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BACTERIAL PATHOGENS RESPONSIBLE FOR BLOOD STREAM INFECTION (BSI) AND PATTERN OF DRUG RESISTANCE IN A TERTIARY CARE HOSPITAL OF LAHORE

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ABSTRACT

The present retrospective analysis was carried out to determine the pattern of bacterial agents responsible for blood stream infection (BSI) in a tertiary care hospital of Lahore and to get an updated knowledge about their antibiotic resistance pattern. It is a cross sectional descriptive study, carried out in the Microbiology Section, Department of Pathology, Services Institute of Medical Sciences (SIMS), Lahore during the period April, 2006 to December, 2006. Among the 1814 blood cultures 1382 (76%) were received from pediatrics/ neonatology wards and 432 (24%) from adult patients. In a total of 508 (27.9%) blood cultures, 465 yielded monomicrobial growth and 43 polymicrobial growth. A total of 454 (97.6%) of the monomicrobial growths were bacterial isolates and 11(2.4%) were Candida Spp. Gram negative bacteria (Enterobacteriaceae + non-fermenter bacteria) comprised the majority of bacterial isolates. Amongst the gram-negative bacteria the most common organism was Klebsiella Spp. while amongst the gram-positive organisms Staph. aureus was the most common isolate. It was seen that 31.25% Staph. aureus isolates were resistant to Oxacillin, 93.7% of Klebsiella Spp. and E. coli isolates were resistant to 3rd generation Cephalosporins and 6.49% of Pseudomonas Spp. and Acinetobacter Spp. whereas resistant to Carbapenems in the present study. As BSI is an emergency, for appropriate management of these cases an updated knowledge about the causative agents and their susceptibility pattern to antibiotics is required to start appropriate empirical antibiotic therapy till the results of the microbiology report are available. The alarming finding is the high resistance seen amongst Enterobacteriaceae against 3rd generation cephalosporins (93.7%), oxacillin resistance among Staph aureus (31.25%) and increasing resistance against Carbepenems among Pseudomonas and Acinetobacter isolates (6.49%). In conclusion there are grave implications of these findings for our already strained health care system as the presence of these multidrug resistant organisms leads to longer hospital stay, more expensive/ toxic drugs and higher mortality.

Keywords: *BSI; Enterobacteriaceae; ORSA; Carbapenems resistance*

INTRODUCTION

Blood stream infection (BSI) is a serious problem that needs immediate attention and treatment. It is a cause of high mortality especially if caused by multidrug resistant bacteria.[1] Bacteriological culture to isolate the offending pathogen and knowledge about sensitivity pattern of the isolates remain the main stay of definitive diagnosis and management of BSI.[2]

The results of bacteriological cultures and antibiotic susceptibility tests take 3-4 days.[3] One key determinant in the ultimate outcome of patients with sepsis is institution of early and appropriate antimicrobial therapy. Thus it is a common practice to institute early empirical therapy with broad-spectrum antibiotics in patients presenting with clinical features suggestive of bacteraemia.[1,3,4] This is only possible with knowledge of the commonly isolated bacteria and their likely susceptibility to antibiotics in a given place.

The present retrospective analysis was carried out to determine the pattern of bacterial agents responsible for blood stream infection (BSI) in a tertiary care hospital of Lahore and to get an updated knowledge about their antibiotic susceptibility pattern. This may help the clinician in selecting the antibiotics for empirical therapy till the results of culture sensitivity are known.

MATERIAL AND METHODS

Present study was based on retrospective analysis of data about blood culture results of specimens submitted for culture to Microbiology Laboratory of Services Institute of Medical Sciences (SIMS), Lahore. One thousand eight hundred and twenty-four blood culture bottles (both paediatric and adult)

containing appropriate amount of blood in Tryptic Soy Broth with SPS were received from the patients admitted to Services Hospital, Lahore during the period April 2006 to December 2006. These were incubated overnight at 35°C. After 24 hour these samples were sub cultured on Blood agar and MacConkey agar plates and incubated at 35°C overnight. Identification of growth was based on colony morphology, Gram staining and appropriate biochemical tests.[5]

Susceptibility to different antibiotics based on the type of growth was performed on Mueller Hinton agar by standard Kirby Bauer method.[6] Sensitivity plates were incubated at 35°C overnight. In the present study, susceptibility of *S. aureus* against Oxacillin (1 ug) was analysed. Similarly, among Enterobacteriaceae, sensitivity pattern for at least two third generation cephalosporins preferably Cefotaxime (30 ug) and Ceftazidine (30 ug) was determined. For Pseudomonas and Acinetobacter species, sensitivity against Carbapenems (Imipenem/ Merpenem) was analysed.

RESULTS

In 1824 blood cultures, 1392 (76%) were received from pediatrics/ neonatology wards and 432 (24%) were received from adult patients. Five hundred and eight (27.9%) blood culture samples were positive for growth. Of these, 465 (91.5%) were monomicrobial and 43 (8.5%) were polymicrobial. Among 465 monomicrobial growths, 454 (97.6%) yielded growth of bacterial isolates and 11 (2.4%) yielded growth of Candida Spp. (Table 1). The table 2 shows common causes of bloodstream infections were gram negative bacilli (Enterobacteriaceae and non-fermenter bacteria). Amongst the gram-negative bacteria the most common organism was Klebsiella

Table 1: *Data showing the results of Blood Cultures.*

Results of culture (N = 1824)	**No**	**%**
Growth positive	508	27.9
Growth negative	1316	72.1
Number of bacterial isolates per culture (N = 508)		
Monomicrobial	465	91.5
Polymicrobial	43	8.5
Pattern of monomicrobial isolates (N = 465)		
Gram positive cocci	221	47.5
Enterobacteriacae	156	33.5
Non fermentor Gram negative rods	77	16.6
Fungi (yeast)	11	2.4

Table 2: *Distribution of isolates obtained from blood cultures positive for monomicrobial growth (N = 465).*

Gram positive cocci	**No**	**%**
S. aureus	112	24.1
Coagulase negative staphylococci	97	20.8
Streptococci	12	2.6
Gram negative bacilli		
Klebsiella species	112	24.1
Pseudomonas species	53	11.4
Acinetbacter species	24	5.1
E coli	21	4.5
Salmonella species	15	3.2
Enterobacter species	4	0.9
Proteus species	2	0.4
Citrobacter species	2	0.4
Candida Spp.	11	2.4

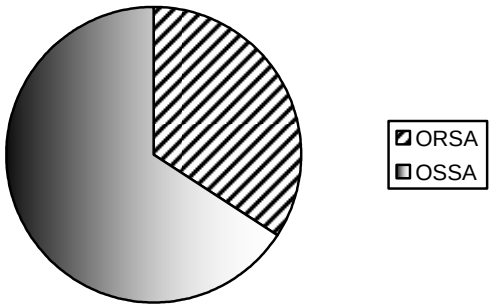

Fig. 1: *Susceptibility of Staph. Aureus to oxacillin.*

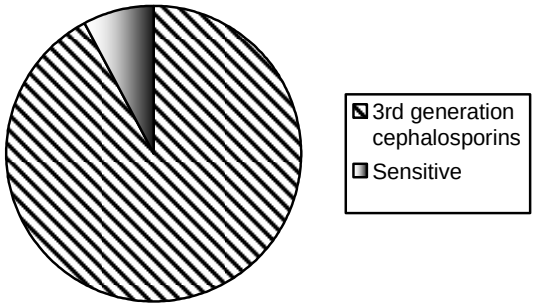

Fig. 2: *Susceptibility of E. coli / Klebsiella spp. To 3rd generation Cephalosporins.*

Spp. Among the Gram-positive organisms Staph. aureus was the most common isolate. On analysis of antibacterial resistance it was seen that 31.25%

Staph. aureus isolates were resistant to Oxacillin, 93.7% of Klebsiella Spp. and E. coli isolates were resistant to 3rd generation Cephalosporins and 6.49% of Pseudomonas Spp. and Acinetobacter Spp. were resistant to Carbapenems in the present study (Figures 1-3).

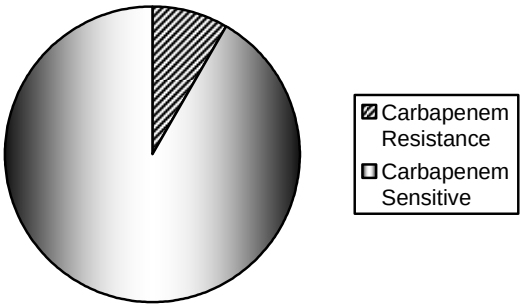

Fig. 3: *Susceptibility of non-fermenter Gram –ive rods to Carbapenems.*

In the Fig. 1 shows percentage of oxacillin resistance among Staph. aureus isolates (35/112; 31.25%).; Fig. 2 shows resistance among Klebsiella Spp. and E. coli isolates to 3rd generation Cephalosporins (119/127; 93.7%), and Fig. 3 shows resistance among Pseudomonas Spp. and Acinetobacter Spp. to Carbapenems (5/77; 6.49%).

DISSCUSION

Prompt diagnosis and effective treatment are necessary to prevent complications and to reduce mortality from BSI. Rapid immunological techniques like C-reactive protein (CRP) assays may help in preliminary diagnosis of BSI.[7] On the basis of prior knowledge of common causative agents and their susceptibility to prescribed antibiotics empiric therapy is started and later changed according to the final culture and susceptibility report.

It is recommended to collect at least two sets of blood cultures. Each set has one aerobic blood culture bottle and one anaerobic blood culture bottle. Two sets increase the yield and strengthen the role of an isolate as pathogen if collected in both sets.[3] In high burden and resource limited settings like several government healthcare institutions in our country most of the time we receive only one bottle of aerobic blood culture. In such a case the yield decreases by 10% and clinical features have to be considered along with other laboratory parameters to consider a common skin flora member to be significant pathogen or a contaminant.[1,3]

In the present retrospective analysis 27.9% of cultures were positive for growth. The rate of positive culture was much higher (59%) in a previous study carried out on blood culture samples collected from patients of suspected BSI from different hospitals in Lahore.[8] In most studies the positivity rate in pediatric patients is higher. In India, it is reported to be between 36-55 percent.[2,9] In a study carried out in Department of Pathology, Agha Khan University Hospital, Karachi, 5840 blood specimens were taken from febrile neutropenic patients. Out of these, 18% were positive for growth.[10] This figure is lower than the one in our study.

Most of the cultures in the present study yielded monomicrobial growth (Table 1). The polymicrobial growth isolation rate was 8.5%. The reported polymicrobial isolation rate varies between 1 to 15 percent. The polymicrobial growth could mean contamination or a severe infection with bad prognosis.[8,11,12]

An interesting finding in the Subcontinent is the isolation of more Gram negative bacteria than Gram positive bacteria in BSI. This is seen in the present analysis as shown in Table 1. Similar findings have also been reported in other studies in Pakistan and India.[8,9] Against these findings, in two centres in Karachi PNS SHIFA (Naval Hospital) and in an analysis of isolates in blood cultures from neutropaenic patients in Aga Khan University Hospital in Karachi, the finding of more Gram positive isolates (53%) may reflect on better isolation of patients and hand washing precautions in ICU/oncology wards of those hospitals.[10,13] Possibly for similar reasons, in Europe and USA blood culture is more likely to yield Gram positive growth.[3,14]

Fungi (Candida spp.) were isolated in 2.4% of cases (Table 1). This is similar to 1.6% reported in CDR weekly.[11] Higher rate of 4% from febrile neutropenic patients obtained in Karachi could be due to the underlying condition of the patients.[10]

In the present study Klebsiella spp. (24.1%) was the most commonly isolated Enterbacteriaceae. This is comparable to the finding of 24.6% in India.[2] In a previous study conducted in Lahore the isolation rate of Klebsiella spp was 6.5%.[8] Mahmood and coworkers have reported up to 34% Klebsiella spp. isolates from neonatal intensive care unit in Karachi.[15] The most commonly isolated non fermenter gram negative bacteria was Pseudomonas spp. (11.4%) in the present study. This is lower than 26.5% reported from different hospitals of Lahore in the year 2000.[10] Acinetobacter isolation rate is increasing in most tertiary care hospitals. In the present study it is 5.1%, which is higher than 2.32% reported in Lahore previously.[10]

Staph. aureus was the most commonly isolated Gram positive bacteria. Thirty one point two five percent of these were oxacillin resistant (ORSA). This finding is similar to ORSA isolation rate in

Karachi.[10] A higher rate of ORSA (43%) has been reported in Rawalpindi by Butt and coworkers.[16] ORSA strains have steadily increased from 10% in 1995 to 29% in 2001 as cause of nosocomial infections in USA.[14] In UK and Ireland the prevalence of Methicillin resistance in Staph. aureus is 42% with annual fluctuation of ≤ 6 percent.[17]

The alarming finding in the present study was the resistance in Klebsiella spp. and E.coli strains to 3rd generation Cephalosporins of (93.7%). This type of resistance is a marker for the presence of ESBL.[18] In India, ESBL production amongst Enterobacteria has been reported to be between 74.4 and 80.9%.[2] In a study carried out in Karachi, 54% of Enterobacteriaceae isolates in the neutropenic patients with BSI have been observed to be ESBL producers.[10] This high rate of resistance to Cephalosporins is due to the abundant use of 3rd generation Cephalosporins in the hospitals.[18] It is a very alarming development as the mortality is much higher with ESBL producing enterobacteriaceae.[19]

Resistance of non fermenter bacteria such as Pseudomonas spp. and Acinetobacter spp. to Carbapenems was 6.5% in the present study as shown in Fig. 3. Carbapenems resistance in pseudomonas (6-8%) was also observed in two studies carried out in Karachi.[10,20] In Taiwan 14-15% Pseudomonas isolates from intensive care were resistant to Carbapenems.[21] Text books report resistance in Pseudomonas to Carbapenems as low as 1%.[22] In India the reported incidence of Pseudomonas resistance to Carbapenems in isolates from diabetic and cancer patients is as high as 26%.[23]

The presence of such resistant strains in our hospitals translates into grave implications. It is time to take action, set up surveillance systems have antibiotic policy implemented and infection control practices established with emphasis on hand washing or the day to revisit pre-antibiotic era is not far.

It is **concluded** that Gram negative bacteria are more likely to be the causative agent in blood stream infection and the most common Gram negative organism isolated was Klebsiella spp, the most common Gram positive isolate was Staph.aureus. The non fermenter gram negative bacteria commonly isolated was Pseudomonas spp. More than 90% Klebsiella spp. were resistant to 3rd generation Cephalosporins. Oxacillin resistant S. aureus were 31%. Resistance to Carbapenems was seen in 6.5% of Non fermenter gram negative bacteria. There are grave implications of these findings for our already strained health care system as the presence of these multidrug resistant organisms leads to longer hospital stay, more expensive/ toxic drugs and higher mortality.

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