ORIGINAL ARTICLE

Bacterial spectrum and antibiogram of pediatric blood stream infections in a tertiary care set-up of Islamabad: A wake-up call to implement antimicrobial stewardship programme

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ABSTRACT

Background: Blood stream infections (BSI) are frequently widespread in the pediatric population targeting over 25 million children yearly with a projected mortality of around three million globally. It remains a significant global health concern especially in developing countries with a substantively high disease burden. Current study is aimed at establishing bacteriologic profile and antibiogram in pediatric patients using blood cultures as a gold standard and to guide towards proper empiric therapy and help preclude adverse consequences of this disease.

Material and Methods: This descriptive, cross sectional study was carried out in Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad from January 2023 till June 2023. Patients aged 1 day till 12yrs with strong clinical suspicion of sepsis were included in the study. Blood cultures were dealt with in the microbiology lab to determine the bacterial spectrum along with their antimicrobial susceptibility.

Results: Out of 3288 blood samples, 723(21.9%) isolates yielded positive growth. The pre-dominant isolates were gram negative rods i.e. 403(55.7%) followed by gram positive bacteria 296(40.9%), while 24(3.3%) isolates yielded Candida spp. *Staph aureus*1 27(17.5%)*, Klebsiella pneumonia* 149(20.6%), *and Pseudomonas aeuroginosa* 81 (11.2%) were identified as the most prevalent isolates. Vancomycin, Linezolid, Imipenem, Meropenem and Colistin showed higher sensitivity against majority of the bacterial isolates.

Conclusion: This study highlights the microbiological profile and antibiogram of pediatric sepsis and underscores the need to implement antimicrobial stewardship programme to contest this ever-rising multi-drug disease burden.

Keywords: Antibiogram, Blood stream infections (BSI), Multi-drug resistance (MDR)

BACKGROUND

Blood stream infections (BSI) are frequently widespread in children contributing as one of the foremost causes of morbidity and mortality in this population.[1] Sepsis targets around 25 million children yearly with estimated 3 million mortalities in neonates and adolescents globally[2]. It remains a significant global health concern particularly in developing countries where an extensively high ailment burden prevails exerting a deleterious influence on health and quality of life.[3] It is noteworthy that the mortality rate of neonatal sepsis is maximum in regions of Asia and sub-Saharan Africa.[4] Though appropriate diagnosis and treatment is crucial for reduction of BSI-associated complications, conversely, prior empiric antibiotic treatments, inadequate consumption of drugs, and meager dietary status altogether escalate this mortality menace more by accentuating multidrug resistance.[5,6] Furthermore, the range of isolates causing bacteremia along with their antibiotic resistance vary amongst different geographical areas and healthcare sites and hence, awareness of the relevant epidemiology and antimicrobial susceptibility at regional, domestic and global levels is essential to direct towards suitable empiric therapy and preclude adverse outcome. For definitive diagnosis of blood stream infections, the gold standard is to isolate the causative bacterial pathogen from blood and sterile body fluids culture.[7]

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Conferring to Infectious Diseases Society of America (IDSA) guidelines on Antimicrobial stewardship program, it is sturdily recommended to establish an institute specific antibiogram for different health care associated infections (HAIs). This can significantly support in formulating and practicing effective treatment within first few hours of hospital admission leading to an active decline in the mortality as well as contest antimicrobial resistance in any health care setting.[8] To our dismay, there is scarce data present in our country on the etiology and susceptibility pattern of blood stream infections (BSI) in pediatric population.

MATERIAL AND METHODS:

This study was conducted at Pakistan Institute of Medical Sciences (PIMS), Islamabad from 1st January 2023 till 30th June 2023. Non-probability consecutive sampling technique was carried out. All data was kept confidential and used solely for research purpose. Approval from Institutional Ethical Committee (No.F.3-1/2023(ERRB)/ Chairman) was taken. Written consent of all study participants was taken from parents/guardians. Children ranging from one day of life till 12 years age who were hospitalized during study period with strong clinical suspicion of bacteremia (supported by other laboratory parameters) and whose blood cultures yielded growth of an identifiable bacterial pathogen (not predominantly encompassed as commensal flora) were included and isolated. Children who received any kind of oral or parenteral antibiotics in last three days of the sample to be drawn and/ or with known focus of infection other than bacteremia were not included in the study. For each patient, demographic data such as gender, age, category of admission, duration of hospital visit and primary diagnosis with comorbidities was recorded.

According to CDC description (2023), all bloodstream infections presenting in >48 hours after hospital admittance reflected hospital-acquired bloodstream infections (HABSI), whereas bloodstream infections presenting before this time were considered as community-acquired bloodstream infections (CABSI).

Data Collection:

Blood sample was drawn from every patient after vigilant antisepsis of venipuncture site and before commencing any kind of antibiotic treatment. These samples were inoculated aseptically in Versa TREK blood culture bottles, labeled properly and dispatched to Microbiology department as soon as possible. Upon arrival in the lab, these bottles were immediately incubated in automated microbial detection system i.e. Versa TREK blood culture machine (Thermo Fisher Scientific, USA) and observed continuously for growth for five days. On the basis of machine identification, a positive signaled blood culture bottle was sub cultured on Blood, Chocolate and MacConkey agar plates. Direct Gram staining was also performed on every sample. After overnight incubation, the colonies grown on culture media were dealt with and identified further based on colony morphology and rapid biochemical tests. Once preliminary Identification was made, isolate specific biochemical tests were performed as well as sensitivity disks were applied on Mueller Hinton agar (according to latest CLSI 2023 guidelines) by adopting “Kirby Baur Disc Diffusion” technique. The definitive identification of isolates up to species level was done with API 20E & API 20 NE (Biomerieux, France) in case of Gram-negative Isolates. For Gram positive isolates, confirmatory biochemical testing was done according to preliminary identification and included DNAse, catalase, coagulase tests and or Lancefield Grouping etc. All statistical data was documented on a specifically designed proforma to keep the record.

Statistical Analysis: Qualitative variables like gender, age and distribution of isolated bacterial pathogens along with their species and strain type as well as their antibiogram were documented as frequency and percentages. Age was represented as mean and standard deviation. Inferential statistics were evaluated by using chi-square test. P-value significance was set at <0.05. SPSS version 28 was used to evaluate the recorded data.

RESULTS

In the course of study, 3288 blood samples were sent to lab in total for blood culture analysis, out of which 723 (21.9%) turned out to be positive. Among these positive cases, male patients were 413(57.1%) while female patients were 310(42.8%). The male to female ratio was 1.3:1. There were 193 (26.6%) children aged below one year, 110 (15.2%) amongst one to five years, 231 (31.9%) aged 5 to 10 years while 189(26.1%) belonged to 10 to 12 years age group. (Table-I). Out of total positive isolates i.e 723, Gram positive bacteria came out to be 296(40.9%) while 403(55.7%) isolates were gram negative while 24(3.3%) isolates yielded *Candida* spp (Table-II).

Bacterial spectrum revealed *Klebsiella pneumoniae* in majority as 149(20.6%), followed by coagulase-negative *staphylococci* (CoNS) 134(18.5%) from the positive blood cultures isolates. *Staphylococci aureus* in 127(17.5%), *Pseudomonas aeruginosa* in 81 (11.2%), E. coli in 79(10.9%), *Salmonella typhi* in 60(8.2%), *Acinetobacter spp.* in 34(4.7%), *Enterococcus spp.* in 29(4.0%) *Candida spp.* in 24(3.3%) and *Bacillus spp.* in 06(0.8%) children (Figure-I).

Table-I: Age and gender wise distribution of isolates (n=723).

Gender wise Distribution		
Gender	**Number (n)**	**%age**
Males	413	57.1%
Females	310	42.8%
Age wise Distribution		
Age Group	**Number (n)**	**%age**
1 day-<1 yr.	193	26.6%
1yr-<5 yr.	110	15.2%
5-<10 yr.	231	31.9%
10-12 yr.	189	26.1%

Table-II: Number and percentage of different isolates (n=723).

Pathogen type	**Number (n)**	**%age**
Gram Positive Bacteria	296	40.9%
Gram Negative Bacteria	403	55.7%
Candida spp	24	3.3%

Table-III: Antibiotic susceptibility pattern of gram-negative blood stream isolates (n=403, 55.7%).

Antibiotics	***Klebsiella pneumonia* n=149(36.9%)**	***Pseudomonas aeuroginosa* n=81(20.01%)**	***E.coli* n=79(19.6%)**	***Salmonella typhi* n=60(14.8%)**	***Acinetobacter baumanni* n=34 (8.4%)**
AMP	IR	IR	6	28	IR
AMC	12	IR	13	NT	17
CRO	16	IR	17	29	17
CAZ	NT	73	19	NT	19
FEP	21	51	31	NT	19
SCF	23	82	35	NT	21
TZP	21	79	33	NT	23
IPM	52	81	76	100	22
MEM	35	83	78	NT	25
CN	47	79	81	NT	79
AK	41	78	83	NT	81
CIP	17	62	23	13	27
LEV	43	71	49	NT	31
CT	100	100	100	NT	98
AZM	NT	NT	NT	98	NT
CAP	NT	IR	NT	29	NT
SXT	NT	IR	NT	27	NT

AMP= Ampicillin, AMC= Co-amoxiclav, CRO= Ceftriaxone, CAZ= Caftazidime, FEP= Cefepime, TZP= Piperacillin-tazobactam, SCF= Cefoperazone-sulbactam, IPM= Imipenem, MEM= Meropenem, CN= Gentamicin, AK= Amikacin, CIP= Ciprofloxacin, LEV= Levofloxacin, SXT= Cotrimoxazole, CAP= Chloramphenicol, CT= Colistin, AZM= Azithromycin, IR= Intrinsic resistance, NT= Not Tested, NR= Not Recommended

Table-IV: Antibiotic susceptibility pattern of gram-positive blood stream isolates (n= 156).

Antibiotics	***Staph. aureus* (MSSA) n= 38 (24.3%)**	***Staph. aureus* (MRSA) n= 89 (57%)**	***Enterococcus* spp. n=29 (18.5%)**
P	7	6	72
AMP	NT	NT	77
FOX	100	0	NT
E	55	52	NR
DA	49	41	IR
DOX	63	56	NR
SXT	67	62	IR
C	43	47	39
CN	87	85	IR
CIP	37	33	37
VA	100	100	93
LZD	100	100	100

P= Penicillin, FOX= Cefoxitin, E= Erythromycin, DA= Clindamycin, DOX= Doxycycline, SXT= Cotrimoxazole, C= Chloramphenicol, CN= Gentamicin, CIP= Ciprofloxacin, VA= Vancomycin, LZD= Linezolid, RIF= Rifampin

DISCUSSION

Blood stream infections (BSIs) is an ever-rising public health distress with fatal nosocomial outcome. Regardless of all progress in advanced countries, sepsis is still a leading health problem particularly in unindustrialized countries ensuing worldwide fatality and growing treatment costs.[9,10] Among these countries, sepsis is common chiefly among children and neonates identifiable to the prevailing poor socio-economic and living circumstances, perinatal complications, insufficient immunization and poor nourishment. In addition, during hospital stay there is a prerequisite for invasive devices that further accentuates this situation serving as a source for pathogens to attack and multiply unimpeded leading to sepsis.[11] Amongst the pediatric population, BSIs initiated by multidrug-resistant(MDR) bacteria poses a frightening threat because these infections are linked with extended ICU stays, high disease burden with meager consequences and high financial impact.[12] Hence, understanding the common causative bacterial agents of sepsis along with their antibiogram can guide towards pertinent empiric therapy and play a dynamic role in subsiding the ever rising danger of resistance to available treatment options.[13]

In the present study, 3288 blood cultures with suspicion of sepsis were received in Microbiology laboratory and analyzed. Out of these, 723(21.9%) revealed positive microbial growth which is in correspondence with a study done by Adnan and colleagues in The Children's Hospital, Multan reflecting the blood culture positivity around 19.9%.[14] Another systematic review done by S.*et al* showed overall percentage of 19.1% positive blood cultures in Africa and 28.0% in Asia respectively.[15] In a study done by Rozina and colleagues, 10.1% cases tested positive for bacterial growth in blood cultures which is a bit lower than our findings.[16] However, Mehta *et al* reported an overall blood culture isolates rate around 44% which is very high as compared to our study.[18]

The current study indicated that the primary pathogens responsible for blood stream infections were gram negative bacteria i.e. 55.7% followed by 40.9%-gram positive cocci and 3.3% isolates were identified as *Candida* species. This is in accordance with the study done by Adnan and colleagues revealing gram negative rods as the most repeatedly isolated strains found among 69 (44.8%) cases.[14] Comparable to this study, gram negative bacteria were predominant in 63.9% cases followed by gram-positive bacteria in 35.8% cases in the study done by S.*et al*.[15] Study done by Rozina and colleagues also showed *Pseudomonas spp*. (33.7%) followed by *Staphylococcus epidermidis* (22.1%) being most prevalent, though other organisms were also detected in varying proportions.[16] On contrary, in a study done by Hafsa and colleagues in Karachi , gram positive cocci were the predominant isolates followed by gram negatives. [17] Another study done by Mehta *et al* also revealed that majority of isolates were Gram Positive cocci (70%); with *Staphylococcus aureus* (53%) being the most predominant organism.[18] In the current study, the gram positive isolate most commonly isolated was *coagulase-negative staph*(CoNS) 134 (18.5%) followed by *S. aureus* 127(17.5 %) which is comparable to the studies done by Rozina and colleagues and Hafsa and colleagues.[16,17] Adnan and colleagues also showed CoNS as the most frequently isolated gram positive cocci in their study.[14] On contrary, Wattal *et al* revealed *S.aureus* as chief pathogen among gram positive cocci.[21] Mehta *et al* also reported *S.aureus* as primary isolate among gram positive cocci.[18]

In the present study, there was an increased prevalence of sepsis in male gender i.e. 57.1% followed by 42.8% females which is comparable to study done by Adnan and colleagues revealing 95 (61.6%) male and 59 (38.4%) females.[14] The blood culture positivity rate for males was also higher i.e. 55% followed by 45% females in a study done by Mehta *et al* in India.[18] This finding can be supported by a gender – bias and fondness for male children in our society that leads to their early presentation at tertiary health care facilities.[19,20] On contrary, a study done by Hafsa and colleagues showed female pre-dominance with 127(63.8%) females and 72(36.20%) males.[17]

In the present study, Gram-negative isolates mainly encompassed enteric coliforms i.e. *Klebsiella spp.* (36.9%), *E.coli* (19.6%), and non-fermenters like *Pseudomonas aeuroginosa* (20.01%), *Salmonella typhi* (14.8%), and *Acinetobacter spp.* (8.4%). Similarly, Hafsa and colleagues also showed that coliforms i.e. *E. Coli* 24 (12.1%), *Pseudomonas aeruginosa* 14(7%), *Klebsiella pneumoniae* 13(6.5%) were common species leading to sepsis.[17] Another study done by Wattal *et al* in India showed *Klebsiella p*neumoniae as the most common species in case of hospital acquired septicemia and *S.typhi* and *S. paratyphi A* as the leading cause of community acquired sepsis.[21] Another study done by Mehta *et al* also exhibited *Klebsiella pneumoniae* and *E.coli* as most common pathogens followed by *Pseudomonas aeruginosa* and *Acinetobacter spp*.[18] On the other hand, Adnan and colleagues reported *Salmonella typhi* as the commonest bacterial agent in 30 (19.5%) cases followed by *Acinetobacter baumannii* in 16 (10.4%) cases.[14] However, *Enterobacter spp.* was identified as the commonest cause of pediatric sepsis in Iran.[22] It can be clearly understood that the different rates of prevalence are most likely due to different geographical locations.

CONCLUSION

In this study, a high antibiotic resistance pattern was observed among the isolated gram negative and gram-positive blood stream infections pathogens signifying the need to implement Antimicrobial Stewardship Programme (ASP) on priority basis in hospital settings. Since, there are very few broad-spectrum antibiotic options left to treat a high multi-drug-resistant disease burden; every institute should establish its antibiogram annually and observe strict compliance to it. This can effectively ensure timely management of sepsis in every hospital setting of Islamabad as well as countrywide. This is the only way forward to combat this alarming health distress.

LIMITATIONS

This was a single Centre study. For antibiotic susceptibility, MIC testing could not be done.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Samia Wazir Khawaja: Substantial contributions to study design, acquisition of data, manuscript drafting or reviewing it critical for important intellectual content, has given final approval of the version to be published, accountable for all aspects of publication

Umme Farwa: Manuscript drafting or reviewing it critical for important intellectual content, has given final approval of the version to be published, accountable for all aspects of publication

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