ORIGINAL ARTICLE

Current Pattern of Bloodstream Infections in a Tertiary Care Hospital of Karachi and Clinical Significance of Positive Blood Cultures

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ABSTRACT

Objective: Blood stream infections (BSI) (septicemias) require prompt empirical therapy based on awareness of the drug susceptibility profiles of locally prevalent pathogens isolated.

Place and Duration of Study: Department of Pathology Dow University of Health Sciences, Karachi, in collaboration with Dr Essa's Diagnostic Centre, from July to November 2008.

Study Design: A cross-sectional prospective study.

Patients and Methods: 324 consecutive blood cultures from patients coming to Civil Hospital Karachi were scrutinized for bacterial isolates and their antibiotic sensitivity profiles were done.

Results: A total of 100 (30.9%) specimens were found positive, of these 78% isolates were gram negative bacteria and 22% gram positive cocci. *Salmonella typhi*, seen less often in adults (20.5%), was the predominant pathogen in children (82.5%). *Escherichia coli*, *Staphylococcus aureus,* Pseudomonas and Klebsiella were isolated in neonates, and Klebsiella, Pseudomonas, Enterobacter and *Acinetobacter* were identified among adult patients. While all *S.typhi* isolates were sensitive to cefixime, ceftriaxone and the fluoroquinolones and increasingly amenable to chloramphenicol, of significance was the percentage of other multidrug resistant bacterial isolates. Methicillin resistant Staphylococcu aureus was isolated from one case.

Statistical Analysis: The results were analysed by applying SPSS version 16 to derive p value.

Conclusion: Amikacin, carbapenems, cefoperazone+sulbactam, fosfomycin and pipericillin+tazobactam are currently the only available drugs still active *in-vitro* on blood isolates, judicious use of antibiotics focused on the compliance and formation of antibiotic policy guide lines is highly recommended.

Key words: Bloodstream infections, septicemia, gram negative bacteria, gram positive bacteria.

INTRODUCTION

Septicemias cause significant morbidity and mortality world wide and are among the most common health-care associated infections.[1, 2] Despite being a major cause of hospital admissions and mortality, there is relatively little information available on community acquired bacteremia in the tropics.[3,4] Respiratory, genitourinary tract and intra -abdominal foci are often identifiable sources of blood stream infections.[5] Bacteremia due to Enterobacteriaceae other than *E. coli* is reported to be associated with increasing mortality as compared to gram positive species.[6]

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The spectrum of organisms causing sepsis change over time and vary from region to region.[7,8] A five-fold increase in the number of cases of sepsis by gram positive cocci have been reported from the developed countries.[9] The epidemiologic data from developing countries show significant differences in the incidence, risk factors, pattern and antimicrobial susceptibility of pathogens, and morbidity, when compared with that of developed countries.[10-13]

There is a dire need, therefore for clinicians to be updated with the current efficiency of commonly prescribed drugs and the selection of antimicrobials for empiric therapy should be based on the susceptibility pattern of local pathogens isolated. On the other hand antibiotic treatment may be

needlessly started based on false positive culture results.[13] This increases the possibility that resistant bacteria may emerge resulting in more difficult-to-treat infections. Bloodstream infection is usually treated with a minimum 10-14 days of antibiotic therapy. This duration of treatment has been shown to be a risk factor for the subsequent emergence of infection with antibiotic resistant bacteria.[14] Previous studies have identified a significant association between administration of inadequate antimicrobial treatment and mortality.

The data of our exercise emphasizes the importance of establishing the current pattern of pathogens and their antibiotic resistant profiles. It is imperative to correctly intemperate positive blood cultures in order to initiate an adequate and prompt antimicrobial regimen.

MATERIAL AND METHODS

This study was carried out at the Department of Pathology, Dow University of Health Sciences, Karachi in collaboration with Dr Essa's Diagnostic Centre, between July-November 2008.

Inclusion criteria: All cases suspected for bloodstream infections on clinical assessment.

Exclusion criteria: Cases already admitted in the hospital and cases already on antibiotic treatment. Blood samples were drawn for two blood cultures from each case. The blood culture medium used was trypticase soya broth supplemented with thyoglycollate broth in 5 ml bottles for adults, 2 ml bottles for children and 1ml bottles for infants..The sample was promptly introduced into each of two blood culture bottles and incubated at 37°C. Daily subculture was made onto blood agar, chocolate agar and McConkey's agar for up to 7 days or until positive growth was noted.

The isolates were identified according to standard procedures[15] and their antibiotic susceptibility profiles determined by the conventional Kirby-Bauer disc diffusion method using antibiotic impregnated discs (Oxoid). Methicillin susceptibility was done for *Staphylococcus aureus*.

Out of 324 blood stream specimens, a total of 100 consecutive positive cultures were obtained . The antibiotics tested on gram positive cocci included ampicillin, amoxicillin+clavulanic acid , ciprofloxacin, erythromycin, gentamicin and vancomycin; and oxacillin for confirmation of MRSA. Antibiotics used for gram-negative bacilli of the *Enterobacteriaceae* family included amikacin, cefotaxime, ceftriaxone, ciprofloxacin and gentamicin. For *S.typhi*, aztreonam, cefixime, cefotaxime, ceftriaxone, ciprofloxacin, chloramphenicol, cotrimoxazole, nalidixic acid and fosfomycin were used.

RESULTS

Among the 324 consecutive samples positive for blood cultures, 100 specimens yielded bacterial growth. Neonates (n=49), children between 1 month-12 years of age (n=26), adults (n=25) (The eldest patient with septicemia was an 80-year old male presenting with unstable angina.(Table 1)

Isolates identified:

Staphylococcus aureus (n=20), followed by *S.typhi*, *Pseudomonas* spp, *E.coli* and *Klebsiella* spp were the most common isolates (Table 2); four other gram negative bacteria were also identified, as well as 2 gram positive cocci: these were *Strep.agalactiae* in a neonate, and enterococci in one child. One *Staphylococcus aureus* isolate was methicillin resistant. The majority of isolates identified (78%) were gram negative rods (Table 2).

The drug susceptibility results of the isolates are presented in Table 3. Fosfomycin, imipenem, pipericillin+tazobactam, cefoperazone+sulbactam and amikacin were the most effective drugs on *Enterobacteriaceae* isolates; only 10 of these, which included *E.coli*, Klebsiella and Citrobacter were

resistant to this drug. Fosfomycin and pipericillin+tazobactam were also more consistent in affording zones on *Pseudomonas* and *Acinetobacter* isolates. Vancomycin was active on all 20 *Staph.aureus* isolates and each of the enterococcus and *Strep.agalactiae* isolates. Ciprofloxacin sensitivity was recorded with all 16 *S.typhi* recovered from the blood specimens scrutinized; 10 of these were resistant to Cefixime. One *Pseudomonas aeruginosa* and one *E.coli* isolate were resistant to every drug tested.

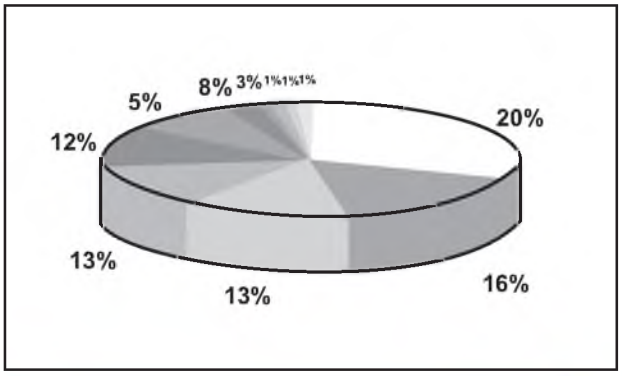

Figure – 1 :

Table1 : Age distribution of patients yielding positive growth on blood culture

Age	Number
0-1 month	49
1 month-12 years	26
12 years-80 years	25
Total	100

Table 2 : Percentage of Blood Culture Isolates from Civil Hospital In-Patients in Karachi

Age	Number	Neonates	Children
Staphylococcus aureus	20	10	4
(Methicillin Sensitive)	19		
MRSA	1		
Salmonella	16	0	13
S typhi	12		
paratyphi	4		
Pseudomonas	13	8	1
Esherichia coli	13	10	1
Klebsiella spp	12	7	1
Acinetobacter spp	8	4	2
Alcaligenes spp	3	1	2
Citrobacter spp	1	1	0
Proteus spp	1	0	0
Enterococcusspp	1	0	1
Streptococcus agalactiae	1	1	0

Table 3 : Antibiotic susceptibility (%) of bacteria isolated from blood cultures

Antibioics	*Enterobacteriaceae*	*S.Typhi*	Non-fermenters	Gram-positive cocci
amikacin 30µg	76		62	
chloramphenicol30µg		48		
cotrimaxozole 25µg	44			66
ciprofloxacin	55	100	65	89
Ceftriaxone30µg	58	99	50	
Cefotaxime30µg	56	96	52	
cefixime	58	90		
Gentamicin10µg	48			62
Fosfomycin50µg	90	92	89	94
aztreonam		83		
imipenem	78		57	
pipericillin+tazobactam	78		49	
Erythromycin15µg				61
Vancomycin30µg				100
cefoperazone +sulbactam	82		82	
ceftazidime + clavulanic acid	63		63	
Methicillin 5µg				19

DISCUSSION

The extent of neonatal sepsis in our study was in keeping with the observation that about 50% to 88% of neonatal deaths in the community are attributable to infectious causes and that 22% to 66% of all admissions in the neonatal unit are due to septicemia and pneumonia.[15] A Nigerian report on neonatal septicemia observed a rate of 59.8% blood culture positivity[16] while studies in Karachi suggested that 43.5% blood cultures from neonates in 1984

and 40% in 1985 were positive.[17, 18, 19] While considering overall blood culture positivity, variable rates have been observed by different workers, possibly reflecting the methodology, manual or automation in use. In our study, while 30.9% of 324 specimens processed yielded growth, a Canadian study found 63% blood cultures positive for pathogens,[20] in Islamabad, 54% were reported positive, and in Lahore, bacterial pathogens were isolated from 60% of blood specimens.[21] Interestingly, in a study carried out in Chandigarh, India only 9.94% of the samples yielded growth.[22]

All our cultures yielded single isolates; this observation is common, unimicrobial growth has been reported in other studies[22,23] and in also those conducted in Multan and Karachi.[24-27]

The spectrum of organisms causing sepsis is known to change over time and in different geographical areas.[21,25]

Coagulase negative staphylococci (CONS) are normally present as commensal organisms on the skin, in recent years they have emerged as significant etiological agents of septicemia.[28] This acceptance has occurred in the face of a positive *staphylococcus* blood culture often being misinterpreted as a "contaminant" by both physician and infection control staff.[29]

Studies reported in Western countries usually show *Strep.agalactiae* as a frequent neonatal isolate. This organism has, however, hardly been reported in studies carried out in Pakistan and other developing countries.[7,24] Our findings include one case of neonatal sepsis due to this Group B *streptococcus*.

Our data differs in the frequency of different gram negative isolates: *S.typhi* among the gram negatives, for example, seen occasionally in adults was the predominant pathogen (81.25%) in children, while *E.coli*, Klebsiella and Pseudomonas were pathogens in all ages.The p-value for pathogens isolated on blood culture s was found to be 0.81.

All our isolates from septicemic patients were aerobic; this not uncommon observation encourages recent recommendations that labs should reserve the practice of routinely setting up anaerobic cultures for only pertinent clinical conditions.[28]

Data from developing countries show important differences in the local pattern of antibiotic sensitivity[30] and multidrug resistance to antibiotics has noticeably increased over the last two decades. This situation is decidedly worse in developing countries due to the misuse of antibiotics, including Pakistan. In our study, 24 of the bloodstream isolates were multidrug resistant; 10 of these were sensitive to only fosfomycin, a drug not in as wide use as other broad spectrum injectables, and one *Pseudomonas aeruginosa* and an *E.coli* isolate were resistant to all the indicated drugs tested.

Our data emphasizes the observation that amikacin offers satisfactory activity (76%) against *Enterobacteriaceae* in particular, whereas ciprofloxacin was less effective (65%) on the non-fermenters including *Pseudomonas* and *Acinetobacter* spp, but active on all our *S.typhi* isolates. Also, cefoperazone+sulbactam acted significantly on all gram-negative isolates (82%) in comparison with ceftriaxone and amikacin, and all gram-positive cocci were found to retain sensitivity to vancomycin. Unfortunately, since antibiotic-resistant strains have emerged we need to control the spread of these resistant strains through infection control programes and continuous monitoring of drug resistant patterns.

CONCLUSIONS

No gold standard other than a positive blood culture exists to confirm septicemia. However, even in the best of hands, blood culture positivity rates may be only 30% in clinically suspected cases. The practice of obtaining three blood cultures from different sites during febrile episodes enhances the chances of obtaining positive results. The life threatening nature of bacteremia and sepsis underscores

the importance of using local surveillance data to guide empirical therapy as a rational strategy to minimize escalating antimicrobial resistance. Regular referral towards latest antibiograms by the clinicians is another important recommendation that needs to be emphasized in our country.

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