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BACTERIAL PATHOGENS RESPONSIBLE FOR BLOOD STREAM INFECTIONS AND THEIR DRUG SUSCEPTIBILITY IN A TERTIARY CARE HOSPITAL

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Abstract:

Objective: *To determine the pattern of bacterial agents responsible for blood stream infections (BSI)*

Methods: *Cross sectional descriptive study was carried out in the Pathology departments of Benazir Bhutto Hospital and Holy Family Hospital Rawalpindi during the period October, 2015 to May, 2017. Blood culture of 1284 bottles containing appropriate amount of blood received from indoor and outdoor patients. Blood agar and MacConkey agar plates were used to subculture the collected sample. The sensitivity of the causative organisms was obtained by collecting samples using antiseptic measures and culturing on BHF culture medium.*

Results: *Gram Negative bacterial growth is responsible for blood infection in 93.3% of cases whereas 6.7% of bloodstream infections are caused by Gram Positive bacterial growth. Mono microbial agent growth causes 92.6% blood stream infections and poly microbial agents cause 7.4% blood stream infection. Bloodstream infections caused by Gram Positive Bacteria are associated with S. Aureus is 38.8% and 1.9% are associated with Streptococcus spp. In bloodstream infections caused by Gram Negative bacteria, Salmonella spp is responsible for 14.2% cases, Klebsiella spp is responsible for 13.5% cases, Acinetobacter spp is responsible for 11.6% cases, E.coli and Pseudomonas are responsible for 6.5% of cases, enterococcus spp is responsible for 3.2 % of cases, proteus and Enterobacter spp is responsible for 6% of cases, candida spp is responsible for 2.5 % of cases. salmonella specie showed susceptibility (100%) to Aztreonam, ceftriaxone, Moxifloxacin, Tigecyclin and meropenam. Klebsiella specie showed susceptibility (100%) to Cefaclor, tegeyclin and vancomycin. Pseudomonas shows susceptibility (100%) to moxifloxacin and cotrimoxazole. Enterococcus shows susceptibility (100%) to linezolid and vancomycin. E.coli shows susceptibility (100%) to gentamycin and meropenam. Streptococcus shows susceptibility (100%) to Augmentin, Ciprofloxacin, Doxycycline, Fusidic Acid, Moxifloxacin, Vancomycin and Staphylococcus Aureus shows susceptibility (100%) to Tigecyclin, Vancomycin.*

Conclusion: *Gram negative bacteria involving mono microbial agent growth is responsible for most of blood stream infections*

Keywords: *Blood stream infections, Benazir Bhutto Hospital, Holy family Hospital, antibiotic Sensitivity Pattern.*

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INTRODUCTION:

The knowledge of bacterial pathogens which cause Bloodstream infection (BSI) is extremely important because these are globally causing high treatment costs, prolonged hospital stay of the patients, and most importantly a very high incidence of morbidity and mortality.(1) Sepsis and septic shock are often associated with blood stream infections causing admission in Intensive care units(ICU).(2)Due to high cost of reagents and culture media and lack of trained technical staff, it is difficult to establish and extend microbiological services in the developing countries.(3)

Spectrum of Blood stream infections consistently vary among different regions of the world and 3 to 4 days are required for results of blood cultures for bacteriological studies and their drug susceptibility.(4)Data from various epidemiological studies have shown marked difference in risk factors, incidence, spectrum of infective agents and their drug susceptibility between developing and developed countries. (5) Clinical microbiology laboratories plays important role in prompt detection of infectious agents causing infections, making early diagnosis and early management.(6) Blood Stream Infections can be caused by both gram positive and gram negative bacterial microorganisms. Gram positive bacterial microorganism includes streptococci, staphylococcus aureus and common Gram negative bacterial agent are Escherichia coli, Klebsiella spp, Enterobacter spp, Proteus spp, Salmonella, Pseudomonas Acinetobacter spp.(7) Bloodstream infections is found to be a growing public health concern, with an estimated1.2 million cases reporting annually in Europe, and 0.5 million attributable deaths. In north America and Europe, blood stream Infection ranks among the top seven causes of death.(8) Blood culture is considered gold standard for the detection of blood stream infection .(9) Increased resistance of bacteria to antibiotics is one of main complication in management of blood stream infections. Drug resistance developed for blood stream pathogens not only limit's therapeutic options but also complicate management.(10) Antibiotics are considered to be the most successful family of drugs to treat the microbial infections in human. Vulnerability of specific microorganism to inhibition or destruction by an antibiotic reduces risk of mortality and morbidity. Different antibiotics are used including Aztreonam, Augmentin, Amikacin, Cefaclor, Gentamycin, Ceftazidime, Ceftriaxone, Ciprofloxacin, Doxycyclin, Fusidic Acid, Cefoxitin, Imepenan, Linezolid, Moxifloxacin, Cotrimoxazole, Cefoperazone + Sulbactam, Piperacillin + Tazobactam, Tigecyclin, Vancomycin, Meropenam. According to evidence up till now the only way possible to reduce mortality rate due to blood stream infection is not just early diagnosis but also appropriate antimicrobial therapy at the earliest. On other hand inappropriate antibiotic use is an important problem and important factor that is responsible for the development of antimicrobial resistance. Excessive use of antibiotic for management of infections promotes antibiotic resistance, increases the chances of drug related adverse effects, which can be prevented by limiting or by appropriate use of antibiotics for treatment of infections/bacterial infections. Drug resistance serious complications causing increase in the use and cost of health care services.(11) Microorganisms present either continuously, intermittently, or transiently in circulating blood are danger to every organ in the body, blood culture is a vital tool to diagnose infections. Drug susceptibility patterns help to identify correct drug therapy for certain bacterial microorganism. Blood stream infection is a challenging situation which can be life threatening sometimes, for reducing complication and mortality rate one of the most important functions of diagnostic microbiology laboratory is timely diagnosis is required by identification and antimicrobial susceptibility testing of pathogens present in blood.(12)

The rationale behind conducting this study is to determine the pattern of bacterial agents responsible for blood stream infection (BSI) in Benazir Bhutto Hospital (BBH) and Holy Family Hospital (HFH)two main tertiary care hospitals of Rawalpindi and to have updated knowledge about their antibiotic susceptibility and resistance pattern. This can help the clinicians in choosing the antibiotics for empirical treatment till the infective agents are identified by culture sensitivity.

MATERIAL/SUBJECTS/PATIENTS AND METHODS:

Cross sectional descriptive study which includes retrospective analysis of data obtained from blood culture results of specimens submitted for culture analysis at Microbiology Section, Department of Pathology, Benazir Bhutto Hospital and Holy Family Hospital, Rawalpindi during the period October, 2015 to May, 2017.Sample from 1284 blood culture of bottles containing appropriate amount of blood in tryptic Soy Broth with sodium polyanethole sulfonate (SPS) were received from indoor and outdoor patients. Data was collected through non probability convenient sampling technique. These were incubated for seven days at 35°C. After 1,3,5,7 days samples were sub cultured using Blood agar and MacConkey agar plates and incubated at 35°C for seven days. Colony morphology was used for identification of growth by using gram staining and appropriate biochemical tests. standard Kirby Bauer method was performed on culture medium to check

Susceptibility to different antibiotics based on the type of growth .(13) Sensitivity plates were incubated for seven days at 35°C. In the present study, susceptibility of S. aureus against Cefoxitin was analysed. Similarly, among Enterobacteriaceae, sensitivity pattern for at least two third generation cephalosporin's preferably Ceftriaxone. For Pseudomonas cefipime and Acinetobacter species, sensitivity against tigecycline was analysed. Data was collected after taking consent, permission from the ERC (ethical review committee) and pathology department of Benazir Bhutto Hospital and Holy Family Hospital, Rawalpindi was taken. Data was analysed using software, SPSS (Statistical Package for the Social Sciences) Version 22. Frequency and percentages were calculated. Results:

Table 1 Results of bacterial growth on blood culture samples

Results Of bacterial growth on blood culture	**%**
Growth Positive	6.7
Growth Negative	93.3

Table 2 Mono microbial and poly microbial growth in BSI

Causative Agent	**%**
Mono microbial	92.6
Poly microbial	12

Table 3 Relationship between BSI cases and associated bacteria

Gram Positive Bacteria	**%**
S. Aureus	38.8
Streptococcus Spp.	1.9
Gram Negative Bacteria	
Salmonella spp.	14.2
Klebsiella spp.	13.5
Acinetobacter spp.	11.6
E. Coli	6.5
Pseudomonas spp.	6.5
Enterococcus spp.	3.2
Proteus spp.	0.6
Enterobacter spp.	0.6
Candida spp.	2.5
Total	100

Table 4: Isolated Organisms And Their Susceptibility To Common Antibiotics.

	Staphylococcus Aureus	**Salmonella Species**	**Klebsiella species**	**Acinetobacter Species**	**Pseudomonas Species**	**E.Coli**	**Enterococci**	**Strepto-cocci**
Aztreonam	-	100%	40%	50%	40%	75%	0%	-
Augmentin	93.3%	66.7%	5.9%	0%	0%	30%	33.3%	100%
Amikacin	-	83.3%	38.5%	0%	50%	100%	0%	-
Cefaclor	89.7%	60%	100%	27%	-	-	0%	-
Gentamycin	66.6%	100%	40%	20%	-	100%	0%	-
Ceftazidime	0%	50%	0%	7.7%	20%	40%	-	-
Ceftriaxone	-	72.2%	5.9%	6.3%	25%	11.1%	0%	-
Ciprofloxacin	20.8%	76.5%	40%	7.7%	37.5%	22.2%	0%	100%
Doxycyclin	93.3%	100%	0%	0%	-	-	33.3%	100%
Fusidic Acid	62.2%	-	-	-	-	-	100%	100%
Cefoxitin	42.3%	100%	-	-	-	-	-	20%
Imepenan	-	55.6%	44.4%	23.1%	66.7%	83.3%	-	-
Linezolid	96%	-	-	-	-	-	100%	100%
Moxifloxacin	80.5%	100%	0%	0%	100%	0%	0%	50%
Cotrimoxazole	19%	50%	57.1%	11.1%	100%	0%	0%	-

Cefoperazone+ Sulbactam	-	88.2%	37.5%	30.8%	50%	87.5%	0%	-
Piperacillin+ Tazobactam	-	92.3%	20%	8.3%	55.6%	80%	33.3%	-
Tigecyclin	100%	100%	100%	92.9%	-	-	-	-
Vancomycin	100%	-	100%		-	-	100%	100%
Meropenam	-	100%	50%	33.3%	0%	100%	0%	-

DISCUSSION:

Study showed that gram negative bacteria causes more bacterial infections than gram positive bacteria and mono microbial agent causes more bacterial infection than poly microbial infections. Gram negative bacteria were more susceptible to anti biotics than gram positive bacteria. Results of our study are in accordance with study "Bacteriological profile and anti biogram of blood culture isolates from a tertiary care hospital of North India" conducted by Shilpi Gupta, Bineeta Kashyap in 2019 , over period of 1year, 3472 blood samples from patients were received at the Microbiology Department. Identification of Bacteriological pathogen and antimicrobial susceptibility testing were performed for all bacterial isolates by following the standard protocol. Results showed Culture positivity in 16.5% of the septicemic cases. The most common isolated bacteria were found to be Escherichia coli (22.4%) than Klebsiella species (19.7%), Staphylococcus aureus (18.3%), and coagulase-negative staphylococci (17.4%). About 26.5% of S. aureus were methicillin-resistant. Vancomycin (100%), gentamicin (87.9%), and ciprofloxacin (73%) showed the highest level of activity among the gram positive isolates.

Most of the gram negative bacteria were multi-drug resistant (67.1%). Imipenem (98.8%), amikacin (90.8%), and cefoperazone/sulbactam combination (81.1%) showed the highest activity among Enterobacteriaceae. Nonfermenters in majority were susceptible to imipenem (88.2%), amikacin (81.6%), and piperacillin/tazobactam combination (72.4%). Gram-negative isolates showed 100% sensitivity toward colistin. Study concluded the bacteriological etiology of sepsis along with the antibiogram of septicemic isolates that may provide necessary information for the formulation of antibiotic policy in effective management of such cases.(14)

Another study "Applicability of an in-house saponin-based extraction method in Bruker Biotyper matrix-assisted laser desorption/ionization time-of-flight mass spectrometry system for identifying bacterial and fungal species in positively flagged pediatric VersaTREK blood cultures" conducted by Ya-LiHuaShun-ChungHsuehbGuan-SyunDing et all in year 2020 showed on analysis of sample that were investigated microbiologist found out that 180 (88.6%) sample tested showed mono microbial bacterial growth and 23 (12.3%) samples showed poly microbial positive blood cultures. Results of study proved that in blood culture samples mono microbial bacterial agent were responsible for more bacterial growth than poly microbial growth agents, which is in accordance with results of this study. (15)

Study conducted in year 2019, "Bacteriological profile and drug resistance patterns of blood culture Isolates: A five year audit from tertiary care hospital". By Fatima Fasih , Samina Baig , Sambreen Zameer et all. showed that blood culture reports were screened for the presence of bacterial growth. Then Frequency of different bacterial isolates along with their antibiotic resistance pattern was noted and analyzed. Results showed that during the study period, 13544 blood cultures were analyzed of which 18% were positive for growth. Among those 97% were bacterial isolates and only 2% were candida species. Among the Gram positive isolates, Coagulase negative Staphylococcus (20%) and Staphylococcus aureus (14%) were the commonest. Among the Gram-negative isolates, Salmonella species (18%) followed by Klebsiella species (15.7%) and E.coli (12.9%) and Pseudomonas species (7%). Staphylococcus aureus was found highly resistant to penicillin (95%), followed by erythromycin (68%), Co-trimoxazole (56%), Fusidic acid (54%) and Oxacillin (48%).Resistance was found to be on lower side against ciprofloxacin (38%), gentamicin (21%), chloramphenicol (13%) and Amikacin (6%).All isolates were sensitive to Linezolid. Salmonella species was resistant to ampicillin (54%) followed by Ciprofloxacin (44%), Cotrimoxazole (44%) and Chloramphenicol (44%). (16).

CONCLUSION:

Gram negative bacteria involving mono microbial agent growth is responsible for most of bloodstream infections.. Gram Negative bacterial growth is responsible for blood infection in 93.3% of cases whereas 6.7% of bloodstream infections are caused by Gram Positive bacterial growth. Mono microbial agent growth causes 92.6% blood stream infections and poly microbial agents cause 7.4% blood stream infection. Bloodstream infections caused by Gram Positive

Bacteria are associated with S. Aureus is 38.8% and 1.9% are associated with Streptococcus spp. In bloodstream infections caused by Gram Negative bacteria, Salmonella spp is responsible for 14.2% cases, Klebsiella spp is responsible for 13.5% cases, Acinetobacter spp is responsible for 11.6% cases, E.coli and Pseudomonas are responsible for 6.5% of cases, enterococcus spp is responsible for 3.2 % of cases, proteus and Enterobacter spp is responsible for 6% of cases, candida spp is responsible for 2.5 % of cases. salmonella specie showed susceptibility (100%) to Aztreonam, ceftriaxone, Moxifloxacin, Tigecyclin and meropenam. Klebsiella specie showed susceptibility (100%) to Cefaclor, tegeyclin and vancomycin. Pseudomonas shows susceptibility (100%) to moxifloxacin and cotrimoxazole. Enterococcus shows susceptibility (100%) to linezolid and vancomycin. E.coli shows susceptibility (100%) to gentamycin and meropenam. Streptococcus shows susceptibility (100%) to Augmentin, Ciprofloxacin, Doxycycline, Fusidic Acid, Moxifloxacin, Vancomycin and Staphylococcus Aureus shows susceptibility (100%) to Tigecyclin, Vancomycin.

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