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A Five-year Review of Bacteremia among Jordanian Children: Pathogens and Antimicrobial Susceptibility Patterns

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The present study was conducted to investigate microorganisms causing bacteremia in Jordanian children and to assess their sensitivity to various groups of antimicrobial. A retrospective study was conducted on a positive blood cultures taken from children aged below 15 years, who attended as outpatient clinics or inpatient at the Princess Rahmah Hospital between 2005 and 2009. Out of 18792 tested blood samples, a total of 1519 isolates were recovered from blood cultures obtained from children patients. The male to female isolates ratio was (1.35:1.0). *Staphylococcus aureus* was the most frequently isolated pathogen (68.2%), followed by *Klebsiella spp.* (23.5%), *Streptococcus spp.* (4.3%), *Enterobacter sp. (2.8%)* and *Pseudomonas spp.* (1.2%). Approximately 80% of varieties of blood isolates were susceptible to vancomycin. Aztreonam was the lowest active antimicrobial agents (16.0%) against varieties of blood isolates. Study concludes that *Staphylococcus aureus* was the main isolate in bacteremic children. Among variety of bacteremia isolates, susceptibility rate was 79.4% to vancomycin. Overall aztreonam resistance was near 84%, and this rate not affected due to type of blood isolates. Careful and continuous monitoring of antimicrobial resistance pattern will help guide appropriate therapeutic selection and may provide early detection of changes in resistance to more potent agents.

Keywords: Antimicrobial resistant; Bacteremia; Pediatric patients.

Bacteremia is a common cause of morbidity and mortality in children (Reimer *et al*., 1997) in both developed and developing countries (Dawodu *et al* 1997, Stoll *et al*., 1998, Bhutta and Yusuf, 1997, and Orrett and Shurland, 2001). Therefore, bacteremia continues to be a serious problem that needs immediate attention and treatment.

For an accurate diagnosis and an appropriate choice of antimicrobials, blood culture, which usually takes a few days, is required. The empirical choice of antimicrobials for the treatment of bacteremia is guided by an awareness of previous culture reports. Up-to-date information on the local etiologic patterns and antimicrobials sensitivities is also important.

Different factors contribute changing the prognosis of the infection such as the type of microorganism, age, underlying disease and where the bacteraemia was acquired (Cisterna *et al*., 2001). However, bloodstream infections in hospitalized patients are usually attributable to the use of central venous lines.

In a prospective five-year study on 344 clinically significant episodes of pediatric septicemia the commonest organisms were *Salmonella spp.* (15.0%), followed by methicillinresistant *S. aureus*. They reported that *Haemophilus influenzae* accounted for 2.0% of all episodes (Cheng *et*

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al., 1991). Another study also reported that of 408 bacterial strains, *Salmonella spp.* were the most commonly isolated (23%), followed by *S. aureus*, *Acinetobacter-Moraxella* (Gedebou *et al*., 1984). The most frequent etiologic agents of bacteraemia cases include *Staphylococcus spp., Streptococcus spp., Enterobacter spp., Escherichia coli, Klebsiella pneumonia and Pseudomonas spp*. (Reimer *et al*., 1997, Cisterna *et al*., 2001).

However, etiology of bacteremia and their sensitivity have been changing over the past years (Gedebou, 1982, Shah and Watanakunakorn, 1979). The rapid emergence of multidrug resistant bacteremia in developing countries is a new potential threat to the survival of newborn babies, who are in a poor health condition. Therefore, this study was conducted to assess the causative organisms and antimicrobials susceptibility pattern of bacteremia pathogens isolated from children between the years of 2005-2009 at the Princess Rahmah Hospital in Irbid, Jordan. The importance of this study is to aid clinicians to facilitate the empiric treatment and management of children with symptoms of bacteremia. Moreover, the data would also help authorities to formulate antibacterial prescription policies.

MATERIALS AND METHODS

This retrospective study was conducted on 18792 blood specimen obtained from sick children (≤ 15 years of age) who attended the Princess Rahmah Hospital as outpatient or inpatient and were diagnosed with bacteremia between 2005 and 2009. A total of 1519 isolates were recovered from blood cultures, and the repeated positive blood cultures were not considered.

The microbiological and antibacterial susceptibility data of the study were obtained from the records of clinical microbiology laboratory of the Princess Rahmah Hospital. These data were filled in a prepared data sheet. Sampling process, culturing, bacterial identification and susceptibility testing for antimicrobials were as follows:

Blood specimens were collected in a blood culture bottle that contained 50 ml of tryptose phosphate broth and 0.02% polyanethol sulfonate (liquid). Following standard aseptic procedure, culture was incubated at 37ºC for 24 hours prior to the isolation and identification of the bacteria.

Based on the Gram-staining characteristics of the bacteria growth in the blood culture bottle was subcultured onto MacConkey agar, Salmonella-Shigella agar, and Nutrient agar and/or blood agar plates. Bacteria isolated from colonies were further characterized by special biochemical and serological methods (Ewing, 1986).

All isolates were tested for their susceptibilities to at least 8 out of 12 antimicrobials using antimicrobial diffusion discs (Bauer *et al*., 1960). Bacterial sensitivity was tested for the following antimicrobials: Amikacin, Amoxicillin-Clavulanic acid, Aztreonam, Cefotaxime, Ceftazidime, Ceftriaxone, Ciprofloxacin, Gentamicin, Imipenem, Pipracillin, Tobramycin and Vancomycin.

Data were analyzed statistically using SPSS (version 15 for Windows) program calculating the frequency and cross tabulations.

This protocol was approved by the Ethics Committee of the Ministry of Health in Jordan (MOH, REC, 08, 0057).

RESULTS

In a five years period (2005-2009), a total 1519 out of 18792 blood samples of children below 15 years of age (55.8% male and 44.2% female) that gave a positive blood culture reaction were studied.

Results showed that the majority of pathogen isolated were *Staphylococcus aureus* (68.2%), followed by *Klebsiella spp.* (23.5%), *Streptococcus spp*. (4.3%), *Enterobacter spp*. (2.8%) and *Pseudomonas spp* (1.2%) (Table 1).

Antimicrobial susceptibility rates for 12 selected antimicrobial agents of different classes used in this study are summarized in Table 2.

The highest susceptibility rate for all different bacterial blood isolates was to vancomycin (79.4%), whereas aztreonam exhibited the lowest susceptibility rate of 16.0% (Figure 1 & Table 2).

DISCUSSION

This current study provides information regarding the main etiological agent *S. aureus* that causes bacteremia in children in both inpatients and outpatient setting and its antimicrobial susceptibility patterns during the years of 2005-

2009. These results are in agreement with other studies that reported *S. aureus* as the most common bacteria isolated from blood of children (Nimri and Batchoun, 2004, Rahman *et al*.,2002 and Sabui *et al*., 1999). An increase in the occurrence of *S. aureus* bacteremia is likely to be related to the increased use of intravascular catheters in medical care centers and puncture wounds (Lark *et al*., 2001, Miller *et al*., 1998).

The second most common organism causing bacteremia in this study was *Klebsiella* spp. (9%). Similar results were reported by Rahman *et al* 2008. However *Klebsiella* was the most common cause of neonatal sepsis in Karachi, Pakistan (Bhutta and Yusuf, 1997). Whereas, *Pseudomonas aeruginosa* was the most common organism (38.3%) followed by *Klebsiella* (30.4%) and *E. coli* (15.6%) (Joshi *et al*., 2000, Orrett and Shurland, 2001, Greenberg *et al*., 1997).

In this study, the occurrence of *Streptococcus spp, Enterobacter spp Pseudomonas spp* were 4.3%, 2.8% and 1.2% respectively. Higher

Table 1. Frequency of isolation of causative organisms of bacteremia in Jordanian children (2005-2009)

Organism	2005 N (%)	2006 N (%)	2007 N (%)	2008 N (%)	2009 N (%)	Total N (%)	M	F
Staph. Aurous	86 (48.0)	110 (65.1)	127 (59.6)	326 (86.2)	387 (66.7)	1036 (68.2)	585	447
Klebsiella spp	70 (39.1)	34 (20.1)	63 (29.6)	34 (9.0)	156 (26.9)	357 (23.5)	210	147
Strepto coccus	8 (4.5)	16 (9.5)	4 (1.9)	7 (1.9)	30 (5.2)	65 (4.3)	40	25
Enterobacter	4 (2.2)	7 (4.2)	19 (8.9)	8 (2.1)	5 (0.9)	43 (2.8)	24	19
Pseudomonas	11 (6.2)	2 (1.1)	00	3 (0.8)	2 (0.3)	18 (1.2)	11	7
Total	179 (100.0)	169 (100.0)	213 (100.0)	378 (100.0)	580 (100.0)	1519 (100.0)	874	645

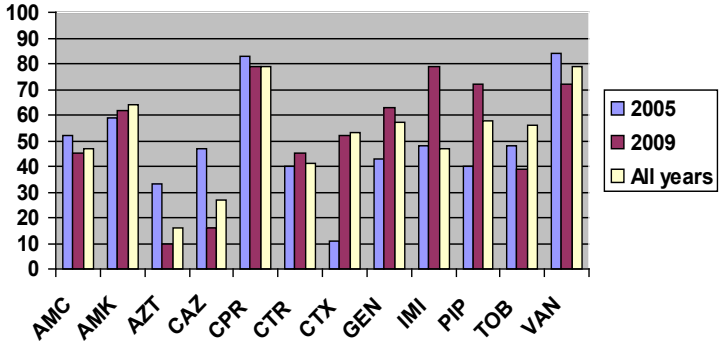
Table 2. Antimicrobial susceptibility among variety of bacteremia isolates in children to various antimicrobials

Drug	2005 N= 179 N (S%)	2006 N= 169 N (S%)	2007 N= 213 N (S%)	2008 N= 378 N (S%)	2009 N= 580 N (S%)	Total N= 1519 N (S%)	Significance 2005 vs. 2009 P-value
AMC	25 (52.0)	50 (48.0)	24 (33.3)	40 (67.5)	373 (45.8)	512 (47.4)	NS
AMK	166 (59.0)	166 (51.8)	203 (58.1)	369 (77.5)	512 (62.3)	1416 (64.0)	NS
AZT	159 (33.3)	165 (20.0)	190 (24.2)	357 (5.8)	211 (9.9)	1082 (16.0)	<0.05
CAZ	162 (46.9)	165 (43.0)	172 (29.6)	322 (27.6)	527 (16.8)	1348 (27.8)	<0.05
CPR	157 (82.8)	168 (74.4)	150 (76.0)	300 (81.0)	177 (79.6)	952 (79.0)	NS
CTR	135 (40.7)	162 (35.1)	184 (39.1)	337 (43.0)	333 (45.3)	1151 (41.7)	NS
CTX	34 (11.7)	115 (51.3)	168 (49.4)	310 (63.8)	510 (52.3)	1137 (53.7)	NS
GEN	114 (43.8)	117 (48.7)	186 (56.9)	331 (55.8)	508 (63.9)	1256 (57.5)	NS
IMI	166 (48.7)	163 (34.3)	197 (44.1)	353 (7.0)	528 (79.1)	1407 (47.4)	<0.05
PIP	159 (40.8)	161 (50.3)	182 (61.5)	349 (49.5)	518 (72.3)	1369 (58.8)	<0.05
TOB	168 (48.8)	160 (71.2)	173 (59.5)	365 (77.5)	504 (39.0)	1370 (56.8)	<0.05
VAN	86 (84.8)	108 (84.2)	158 (68.3)	332 (91.5)	489 (72.8)	1173 (79.4)	<0.05

N= Number of isolates

S = Sensitive

(Amoxicillin-Clavulanicacid (AMC), Amikacin (AMK), Aztreonam (AZT), Ceftazidime (CAZ), Ciprofloxacin (CPR), Ceftriaxone (CTR), Cefotaxime (CTX), Gentamicin (GEN), Imipenem (IMI), Pipracillin (PIP), Tobramycin (TOB), Vancomycin (VAN))



N= Number of isolates
S = Sensitive
(Amoxicillin-Clavulanicacid (AMC), Amikacin (AMK), Aztreonam (AZT), Ceftazidime (CAZ), Ciprofloxacin (CPR), Ceftriaxone (CTR), Cefotaxime (CTX), Gentamicin (GEN), Imipenem (IMI), Pipracillin (PIP), Tobramycin (TOB), Vancomycin (VAN))

Fig. 1. Antimicrobial susceptibility among variety of bacteremia isolates in children to various antimicrobials

occurrence of these blood isolates was reported in different literature (Nimri and Batchoun,2004, Joshi *et al*., 2000, and James *et al*., 2005).

During the study period, the most effective antimicrobial agent against variety of bacteremia isolates was vancomycin (79.4%), followed by ciprofloxacin (79.0%), amikacin (64.0%), pipracillin (58.8%) gentamicin (57.5%) and tobramycin (56.8%), while the lowest susceptibility rate was to ceftazidime (27.8%), and aztreonam (16.0%).

Susceptibility rates of different blood isolates showed improvement to amikacin, cefotaxime, ceftriaxone, gentamicin, imipenem and pipracillin in comparison between the years of 2005 vs. 2009. This increment was significant ($P<0.05$) for imipenem and pipracillin. The cause of significant improvement in the activity of imipenem and pipracillin is may due to little use of these medicines in treatment of bacterial infection in children. In contrast, susceptibility rates of variant blood isolates showed significant decreases ($P<0.05$) to aztreonam, ceftazidime, tobramycin and vancomycin in comparison between the years of 2005 vs. 2009. The cause of significant decrement in the activity of tobramycin and vancomycin is may due to intensive use of these medicines in treatment of bacterial infection in children. By the way, amoxicillin-clavulanic acid, and ciprofloxacin also showed decreases in their activity, but this decrement was not significant. Similar results for vancomycin, ciprofloxacin and amoxicillin-cavulanate were reported in the literature[23, 24, 25].

In conclusion, bacteremia in children is mainly caused by *Staphylococcus aureus* organisms, which develop resistance to commonly used antimicrobials. This emergence of multiple drug resistance calls for a continuous monitoring and reviewing of antimicrobial policy in the hospital and the country at large. Therefore, this study is important for clinician in order to facilitate the empiric treatment of children with symptoms of bacteremia. Moreover, the data would also help authorities to formulate antimicrobial prescription policies.

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