ORIGINAL ARTICLE

Sepsis in Infants: Analysis of Bacterial Pathogens and their Antibiotic Susceptibility, A Study at Government Tertiary Care Hospital, Karachi

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ABSTRACT

Objective: To assess the frequency of causative bacterial pathogen of sepsis in infant, their antibiotic susceptibility and to determine resistance pattern in commonly used antibiotics.
Place and Duration of Study: Central Lab Civil Hospital, Karachi, 6 months.
Study Design: Retrospective Descriptive observational study.
Patients and Method: All 1414 reports of blood samples send for culture/sensitivity of infants admitted in Civil Hospital Karachi during the study period were scrutinized for bacterial pathogen, their frequency, antibiotic susceptibility and resistance pattern.
Result: Out of 1414 infants, 604 (42.7%) had positive blood culture. Gram positive bacteria were predominant (54.1%) than gram negative (45.9%). Male: female ratio was found to be approximately 1:0.9. Total 9 organisms were isolated, in which staphylococcus aureus predominates followed by Pseudomonas aeruginosa and Escherichia coli respectively. The overall sensitivity of the organism to Amikacin and Cefotaxime were 60.87%and 36.67% respectively which are currently in use as empirical therapy in pediatric ward of CHK. The organisms were most sensitive to Vancomycin (95.54%), Sparfloxacin (94.16%), Linezolid (93.56%), while mostly resistant to kanamycin (56.21%), cephalosporins (55.9%), Gentamycin (54.31%) and amoxicillin (51.11%).
Conclusion: Gram positive organisms were identified as the major threat for sepsis in infants. An emerging pattern of resistance was observed against commonly used antibiotic so there is a need to control the spread of these resistant strains through infection control programs and continuous monitoring of drug resistant patterns.

Key words: Septicemia in infants, culture and sensitivity pattern, drug resistance.

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INTRODUCTION

Sepsis is defined as systemic inflammatory response syndrome resulting from suspected or proven infection.[1] According to an estimate of World Health Organization (WHO), out of 4 million neonatal deaths occurring around the world every year,[2] approximately 98% of these deaths occur in developing countries.[3] Neonatal sepsis is a predominant cause of morbidity and mortality and reason for frequent hospital admissions of children in developing countries.[4]

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Pakistan accounts for about 7% of global neonatal deaths.[5] One third of these deaths occur due to infections.[6] Infants are at highest risk, with 10 times higher than that of older children. Low and very low-birth-weight (VLBW) babies make up nearly one fourth of the pediatric sepsis population.[7]

Sepsis in children is a life-threatening emergency and any delay in treatment may cause death. Initial signs of sepsis are slight and nonspecific. Therefore, in suspected cases, empirical antibiotic therapy should begin immediately without awaiting the results[8] of blood culture and sensitivity reports. Early treatment and appropriate use of antibiotics minimize the risk of severe morbidity and mortality in sepsis and reduce the emergence of multi-drug resistant organisms in intensive care units by rational antibiotic use.[9]

The distribution of pathogens causing sepsis in a specific hospital unit is usually considered when empiric antibiotics are selected.[10] The bacteriological profile of neonatal septicemia is constantly under change with advances in early diagnosis and treatment. Thus the rational protocol for sepsis management must be based on adequate knowledge of the causative organism and their antibiotic sensitivity pattern in related area.[4]

In Pakistan, a very little data is available on infant's sepsis and their antibiotic susceptibility and resistance. So we have planned to provide the health management an open access to those antibiotics which are more sensitive to common bacteria now a day.

METHODOLOGY

The study was conducted at central lab CHK during the period of December 2010 -May 2011. A 5ml Blood sample of infants under one year of age admitted in pediatric wards of CHK with clinical sign and symptoms of sepsis as defined by WHO, were received by the lab for Culture and sensitivity. The blood was aseptically drawn and inoculated into the BD BACTEC culture bottle and incubated for 5days. Sub culture was done on Blood Agar, Chocolate Agar and Mc.Conkeys Agar and incubated at 37^0C aerobically. The plates were then examined for any bacterial growth. Gram staining and various biochemical and serological test were done for identification and antibiotic susceptibility was checked by Kirby Baur Disc diffusion technique. Blood culture reports were developed and a copy of the same was sent to the concerned unit. The data was analyzed through SPSS version 16.0 and frequency and percentages were calculated for each qualitative variable. The effective antibiotics were determined by applying chi-square test with significant values $P < 0.05$. Isolates showing intermediate level of resistance were classified as sensitive.

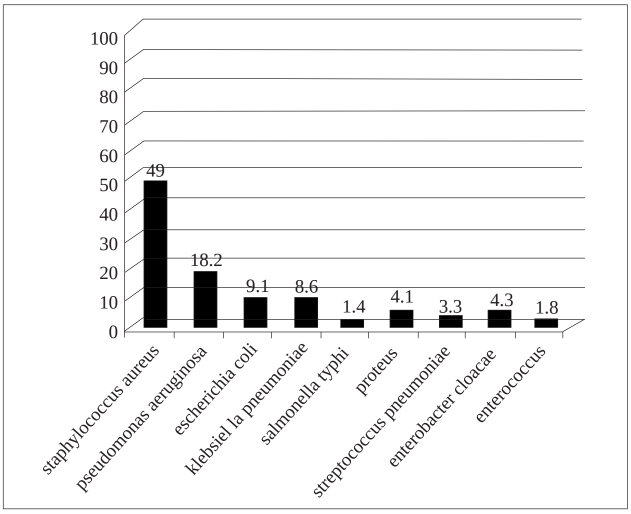
RESULTS

During the study period of 6 months, total 1414 blood samples of infants (under one year of age) suspected with sepsis were included. Out of these, 604 (42.7%) had positive blood culture. Of these, 322 (53.3%) were males and 282 (46.7%) were females. Male: female ratio was approximately 1:0.9. In 604 positive blood culture reports, Gram positive bacteria was found in 54.1% as compared to gram negative (45.9%). A total 9 organisms were isolated; in which staphylococcus aureus (49%) predominates followed by Pseudomonas aeruginosa (18.2%) and Escherichia coli (9.1%) respectively (Graph 1).

The antibiotic sensitivity pattern of the bacterial isolates was also analyzed. The overall sensitivity of the organisms was found with Amikacin and Cefotaxime (60.87%and 36.67% respectively) which are currently in use as empirical therapy in pediatric ward of CHK. Overall, the organisms were most sensitive to Vancomycin (95.54%), Sparfloxacin (94.16%), Linezolid (93.56%), while resistance was mostly to cephalosporins, (Cefaclor 81.55%, Cephradine 78.85%, Cefixime 75.69%, and Cefuroxime 75.47%), kanamycin 56.21%, Gentamycin 54.31% and amoxicillin 51.11%. (Graph 2)

According to the Sensitivity and resistance pattern of bacterial isolates, sparfloxacin and vancomycin were found to be most sensitive with most of the bacterias, where as amoxicillin and Kanamycin was the most resistant to the isolated bacteria. (Table I)

Graph 1: Frequency of Bacterial Pathogens (In Percentages)



DISCUSSION

Sepsis is a predominant cause of morbidity and mortality and reason for frequent hospital admissions of children. It is a life-threatening emergency and any delay in treatment may cause death. In our study positive blood cultures were found to be 42.7%.This suggests that sepsis in infants remained major cause of morbidity in hospitals. Similar studies were conducted in 2002 and 2008 in CHK which showed 55.2%[11] and 30.9%[12] positive cultures respectively, showing these percentages are not varying much in the same hospital within 10 years. Different researches in Pakistan showed different results such as 40% positive cultures in Islamabad,[13] 32% in Lahore,[14] 62.8% in Peshawar.[15]

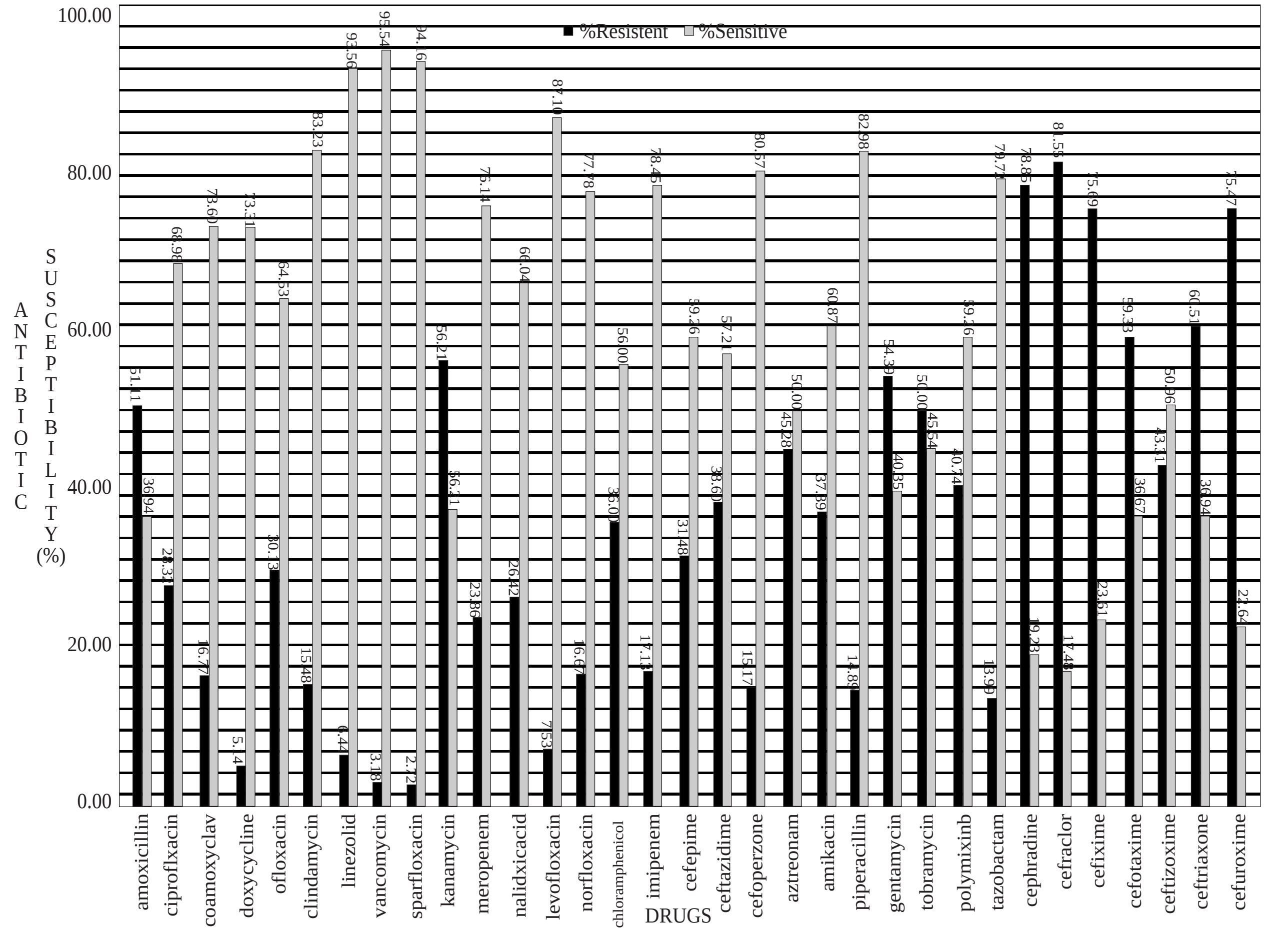
In our study, all cultures yielded single pathogen. This is similar to other studies conducted in Karachi[12] and Lahore.[16]

Gram positive cocci were most frequent 54.1% which is in contrast to previous studies in CHK,[11,12] Pakistan[14,15,17] and neighboring countries.[18-20] However, in a study[21] gram positive organisms were found to be the main cause of neonatal sepsis in Karachi. Similar predominance of Gram-positive organisms was reported in different centers in Nigeria.[22,23]

Table I: Sensitivity Pattern of Bacterial Isolates

NO.	Bacteria	Most Sensitive Antibiotic	Total Used	Sensitivity	Most Resistant Antibiotic	Total used	Resistance
1.	Staphylococcus Aureus	1.sparfloxacin	116	97.41%	1.kanamycin	270	57.78%
		2.vancomycin	292	97.26%	2.amoxicillin	294	52.04%
		3.linezolid	293	93.52%	3.ciprofloxacin	264	39.05%
		4.clindamycin	288	85.42%	4.ofloxacin	291	38.14%
		5.coamoxyclav	290	83.45%	5.cefepime	66	34.85%
2.	Pseudomonas Aeruginosa	1.sparfloxacin	47	93.62%	1.Gentamycin	110	54.55%
		2.ceftazidime	106	77.36%	2.tobramycin	108	49.07%
		3.ciprofloxacin	93	90.32%	3.aztreonam	103	44.66%
		4.Pipera/tazobactam	58	89.66%	4.polymixinb	106	41.51%
		5.amikacin	110	64.55%	5.imipenem	108	18.52%
3.	Escherichia coli	1.sparfloxacin	26	96.15%	1.cefixime	53	77.36%
		2.levofloxacin	51	90.20%	2.cefaclor	53	71.70%
		3.cefoperzone	35	77.14%	3.cephradine	52	67.31%
		4.ofloxacin	53	75.47%	4.cefuroxime	51	62.75%
		5.Pipera/tazobactam	27	74.07%	5.ceftriaxone	51	52.94%
4.	Klebsiella pneumoniae	1.levofloxacin	48	91.67%	1.cefaclor	48	91.67%
		2.ofloxacin	49	85.71%	2.cefixime	48	93.75%
		3.ciprofloxacin	45	82.22%	3.cefuroxime	49	98.14%
		4.cefoperzone	13	76.92%	4.ceftriaxone	48	87.54%
		5.ceftizoxime	46	50%	5.cefotaxime	45	80%
5.	Salmonella typhi	1.ofloxacin	7	100%	1. amoxicillin	9	66.67%
		2.sparfloxacin	5	100%	2.ceftizoxime	8	50%
		3. imipenem	9	88.9%	3.ceftizoxime	2	50%
		4. levofloxacin	9	88.9%	4.chloramphenicol	9	44.4%
		5. norfloxacin	9	88.9%	5.cefixime	9	44.4%
6.	Proteus	1.cefoperzone	20	95%	1.amoxicillin	15	60%
		2.norfloxacin	18	94.44%	2.cefotaxime	19	57.89%
		3.Pipera/tazobactam	18	94.44%	3.ceftriaxone	25	56%
		4.levofloxacin	25	92%	4.ceftizoxime	24	45.83%
		5.ofloxacin	24	87.5%	5.cefixime	11	45.45%
7.	Streptococcus pneumoniae	1.vancomycin	20	95%	1.kanamycin	18	38.89%
		2.linezolid	20	95%	2.ofloxacin	20	20%
		3.coamoxyclav	20	90%	3.clindamycin	20	25%
		4.amoxicillin	18	88.89%	4. -		
		5.ciprofloxacin	20	75%	5. -		
8.	Enterobacter cloacae	1.levofloxacin	26	96.15%	1.amoxicillin	23	60.8%
		2.imipenem	26	92.30%	2.cefixime	23	60.86%
		3.cefoperzone	25	92%	3.cefotaxime	26	50%
		4.Piper/tazobactam	6	100%	4.ceftizoxime	26	46.15%
		5.ofloxacin	22	86.36%	5.ceftriaxone	25	40%
9.	Enterococcus	1.imipenem	11	81.81%	1 -		
		2.Coamoxyclav	11	72.72%	2. -		
					3. -		

Graph 2: Combined Susceptibility Pattern of Antibiotics in All Bacterial Pathogens



The male gender Preponderance in our study is similar with few other previous studies.[13,15,16,18-20]

Staphylococcus aureus emerged as most frequent causative agent of septicemia in our study (49%). As it is a normal flora of skin, lack of awareness about safety protocols during medical procedures in overall society may be a cause of such high prevalence. Other two common organisms were Pseudomonas auregnosa (18.2%) and Escherichia coli (9.1%). We found change in frequency of different organism in CHK with time as in 2008, Escheria coli and Staphylococcus aureus were most common[12] while in 2005, klebsiella pneumoniae was the major isolate (24%) followed by staphylococcus aureus (22%).[11] Studies outside Karachi showed high incidence of Escherichia coli in Lahore[14] and Multan[9] and enterobacter in Islamabad.[13] Among neighboring countries, enterobacter was most common in Iran,[19] pseudomonas and klebsiella in India[18] and Bangladesh.[20] Thus different geographical areas have different prevalence.

Group B streptococcus (GBS) was not isolated from any culture in our study, the same has been reported in most of the studies in Pakistan.[14,11,15] However, a single isolate was reported in a previous study at CHK,[12] AKU[24] Karachi and Peshawar[25] which showed incidence of sepsis with GBS. In contrast, western countries reported GBS as their frequent isolate.[26] This difference may be because of presence of strains of low virulence, low prevalence of colonization of GBS in pregnant women or simply because of low socioeconomic condition resulting in death of most early onset sepsis (EOS) babies at home which remain unreported.

In our study, Staphylococcus aureus showed high resistance to ampicillin (75%) which corresponds with other studies.[11,13,19,20] This demonstrates that the use of this drug is now inappropriate. However, it remained sensitive to vancomycin (97%) as reported by others also.[10,12,14,17] This suggests that guidelines should be made for prudent use of Vancomycin, in an attempt to prevent the spread of vancomycin resistant strains.

Over all, Flouroquinolones remained highly sensitive in most of the organisms.[13,25] Among them, ciprofloxacin showed overall 68.9% sensitivity. This indicates that it may be a good choice for septicemia in infants as it is inexpensive, penetrates CSF, has good oral bioavailability[27] and has an acceptable safety profile in infants.[28,29]

There is considerable degree of resistance in Cephalosporins ranging from 15% (cefoperzone) to 81.55% (cefaclor). Similar degree of resistance is reported in different studies as well.[9,13,15,17] Cefotaxime (an empirical therapy drug in CHK) showed considerable resistance (59.33%) against gram negative rods. This emerging pattern of resistance is supported by the work of A. Mahmood et al,[17] Batool A et al[11] and others[9,13,15,19] suggesting that the cautious use of cefotaxime should be promoted as resistance to this may evoke a great challenge for physicians in choosing antimicrobial therapy, as the treatment options for cephalosporin resistant strains are limited.

Aminoglycosides showed moderate degree of resistance against most of gram negative rods ranging from 37% (amikacin) to 56% (kanamycin). In contrast, in a study[11] conducted in in CHK reported significant resistance for aminoglycosides, same was found in other studies.[14,15,30] However, in our study among aminoglycosides, Amikacin showed good sensitivity and this pattern is consistent to that found by Mahmood et al in Karachi[17] and Shams et al[13] in Islamabad.

Amikacin and Cefotaxime are currently used as empirical treatment in infants at our hospital which showed 60.87% and 36.67% sensitivity respectively. However, the observation in the present study may not be conclusive because the sensitivity of Amikacin and cefotaxime is not tested for gram positive cocci (Staph. Aureus) in CHK Lab, hence, it is highly recommended that lab should check these drugs, as they are important therapy against Staphylococcus and pseudomonas and we are lacking current susceptibility pattern of most prevalent organisms to them, in our setup.

CONCLUSION

We conclude from our study that Staphylococcus aureus is a major cause of sepsis in infants admitted in CHK. Moreover, the frequency of bacterial pathogens and antibiotic susceptibility is varying geographically and with time. Also, the antibiotic susceptibility profile of different organisms is showing considerable resistance to conventional antibiotics. Therefore, routine bacterial surveillance and study of their resistance patterns is essential for formation of antibiotic policy guidelines, and such a study should be carried out in every hospital on periodic basis. In this context, we propose the continuation of use of Amikacin in our current empirical therapy. In order to reduce morbidity and mortality it is crucial to consider latest guidelines and prudent use of antibiotics focused on accurate dosage.

LIMITATIONS

According to our limitations, we were unable to differentiate between early and late onset of sepsis as records were available for age in years only. Secondly, in our setup, methicillin is not tested for staphylococci so MRSA strains prevalence is still indefinable.

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