact that, elderly are more susceptible to infection.

In the present study, the frequency of isolation of Gram-negative bacteria (n=80, 51.28%) was found to be more than Gram-positive bacteria (n=69, 44.23%). It is in accordance With the studies of Mehta et al,[10]Mehdinejad et al,[11]Barati et.al,[12]and Ayobola et.al,[13]Who reported similar incidences.However, in contrast some studies like Cina et.al,[14] Kamga et.al,[15]Anbumani et.al[16]and Karlowsky et.al.[17] have shown a higher incidence of Gram-positive organisms then Gram-negative organisms.

In the present study as expected E.coli (n=23, 14.7%) was the most frequently encountered species followed by K. pneumonia (n=17, 10.8%), S. aureus (n=17, 10.8%), E. faecium (n=16, 10.2%), S. hemolyticus (n=11, 7%) all accounting for around (n=84, 54%) of totale isolates. Frequency of E. coli and K. pneumoniae was more in female i.e (n=13, 13.4%) and (n=9, 9.2%) respectively where S. hominis and S. paucimobilis where more prevalent in male i.e (n=4, 6.7%) and (n=4, 4.1%).

In the present study, the predominant Gram-negative isolates were E.coli (n=23, 14.7%) followed by K. pneumonia (n=17, 10.8%) which was in concordance with other studies.[18-22] In contrast to this finding, a study from Mumbai revealed that, Pseudomonas species was the most common cause (30.37%) and E.coli amounted upto 16.06%.[23]

The Gram-positive isolate was S. aureus (n=17, 10.8%) followed by E. faecium (n=16, 10.2%) This findings is similar to other studies Where S. aureus was the most common isolate.[23,24,25] This is in contrast with other studies where coagulase negative Staphylococci has contributed to the blood stream infection in patients. [21, 26, 27]
In the present study, the Gram-negative isolates E.coli (n=23) resistance to orally active compound ampicillin was (n=20/21, 95.45%) Resistance to ceftriaxone was (n=20/22, 90.9%) However, in contrast some studies like shilpi gupta et.al.[28] have shown Majority of E. coli were sensitive to immipenem (98.77%) K. pneumonia (n=17) resistance to Tetracycline was (n=10/10, 100%), Ceftazidime was (n=14/15, 93.33%), Cefotaxime was (n=13/14, 92.85%), the Gram-positive isolate S.aureua (n=17) was susceptible to vancomycin(n=17/17, 100%) and linezolid(n=16/17, 94.11%), E. faecium (n=16) was susceptible to vancomycin(n=14/16, 87.5%) and linezolid(n=16/16, 100%), S. hemolyticus (n=11) was susceptible to vancomycin(n=9/11, 81.81%) and linezolid(n=11/11, 100%) This correlates with other studies conducted by Mehta M. et.al,[29]Sharma M et.al,[30]Atul G et.al,[31] Mustafa M et.al.[32] The Candida species C.tropicalis (n=3) wrew equally susceptible to Voriconazole, Flusytosine, Micafugin and caspofungin i.e. 100%. Resistance rate for fluconazole were 50%. C.albicans (n=2) were (n=2/2, 100%) susceptible to Flusytosine, Fluconazole, Voriconazole, Ampphptericin-B, Micafungin, Caspofungin.

Conclusion

E.coli remains the most Common etiological agent of BSI. Majority of BSI was shown in old age patient. In critical care units are important contributors in BSI infection. Drug resistance is evolving thret reduce patient hospital stay and rational use of antimicrobials.

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Table: 1 Distribution of bacterial and fungal isolates from Blood stream infection throughout the Study period (n= 156)

Organism	Frequency (%)
A. bumanii	11(7.05)
B. cepacia	2(1.2)
C. albicans	2(1.2)
C. glabrata	1(0.6)
C. krusei	1(0.6)
C. tropicalis	3(1.9)
C. utilis	1(0.6)

E. cloacae	1(0.6)
E. coli	23(14.7)
E. feacalis	3(1.9)
E. facium	16(10.2)
E. cloacae complex	3(1.9)
K. pneumoniae	17(10.8)
Pantoea sp	1(0.6)
P. shigelloides	1(0.6)
P. aereginosa	3(1.9)
Pseudomonas	3(1.9)
S. agalactiae	1(0.6)
S. aureus	17(10.8)
S. epidermis	10(6.4)
S. hemolyticus	11(7)
S. hominis	7(4.4)
S. mltophilia	1(0.6)
S. pneumoniae	2(1.2)
S. typhi	8(5.1)
S. paucimobilis	7(4.4)

Table: 2 Antimicrobial drug resistance of Gram negative Blood pathogens (n=58)

Antimicrobial agent	**E. coli n=23(%)**	**K. pnemoniae n=17(%)**	**A,bumanii n=10(%)**	**S. typhi n=8(%)**
Ampicillin-suibactum	12/18(66.66)	12/14(85.71)	6/8(62.5)	NA*
Aztreonam	12/13(92.30)	7/8/(87.5)	NA*	NA*
Amikacin	4/23(17.39)	8/16(50)	7/9(77.77)	NA*
Amoxicillin clabulanic Acid	12/22(54.54)	12/15(80)	NA*	NA*
Ampicillin	21/22(95.45)	NA*	NA*	NA*
Cefepime	12/22(54.54)	13/15(86.66)	6/8(37.5)	NA*
Cefepime/tazobactum	7/17(41.17)	9/13(69.23)	5/8(87.5)	NA*
Cefotaxime	20/21(95.23)	13/14(92.85)	NA*	NA*
Ceftriaxone	20/22(90.9)	14/16(87.5)	7/9(77.77)	NA*
Cefuroxime	20/23(86.95)	14/16(87.5)	1/1(100)	NA*
Ceftazidime	16/19(84.21)	14/15(93.33)	6/8(75)	NA*
Co-trimoxazol	17/21(80.95)	10/17(58.82)	3/8(37.5)	NA*
Ciprofloxacin	15/20(75)	9/14(64.28)	7/9(77.77)	4/8(50)

Ertapenem	4/22(18.18)	12/17(70.58)	NA*	NA*
Imipenem	4/20(20)	12/17(70.58)	7/9(77.77)	NA*
Meropenem	5/22(22.7)	12/17(70.58)	7/9(77.77)	NA*
Doripenem	2/2(100)	NA*	NA*	NA*
Levofloxacin	12/16(75)	7/12(58.33)	6/8(75)	NA*
Gentamicin	10/22(45.45)	9/16(56.25)	7/9(77.77)	NA*
Cefoperazone-sulbactum	5/20(25)	11/16(68.75)	5/8(62.5)	NA*
Piperacillin	1/2(50)	NA*	NA*	NA*
Piperacillin/tazobactum	7/21(33.33	12/17(70.58)	7/9(77.77)	NA*
Ticarcillin-clavulanic Acid	NA*	NA*	2/2(100)	NA*
Ticarcillin	NA*	NA*	2/2(100)	NA*
Tettracycline	8/12(66.66)	10/10(100)	5/6(83.33)	NA*
Tobramycin	5/19(26.31)	10/17(58.82)	6/9(66.66)	NA*
Colistin	1/7(14.28)	NA*	NA*	NA*
Tigecycline	NA*	10/14(71)	NA*	NA*

Table: 3 Antimicrobial drug resistance of Gram positive Blood pathogens (n=54)

Antimicrobial agent	***S. aureus* n=17(%)**	***E. faecium* n=16(%)**	***S. hemolyticCus* n=11(%)**	***S. epidermIs* n=10(%)**
Penicillin	N/A	11/15(73.33)	10/10(100)	10/10(100)
Ampicillin	1/1(100)	10/12(83.33)	N/A	N/A
Erythromycin	6/14(42.85)	1/1(100)	9/11(81.81)	3/4(75)
Clindamycin	7/16(43.75)	2/2(100)	5/9(55.5)	7/10(70)
Linezolid	1/16(6.25)	2/16(12.5)	0/11(0)	1/8(12.5)
Vancomycin	0/17(0)	4/16(25)	0/10(0)	0/10(0)
Tecoplanin	0/3(0)	2/5(40)	0/3(0)	0/1(0)
Oxacillin	8/16(50)	N/A	10/10(100)	10/10(100)
HL streptomycin	0/1(0)	5/10(50)	N/A	N/A
HL gentamicin	1/1(100)	10/13(76.92)	N/A	N/A
Ciprofloxacin	N/A	1/1(100)	N/A	N/A
Levofloxacin	13/17(76.47)	1/1(100)	8/10(80)	7/10(70)
Tetracycline	1/16(6.25)	1/1(100)	5/9(55.55)	3/9(33.33)
Nitrofurantoin	N/A	1/1(100)	N/A	N/A
Cotrimoxazole	12/17(70.58)	N/A	8/11(72.72)	8/10(80)
Gentamicin	2/16(12.5)	N/A	6/11(54.54)	5/10(50)