REPORT

PAEDIATRIC NOSOCOMIAL INFECTIONS: RESISTANCE PATTERN OF CLINICAL ISOLATES

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ABSTRACT

Hospital acquired infections are transmitted to patients by hospital personnel and other patients, or they may arise from patient's own endogenous flora. Children are one of the most susceptible subjects associated in the hospital-acquired infections and have a higher prevalence rate for infections. This problem is at its extremes in developing countries like Pakistan where in most of cases the severity depends on the hygienic conditions of the Hospitals and lack or lapse of infection control measures.

To have a surveillance type of data in this regard, one hundred and twenty four isolates of *Pseudomonas aeruginosa*/Pseudomonas species, *Staphylococcus aureus* (MRSA/MSSA) and *Klebsiella* species, that are commonest among the nosocomial infection causing organisms, were collected from pediatric hospital settings in Karachi. A study of incidence and resistance pattern by Kirby Baur disc diffusion method, with selected antimicrobials, was carried out.

These isolates were resistant against most antimicrobials tested. Drugs like mmipenem, meropenem, amikacin, vancomycin (especially in MRSA or BRSA), Fucidic acid (for burns and other infections) and some of the 3rd generation cephalosporins were found quite effective.

Keywords: Nosocomial, antimicrobics, resistance, pediatric.

INTRODUCTION

The term Nosocomial infection (NIs), or Hospital-acquired infection, is applied to any clinical infection that causes illness which was neither present nor was in incubation period when the subject entered the hospital. The sources and mode of NIs are airborne spread, water-borne spread, food acquired spread and contact spread (Suggs, 1999). Microorganisms on the hands of staff may be resident (present but not removed by washing) or transient (recently acquired from another source), Inoculation mode of spread; blood transfusion and tissue donation, infection by accidental inoculation, infection from contaminated infusion fluids are the examples of infections spread by inoculation in a Hospital. Spread by Indwelling medical devices; cannulae used for different admixtures and drug administrations lead to bacterial colonization and resultant infection (Maki *et al*., 1973; Nejjari *et al.,* 2000 and Su *et al*., 2001).

Unlike adults, children, especially the neonates are more susceptible to such kind of infections. In the present study the intrauterine and perinatal infections of maternal origin such as rubella, listeriosis and group B streptococcal and candida infections were not included. Neonatal intensive therapy units usually have a prevalence of about 20% nosocomial infections due to virulent and usually antibiotic resistant strains because of following reasons:

1 Children admitted usually have weak immune system, so they may acquire the colonization of any type of organism.
2 Ill babies require more handling hence the chances of spread by contact are more.

EXPERIMENTAL

Collection of specimens

One hundred and twenty four isolates of *Pseudomonas aeruginosa*, *Pseudomonas sp. Staphylococcus aureus* and Klebsiella sp., recovered from cases of hospital-acquired infections were collected from pediatric hospital settings of Karachi during July and December 2001. The age of patients ranged from 8 months to 12 years. The isolates were identified on the basis of biochemical reactions and maintained on trypticase soy agar till tested for antimicrobial sensitivity by Kirby-Bauer method.

Briefly

- Isolates and the control strains were brought to room temperature and were inoculated in Mueller Hinton broth tubes.
- The tubes were incubated at 37°C for 2-4 hours so that turbidity could be matched to Macfarlane No5 standard. If required turbidity was adjusted with sterile Muler Hinton broth.

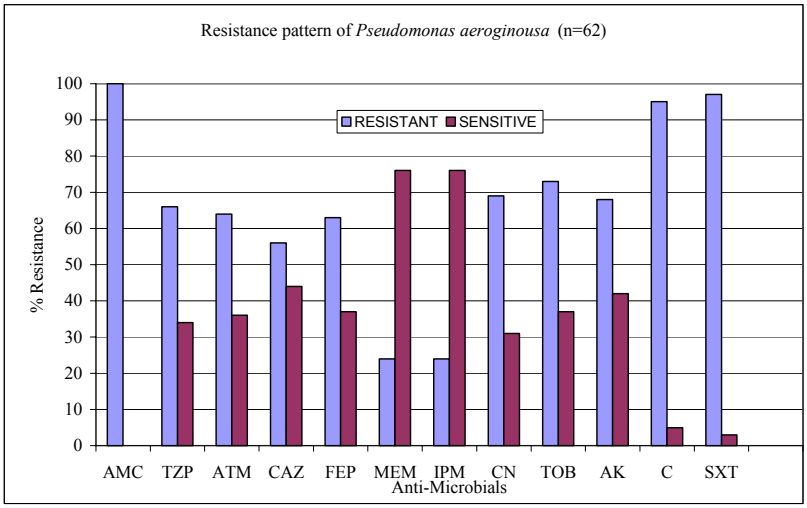

Fig. 1: Resistance in *Pseudomonas aeroginousa*

Key: AMC=Co-amoxiclav, TZP=Tazobactam, ATM=Aztreonam, CAZ=Ceftazidime, FEP=Cefipime, MEM=Meropenem, IPM=Imipenem, CN=Gentamycin, TOB=Tobramycin, AK=Amikacin, C=Chloramphenicol, SXT=Co-trimoxazole*

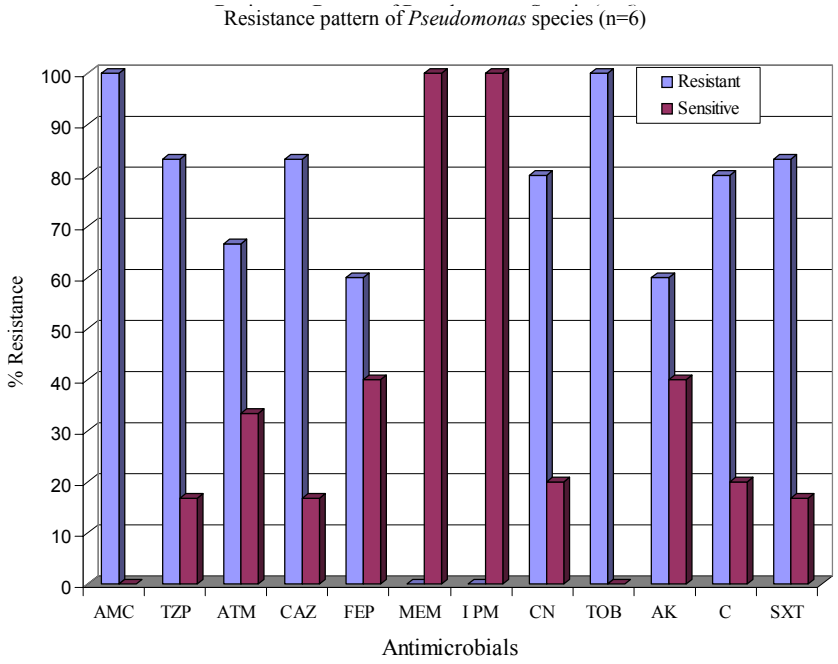

Fig. 2: Graphical representation of resistance in *Pseudomonas* sp.

Key: AMC=Co-amoxiclav, TZP=Tazobactam, ATM=Aztreonam, CAZ=Ceftazidime, FEP=Cefipime, MEM=Meropenem, IPM=Imipenem, CN=Gentamycin, TOB=Tobramycin, AK=Amikacin, C=Chloramphenicol, SXT=Co-trimoxazole.

- Petri dishes of Muller Hinton agar for sensitivity were dried and labeled.
- Test- organism was inoculated on agar using a sterile cotton swab.
- Antibiotic discs were then placed on agar using a sterile forcep.
- Petri plates were incubated at 37°C for 24 hours.
- A ruler was used to measure the zone of inhibition. For determination of sensitivity, appropriate interpretive zone diameters were used as per National Committee for Clinical Laboratory Standards USA, recommendations (NCCLS).

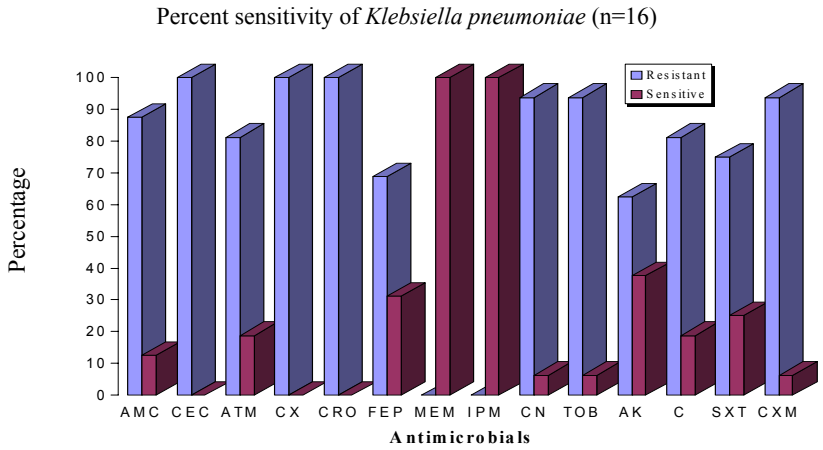

Fig. 3: Graphical representation of resistance in *Klebsiella pneumoniae*.

Key: AMC=Co-amoxiclav, CEC=Cefaclor, ATM=Aztreonam, CX=Cloxacillin, CRO=Ceftriaxone, FEP=Cefipime, MEM=Meropenem, IPM=Imipenem, CN=Gentamycin, TOB=Tobramycin, AK=Amikacin, C=Chloramphenicol, SXT=Co-trimoxazole, CXM=Cefuroxime*.

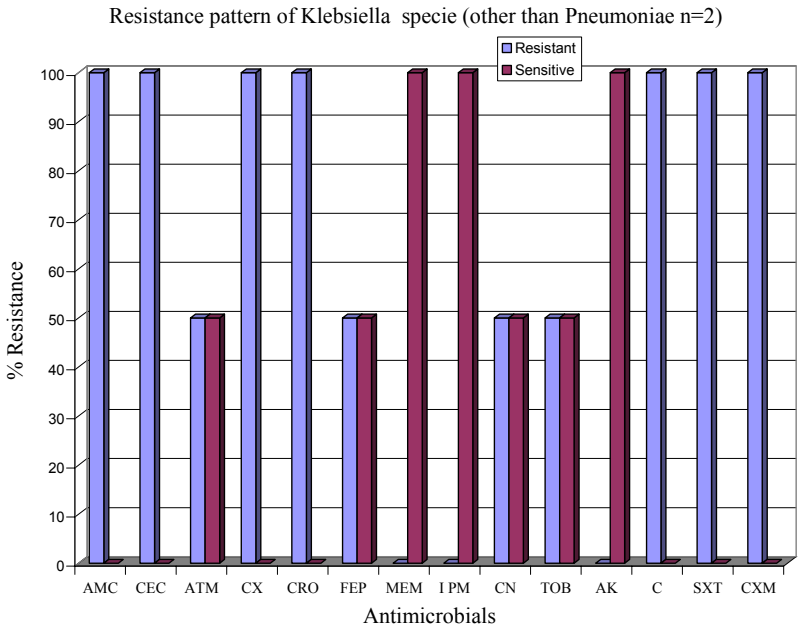

Fig. 4: Graphical representation of resistance in *Klebsiella* sp.

Key: AMC=Co-amoxiclav, CEC=Cefaclor, ATM=Aztreonam, CX=Cloxacillin, CRO=Ceftriaxone, FEP=Cefipime, MEM=Meropenem, IPM=Imipenem, CN=Gentamycin, TOB=Tobramycin, AK=Amikacin, C=Chloramphenicol, SXT=Co-trimoxazole, CXM=Cefuroxime*.

RESULTS AND DISCUSSION

Nosocomial infections are the most difficult and tedious to manage and control. This study was conducted to find out the incidence of hospital acquired infections in paediatric settings in the city as well as to generate data regarding the antibiotic sensitivity pattern of isolates causing such infections. So that initiation of empirical therapy could be made more effective in such infections.

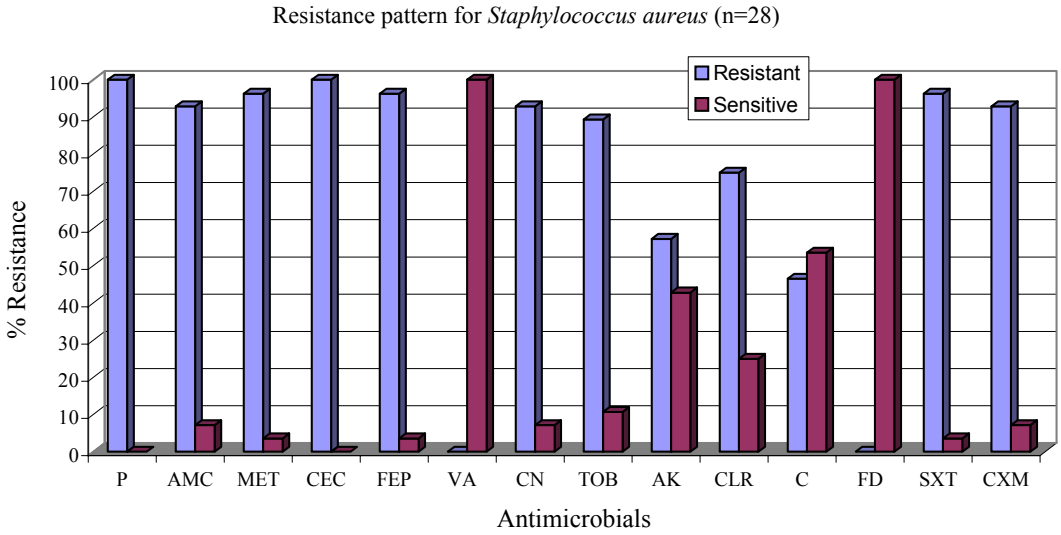

Fig. 5: Graphical representation of resistance in *Staphylococcus aureus.*

Key: P=Penicillin, AMC=Co-amoxiclav, MET=Methicillin, CEC=Cefaclor, FEP=Cefipime, VA=Vancomycin, CN=Gentamycin, TOB=Tobramycin, AK=Amikacin, CLR=Clarithromycin, C=Chloramphenicol, FD=Fucidic Acid, SXT=Co-trimoxazole, CXM=Cefuroxime.

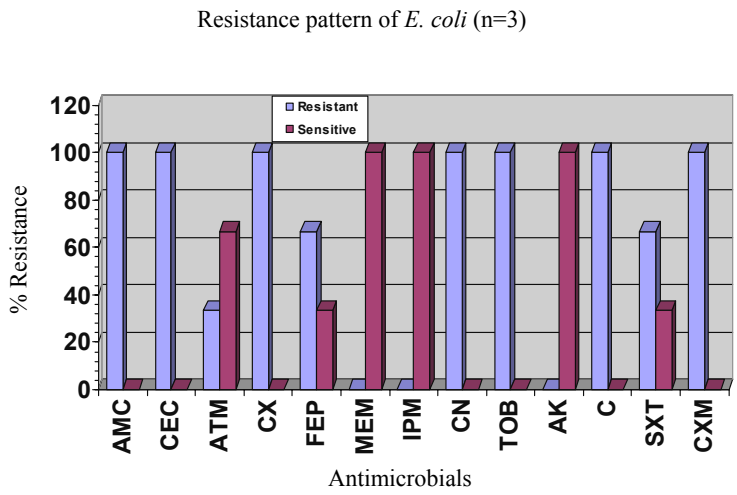

Fig. 6: Graphical representation of resistance in *E. coli.*

Key: AMC=Co-amoxiclav, CEC=Cefaclor, ATM=Aztreonam, CX=Cloxacillin , FEP=Cefipime, MEM=Meropenem, IPM=Imipenem, CN=Gentamycin, TOB=Tobramycin, AK=Amikacin, C=Chloramphenicol, SXT=Co-trimoxazole, CXM=Cefuroxime*.

In a study *Pseudomonas aeruginosa* were sensitive to amikacin (89.7%), tobramycin (75.81%), norfloxacin (68.48%), piperacillin (68.25%) and ceftazidime (58.81%) and few isolates were resistant to gentamicin, carbenicillin, tobramycin, ceftazidime and augmentin (Ahmad *et al*., 1995). Majority of the isolates in the present study were *Pseudomonas aeruginosa* (n = 62). Their sensitivity to imipenem and meropenem was 76%. All isolates were resistant to augmentin, ceftazidime, chloramphenicol, gentamycin, tobramycin and cotrimoxazole (table 1 and fig. 1). Antibiotic-resistant Gram-negative organisms are a significant risk to severely ill children and in many instances these are imported into the unit or rapidly acquired from environmental reservoirs (Toltzis *et al*., 1997).

Table 1: Percentage distribution of resistance in *Pseudomonas aeroginousa* against different antibiotics

Resistance pattern of *Pseudomonas aeroginousa*												
Isolates	AMC	TZP	ATM	CAZ	FEP	MEM	IPM	CN	TOB	AK	C	SXT
62	0	33.87	35.48	43.54	37.09	75.80	75.80	30.64	27.41	32.25	4.83	3.22

Table 2: Percentage distribution of resistance in *Pseudomonas* sp. against given antibiotics

Resistance Pattern for *Pseudomonas sp.* (other than aeroginousa)												
Isolates	AMC	TZP	ATM	CAZ	FEP	MEM	IPM	CN	TOB	AK	C	SXT
6	0	16.66	33.33	16.66	40.0	100	100	20	0	40.0	20	16.66

Table 3: Percentage distribution of resistance in *Klebsiella pneumoniae* against given antibiotics

Resistance pattern for *Klebsiella pneumoniae*.														
Isolates	AMC	CEC	ATM	CX	CRO	FEP	MEM	IPM	CN	TOB	AK	C	SXT	CXM
16	12.5	0	18.75	0	0	31.25	100	100	6.25	6.25	37.5	18.75	25.0	6.25

Table 4: Percentage distribution of resistance in *Klebsiella* sp. against given antibiotics

Resistance pattern for *Klebsiella sp.* (other than *pneumoniae*)														
Isolates	AMC	CEC	ATM	CX	CRO	FEP	MEM	IPM	CN	TOB	AK	C	SXT	CXM
2	0	0	50	0	0	50	100	100	50	50	100	0	0	0

Table 5: Percentage distribution of resistance in *Staphylococcus aureus* against given antibiotics

P	AMC	MET	CEC	FEP	VA	CN	TOB	AK	CLR	C	FD	SXT	CXM
100	92.6	96.4	100	96.4	0	92.8	89.3	57.2	75	46.5	0	96.4	92.8

Key: P=Penicillin, AMC=Co-amoxiclav, MET=Methicillin, CEC=Cefaclor, FEP=Cefipime, VA=Vancomycin, CN= Gentamycin, TOB=Tobramycin, AK=Amikacin,

Table 6: Percentage distribution of resistance in *E. coli.* against given antibiotics

Isolates	AMC	CEC	ATM	CX	FEP	MEM	IPM	CN	TOB	AK	C	SXT	CXM
3	100	100	33.33	100	66.66	0	0	0	0	0	100	33.33	100

Pseudomonas sp. represents about 5% (n=6) of the isolates tested. The five most effective antimicrobials against *Pseudomonas aeruginosa* were meropenem (76%), imipenem (76%), then CAZ (44%), FEP (37%) and ATM (35%). While 100% Pseudomonas sp. were sensitive to meropenem and imepenem. Cefipime and amikacin inhibited 40% isolates of Pseudomonas species and aztreonam could inhibit only 33% isolates (table and fig. 2). *Klebsiella pneumoniae* resistant to third-generation cephalosporins and gentamicin was isolated from two patients in a paediatric intensive care unit (Grogan *et al.,* 1998). The organism was also isolated from a nurse and from the father of one of the children in a study (French *et al*., 1996). High incidence of strains of *Klebsiella pneumoniae* resistant to cephalosporins of the 3rd generation have been observed (Kolar *et al.,* 1995). In the present study *Klebsiella pneumoniae* was the third most common organism (13%) causing Nosocomial Paediatric Infections (table 3). Usually prescribed antimicrobials failed to inhibit this organism and the most effective antimicrobials against such organisms were meropenem (100%), imipenem (100%). While amikacin (36%) cefipime (32%) and co-trimoxazole (19%) did not exhibit significant activity against these isolates (fig. 3).

Klebsiella sp., (table 4) the effective antimicrobials like meropenem and imipenem among the carbapenems and amikacin among the aminoglycosides that shown 100%

activity. Others were gentamicin and tobramycin, ATM and FEP (fig. 4)

Methicillin-resistant *Staphylococcus aureus* (MRSA), endogenous in healthy people, often causes nosocomial infections (Suzuki *et al.,* 1997). In a study, a total of 40 MRSA cases out of 991 acutely burned children were identified (Sheridan *et al*., 1994). In another study, 878 methicillin-resistant *Staphylococcus aureus* (MRSA) strains were recovered from the pediatric hospital in Lisbon (Sa-Leao *et al.,* 1999). In a study, one hundred thirty-two (26.4%) of children were colonized with *S. aureus*. In another study 11 (8.3%) of the *S. aureus* isolates were MRSA (Suggs *et al*., 1999). Significant increase in nosocomial infections by multi-resistant Staphylococcus (*Staphylococcus aureus*) with *in-vitro* and *in-vivo* resistance to Teicoplanin was observed (Tuo *et al.,* 1995). Present study shows that *Staphylococcus aureus* was the second most common agent (n = 28) causing a highly resistant type of infection that could not be controlled by conventional antibiotic therapy (table 5). In most cases only Vancomycin and fucidic acid were the effective antimicrobials (100%). Other than vancomycin and fucidic acid, chloramphenicol and amikacin (53 and 47% respectively) were found effective (fig. 5).

Data are limited on the prevalence, patterns of resistance and risk factors associated with resistant organisms, including *E. coli*, in children. Selective antimicrobial pressure and multiple admissions to hospital were among the risk factors associated with antimicrobial resistance (Allen *et al*., 1999). Although *E. coli* is one of the most abundantly existing organisms associated in the PNIs its occurrence is not that much in the present study. In this study only 3 strains were included and were susceptible to usually applied antimicrobials.

Based on the above facts it is concluded that the usually prescribed antimicrobials fail to control the paediatric nosocomial infections and tend to result in the use of much pharmacoeconmically inappropriate par-enteral antimicrobials. The antimicrobials like imipenem, meropenem, amikacin, vancomycin (especially in MRSA or BRSA), and Fucidic acid (for burns) and some of the 3rd generation cephalosporins were found most effective and hence can be useful provided that these are used in appropriate dosage and regimen.

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