Bacteriological Profile and Antimicrobial Sensitivity Pattern of Blood Isolates in Children: A Hospital Based Study in Kathmandu, Nepal

Rai GK*, Manandhar R**, Karki S***, Prajapati B*, Thapa UB****, Mahat T****, Singh G****
*Senior consultant paediatrician, **Pathologist, ***Paediatrician, ****Senior medical technologist.

ABSTRACT

INTRODUCTION: Antimicrobial sensitivity pattern changes over time. Periodic monitoring of microorganisms and evaluation of their antibiotic sensitivity is very important for the rational use of antibiotics. Objective: This study was conducted to evaluate the bacteriological profile and antimicrobial sensitivity pattern of blood isolates in children.

METHODS: This retrospective hospital based study was conducted over one year period. Records of all blood samples collected for culture from children aged 1 day to 14 years were reviewed and all positive samples were analyzed for types of isolates and their antibiotic sensitivity.

RESULT: Out of 10883 blood samples collected, 419 samples yielded organisms. The most common blood isolate was *Staphyloccus* aureus (37.0%) followed by *Escherichia coli* (27.4%), *Salmonella sp* (14.4%), Coagulase negative *Staphylococci* (6.9%), *Neisseiria elongata* (4.7%), *Klebsiella sp* (3.6%) and *Streptococcus sp* (3.4%). *Pseudomonas aeruginosa*, *Streptococcus faecalis, Serratia marcescens* and *Hafnia alves* were the least frequent blood isolates. The most effective antibiotic for *Staphylococcus aureus* was amikacin (95.7%) followed by ofloxacin (84.6%), chloramphenicol (82.4%), vancomycin (80.0%) and ciprofloxacin (78.4%) while the least effective was cephalexin (2.6%) followed by cloxacillin (9.1%), cefixime (19.1%) and ceftazidime (20.6%). Similarly, the most effective antibiotic for E coli was amikacin (87.9%) followed by ofloxacin (82.9%), ciprofloxacin (82.4%) and tobramycin (88.3%) where as the least effective antibiotic was cephalexin (1.4%) followed by cefixime (22.2%), ceftazidime (23.2%) and cefotaxime (48.9%).

CONCLUSION: The most frequently isolated organisms were found to be acceptably sensitive to amikacin, chloramphenicol, ofloxacin and ciprofloxacin but highly resistant to other commonly used antibiotics like amoxicillin, ampicillin, cephalexin, cefixime, cloxacillin, cefotaxime, ceftriaxone and ceftazidime.

KEY WORDS: antimicrobial sensitivity, antimicrobial resistance, bacteriological profile, blood culture, blood isolates

INTRODUCTION

Infectious diseases are the major cause of morbidity and mortality in infants and children worldwide.[1] About 60.0% of these infections are viral and self limiting [2] and do not need antibiotics for their treatment unless they are complicated by bacterial super-infection. Despite this fact, antibiotics have been in use irrationally and inappropriately in our communities and such practice has been reported to be as high as 85.0%.[2] Such irrational practice is considered as one of the causes of increasing prevalence of drug resistant organisms posing a great challenge to medical personals. Antimicrobial sensitivity pattern is also changing rapidly as the microorganisms evolve new resistant mechanisms themselves spontaneously. [3]

Correspondence :
Dr. Ganesh Kumar Rai,
Kanti Children's Hospital, Kathmandu, Nepal
E-mail: drganeshrai@gmail.com

Infections associated with bacteremia may range from self-limiting episodes to potentially life threatening

conditions like septicemia and septic shock.[4] The incidence of bacteremia varies widely, ranging from 25 to 50%.[5] Early diagnosis and appropriate treatment of blood stream infections is of outmost importance to substantially reduce the incidence of shock and increase survival of patients.[4] Isolation of microorganisms from blood culture is the gold standard for the confirmation of such conditions.[6]

Prudent and potent antibiotic use not only prevents the emergence and spread of resistant strains of microorganisms but also benefit the patient and a nation as a whole.[7] Choice of appropriate antibiotics is, therefore, crucial for the management of patients and reduction of the complications. However, such choice is complicated by increasing antibiotic resistance worldwide.[4] Effective management of patient needs evidence based rational prescription practices. Frequent periodic review of causative organisms and their sensitivity pattern will help rationalize such prescription practices.[8,9] There is a great need of continuing resistance surveillance of antibiotics for rational use of antimicrobial agents and reduction of multi-drug resistant strains of microorganisms.[4] Such prevalence studies or surveys of microorganisms and their sensitivity patterns also provide the rational for preventive strategies like the vaccination programs against certain organisms.[10] Therefore, this study was conducted to analyze the blood isolates and their antimicrobial sensitivity pattern in infants and children at Kanti Children's Hospital.

METHODS

This was a retrospective study conducted at Kanti Children's Hospital, Kathmandu, Nepal over the time period of one year, from April 2011 to March 2012. Children of age group ranging from 1day to 14 years attending the inpatient & outpatient department of KCH were enrolled. Blood samples collected for culture from these children were analyzed for the growth & types and their antibiotics sensitivity. Three ml of blood was collected by aseptic venipuncture and mixed in 30 ml of brain heart infusion (BHI) broth for culture. If the collected blood volume was not adequate (less than 3 ml) the volume of the broth was made 90% of the amount of blood collected. Blood samples collected were subjected to bacteriological culture and incubated at 37^{0}C over night followed by sub-culture on blood agar and MacConkey agar. Incubation was continued for growth negative cultures for 72 hours sub-culturing at 48 and 72 hours. Growth negative cultures even after this period were regarded as negative.

Blood isolates were subjected to antibacterial susceptibility testing following Kirby Bauer disc diffusion technique using Mueller Hinton agar. The antibiotic impregnated discs were placed on the surface of the agar plate and incubated at 37^{0}C for 18 hours. Diameter of the zone of inhibition was measured for individual antibiotic and interpreted as sensitive, intermediate and resistant on the basis of zone size as per manufacturer's instruction.

Antimicroibioal discs used in this study were amikacin, amoxicillin, amoxiclav, ampicillin, cefixime, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, ciprofloxacin, cotrimoxazole, cloxacillin, cephalexin, erythromycin, gentamycin, nalidixic acid, norfloxacin, ofloxacin, penicillin, tobramycin and vancomycin. However, only 6-7 antimicrobial discs were tested for each culture positive sample. If the culture positive sample was found resistance to all 6 or 7 antimicrobials it was tested for other antimicrobials. Selection of the antimicrobial discs to be used was based on the availability of the discs in the hospital laboratory.

The variables investigated were age and sex of the child, species of the blood isolates and their antibacterial sensitivity pattern as these were the only information available in the records. Data analysis was done using SPSS software package version 16.

Permission to undertake this study was taken from the institutional review committee of Kanti Children's Hospital.

RESULTS

Total number of blood samples collected for culture during one year period was 10883, among them 419 samples yielded organisms with the positivity rate of 3.9%. Out of 419 positive samples, samples from male patients predominated females (57.5% vs 42.5%). Blood samples from neonates constituted more than one third (43.0%) of the samples (Table 1).

Table 1: Positive samples by age and sex (n=419)

Age-group	Male		Female		Total	%
	No	%	No	%		
<1 month	101	56.1	79	43.9	180	43.0
1-11 months	55	67.1	27	32.9	82	19.6
1-5 yrs	47	54.0	40	46.0	87	20.7
6-10 yrs	32	54.2	27	45.8	59	14.1
10-14 yrs	6	54.5	5	45.5	11	2.6
Total	241	57.5	178	42.5	419	100.0

Out of 419 isolates, gram negative bacteria were predominant over gram positive (52.7 vs 47.3%).

The most common blood isolate was *Staphyloccus aureus* (37.0%) followed by *Escherichia coli* (27.4%). *Pseudomonas aeruginosa, Streptococcus faecalis, Serratia marcescens* and *Hafnia alvei* were the least frequent isolates each constituting 0.3 % of the total. *Salmonella sp* accounted for 14.4% of the total isolates. Most of the isolates were from the samples from neonates (43.0%) except *Salmonella sp, Neisseria elonga*ta and *Streptococcus sp*. Antibiotic sensitivity pattern of *Salmonella sp* is not included in this study (Table 2).

Table 2: Distribution of blood isolates by age-group (n=419)

Blood isolates	Age-group					Total
	<1 month %	**1-11 months %**	**1-5 yrs %**	**6-10yrs %**	**>10yrs %**	
S aureus	86	34	19	13	3	155
	55.5	21.9	12.3	8.4	1.9	37.0
E-coli	60	30	16	9	0	115
	52.2	26.1	13.9	7.8	0.0	27.4
Salmonella sp	0	0	25	27	8	60
	0.0	0.0	41.7	45.0	13.3	14.4
Coagulase negative *Staphylococci*	12	8	7	2	0	29
	41.4	27.6	24.1	6.9	0.0	6.9
Neisseiria elongate	3	2	11	4	0	20
	15.0	10.0	55.0	20.0	0.0	4.7
Klebsiella sp	10	2	2	1	0	15
	66.7	13.3	13.3	6.7	0.0	3.6
*Streptococcus sp**	5	2	5	2	0	14
	35.7	14.3	35.7	14.3	0.0	3.4
Other gram negative bacteria#	4	4	2	1	0	11
	36.4	36.4	18.2	9.0	0.0	2.6
Total	180	82	87	59	11	419
	43.0	19.6	20.7	14.1	2.6	100.0

**Streptococcus sp* included *Streptococcus pyogenes* (6), *Streptococcus pneumoniae* (4), *Streptococcus viridans* (3) and *Streptococcus faecalis* (1); #other gram negative bacteria included *Enterobacter sp* (6), *Proteus vulgaris* (2), *Pseudomonas aeruginosa* (1), *Serratia marcescens* (1) and *Hafnia sp* (1)

Among the most frequently tested antibiotics for *S aureus*, it was least resistant to amikacin (4.3%) followed by ofloxacin (15.4%), chloramphenicol (17.6%), vancomycin (20.0%) and ciprofloxacin (21.6%) while it was most resistant to cephalexin (97.4%) followed by cloxacillin (90.9%), cefixime (80.9%) and ceftazidime (79.4%) as depicted in table 3.

E coli was found to be least resistant to amikacin (12.1%) followed by ofloxacin (17.1%), ciprofloxacin (17.6%) and tobramycin (21.7%) and most resistant to cephalexin (98.6%) followed by cefixime (77.8%), ceftazidime (76.8%) and cefotaxime (51.1%) among the frequently tested antibiotics as shown in table 4.

The most effective antibiotic for coagulase negative *Staphylococci* (CoNS) in vitro was amoxycillin (100.0%) followed by amikacin (95.8%), ciprofloxacin (92.6%), ofloxacin (89.5%), chloramphenicol (74.6%) and cefotaxime (81.8%) where as the least effective was cloxacillin (0.0%) followed by ampicillin (11.1%) and cefixime (27.2%) as seen in table 5.

Table 3: Antimicrobial sensitivity pattern of *Staphylococcus aureus* (n=155)

Antibiotics	Sensitivity pattern						
	Total	Sensitive	%	Intermediate	%	Resistance	%
Chloramphenicol	148	118	79.7	4	2.7	26	17.6
Amikacin	139	126	90.6	7	5.0	6	4.3
Ciprofloxacin	139	94	67.6	15	10.8	30	21.6
Ceftazidime	136	19	14.0	9	6.6	108	79.4
Cefixime	115	13	11.3	9	7.8	93	80.9
Cefotaxime	89	50	56.2	10	11.2	29	32.6
Cloxacillin	88	7	8.0	1	1.1	80	90.9
Vancomycin	56	36	72.0	4	8.0	10	20.0
Ofloxacin	52	37	71.1	7	13.5	8	15.4
Tobramycin	42	23	54.8	7	16.7	12	28.5
Cephalexin	39	1	2.6	0	0.0	38	97.4
Ampicillin	27	5	18.5	1	3.7	21	77.8
Amoxycillin	5	2	40.0	0	0.0	3	60.0
Amoxiclav	4	1	25.0	0	0.0	3	75.0
Ceftriaxone	3	2	66.7	0	0.0	1	33.3
Gentamycin	2	2	100.0	0	0.0	0	0.0
Cotrimoxazole	1	1	100.0	0	0.0	0	0.0

Table 4: Antimicrobial sensitivity pattern of *E coli* (n=115

Antibiotics	Sensitivity pattern						
	Total	Sensitive	%	Intermediate	%	Resistance	%
Chloramphenicol	112	57	50.9	12	10.7	43	38.4
Ceftazidime	112	9	8.0	17	15.2	86	76.8
Ciprofloxacin	108	61	56.5	28	25.9	19	17.6
Amikacin	107	89	83.2	5	4.7	13	12.1
Cefotaxime	92	20	21.7	25	27.2	47	51.1
Ofloxacin	82	36	43.9	32	39.0	14	17.1
Cephalexin	70	0	0.0	1	2.4	69	98.6
Cefixime	63	10	15.9	4	6.3	49	77.8
Tobramycin	23	15	65.2	3	13.0	5	21.7
Ceftriaxone	8	1	12.5	3	37.5	4	50.0
Amoxiclav	6	1	16.7	0	0.0	5	83.3
Amoxycillin	5	0	0.0	0	0.0	5	100.0
Ampicillin	5	0	0.0	0	0.0	5	100.0
Cloxacillin	4	1	25.0	0	0.0	3	75.0

Table 5: Antimicrobial sensitivity pattern of *CoNS* (n=29)

Antibiotics	Sensitivity pattern						
	Total	Sensitive	%	Intermediate	%	Resistance	%
Ciprofloxacin	27	24	88.9	1	3.7	2	7.4
Chloramphenicol	26	21	80.8	1	3.8	4	15.4
Amikacin	24	22	91.6	1	4.2	1	4.2
Cefixime	22	3	13.6	3	13.6	16	72.8
Ceftazidime	20	10	50.0	3	15.0	7	35.0

Ofloxacin	19	16	84.2	1	5.3	2	10.5
Amoxycillin	12	7	58.3	5	41.7	0	0.0
Cefotaxime	11	9	81.8	0	0.0	2	18.2
Ceftriaxone	10	7	70.0	1	10.0	2	20.0
Ampicillin	9	1	11.1	0	0.0	8	88.9
Tobramycin	7	4	57.1	1	14.3	2	28.6
Cloxacillin	5	0	0.0	0	0.0	5	100.0
Vancomycin	4	4	100.0	0	0.0	0	0.0
Penicillin	1	1	100.0	0	0.0	0	0.0
Cotrimoxazole	1	1	100.0	0	0.0	0	0.0
Gentamycin	1	1	100.0	0	0.0	0	0.0
Erythromycin	1	0	0.0	0	0.0	1	0.0

Neisseria elongata was found to be 100.0% sensitive to ciprofloxacin, ofloxacin, cefotaxime, chloramphenicol and amikacin. Its sensitivity to ceftazidime, ampicillin, cefixime and cloxacillin was 94.4%, 92.3%, 90.0% and 83.3% respectively. However, it was 100.0% resistant to tobramycin.

Among the commonly tested antibiotics, *Klebsiella sp* was shown to be most sensitive to ciprofloxacin (92.3%) followed by ofloxacin (91.6%), amikacin (61.5%), chloramphenicol (58.3%) and least sensitive to ceftazidime (21.3%) and cefotaxime (27.3%). These isolates were found to be 100.0% resistant to cephalexin, cefixime, amoxycillin and ampicillin.

Streptococcus species were found to be 100.0% sensitive to chloramphenicol and bacitracin. Other antibiotics in order of in vitro efficacy were ciprofloxacin (83.3%), erythromycin (71.4%) and cotrimoxazole (66.7%). They were least sensitive to optochin (20.0%) followed by ceftazidime (33.4%), ampicillin (40.0%), penicillin (45.5%) and amoxycillin (50.0%) among the commonly tested antibiotics.

Other gram negative bacteria as mentioned in table 2 were shown to be 100.0% sensitive to ciprofloxacin. After ciprofloxacin, these bacteria were found to be most sensitive to chloramphenicol (90.0%) followed by ofloxacin (71.4%) and amikacin (67.7%) among the most frequently tested antibiotics. They were least sensitive to cefixime (10.0%) followed by cefotaxime (12.5%) and ceftazidime (40.0%). These isolates were seen to be 100.0% resistant to ampicillin, amoxycillin and ceftriaxone.

DISCUSSION

The present study highlights the pattern of blood isolates and their sensitivity pattern in children.

Newborns constituted the most common age group (43.0%) among positive blood isolates in this study which is in consistent with the findings by Karki et al[9] (64.0%), Meremikwu et al[8] (50.8%) and Al-Zamil[11] (35.0%) although the percentages constituted by the newborns varied considerably among these studies. The predominance of newborns is most probably due to their large share in the hospital consultations and likelihood of requiring more screening tests for sepsis.

The positivity rate of blood isolates in the present study was found to be only 3.9% which is similar to the findings reported by Anandan et al[12] (3.1), Karki et al[9] (4.2%) and Ladhani et al[13] (6.0%). However, this observation is in contradiction to the rates observed by other studies, that reported the rates to be much higher ranging from 12.7 to 44.9%.[8, 14,15,16,17] Use of antibiotics prior to the visit to our hospital may be one of the possible reasons for such low yield in our study. Another reason of such low yield could possibly be inadequate amount of blood drawn for culture as it is not often easy to draw required amount of blood from young infants and small children due to different valid reasons. However, this limitation was taken care of by making the volume of the broth 90% of the amount of blood collected in our study. One more possible reason may be shortcomings in culture media and laboratory techniques as postulated by Shrestha et al.[15]

S aureus was the most common blood isolate in this series accounting for 37.0% of the total isolates. This observation is in agreement with the findings by Karki et al[9], Makoka et al[14] and Al-Zamil[11] but the percentage constituted by this organism differed in these studies (65.0%, 48.0% and 18.7% respectively). However, in contrast to this study, the findings of the study

conducted by Bhat et al seven years back, among neonates in India showed *S aureus* to be the 4th most common blood isolated organism accounting for 9.2% of the total. Another study in India reported *S aureus* to be the second most common blood isolate (22.5%) after *Klebsiella pneumoniae*.[17] *S aureus* is considered a common skin commensal and its high incidence could be due to contamination in some cases as argued by Ladhani et al.[13] However, each venipuncture was carried out following strict aseptic technique to reduce the contamination in our study. Another possible reason for such varied reported incidence might be due to different age groups of the study population and time and place of studies.

Among the most frequently tested antibiotics for *S aureus* in the present study, amikacin was found to be the most effective antibiotic in vitro (95.7%) followed by ofloxacin (84.6%), chloramphenicol (82.4%), vancomycin (80.0%) and ciprofloxacin (78.4%) where as it was shown to be most resistant to cephalexin (97.4%) followed by cloxacillin (90.9%), cefixime (80.9%) and ceftazidime (79.4%). Antibiotic sensitivity pattern of blood isolates done about 4 years ago in the same setting by Karki et al[9] in *S aureus* was almost similar to the findings of the present study. However, chloramphenicol was found to be the most effective antibiotic by them. In the contrary, Ladisch et al[18] observed that all isolates of *S areus* were sensitive to oxacillin and cephalothin and 76.0% resistant to penicillin. Ladhani et al[13] also reported cloxacillin (99.0%), gentamycin (99.0%) and chloramphenicol (96.0%) to be very effective antibiotic for *S aureus* and 92.0% penicillin resistant. The efficacy of cefotaxime, erythromycin, ciprofloxacin and cotrimoxazole observed by Ladhani et al[13] was below 50.0%. *S aureus* was also found to be highly resistant to ampicillin/amoxicillin (95%), penicillin G (95%), cephalexin/cephradine (44%)] by the Saudi Arabian study[11] conducted about 7 years ago, however, amoxicillin/clavulanic acid had reasonable efficacy (76.0%). The most effective antibiotic for *S aureus* observed by the Malawian study[14] conducted about 4 years ago was clindamycin (90.2%) followed by gentamycin (80.1%) oxacillin (68.7%) and chloramphenicol (68.5%) while least effective antibiotics were cotrimoxazole (30.7%) and erythromycin (58.2%. Vancomycin which is considered to be one of the drugs of choice for MRSA was found only 80.0% effective in the present study and defers to the findings by Ladhani et al[13] who found it 100.0% effective. Another drug of choice for MRSA, clindamycin, which was not tested in our study, was found to be 90.2% effective by Makoka et al.[14] Amikacin was found to be one of the effective drugs (76.2%) for *S aureus* by Ladhani et al.[13]

E coli was the second most commonly isolated bacteria in the present study which corroborates the findings reported by Karki et al[9] and Makoka et al. [14] In the contrary, *E coli* was not found to be common isolate by Shrestha et al[15] (3.8%) and Bhat et al[16] (4.4%). Another study reported *E coli* to be the most common isolate accounting for 53.7% of the total isolates among neonates.[19]

Amikacin was found to be the most effective antibiotic in vitro (87.9%) followed by ofloxacin (82.9%), ciprofloxacin (82.4.6%) and tobramycin (78.3%) while cephalexin was the least effective antibiotic (1.4%) followed by cefixime (22.2%), ceftazidime (23.2%) and cefotaxime (48.9%) against *E coli* among the frequently tested antibiotics in our study. Surprisingly, *E coli* was found to be more sensitive to amikacin, ofloxacin and ciprofloxacin as compared to the findings reported by Karki et al[9] 4 years ago in the same setting. It appears that antibiotic resistance is not only increasing but also decreasing to some organisms over time. This could be due to the phenomenon of antibiotic cycling[20] that may be taking place spontaneously. The findings reported by Shrestha et al[15] about 7 years ago showed the similar sensitivity pattern to ofloxacin and ciprofloxacin, however, amikacin was found to be 100.0% effective while chloramphenicol, cefotaxime, amoxicillin and gentamycin were 91.7%, 83.4%, 75.0% and 75.0% effective respectively. In the contrary, amikacin was found only 70.0% effective against *E coli* by Bhat et al.[16] Cefotaxime, cotrimoxazole and gentamycin were 40.0% effective; tobramycin, ciprofloxacin and ampicillin were 20.0% effective and ceftazidime was only 10.0% effective. The least effective antibiotic for *E coli* observed by Al-Zamil[11] was ampicillin and amoxicillin (35.0%) followed by cotrimoxazole (50.0%) and amoxiclav (63.0%).

Coagulase negative *Staphylococc*i (CoNS) constituted 6.9% of the isolates in this series which is much lower than the findings reported by Kumar et al[17] (18.7%), Shrestha et al[21] (21.3%) and Shrestha et al[15] (48.4%). The discrepancies in the incidence of this organism observed by different studies might

be due to differences in the age groups of the study population. Another possible reason could be contamination in some of the cases. The most effective antibiotic for coagulase negative *staphylococci* (CoNS) was found to be amoxycillin (100.0%) followed by amikacin (95.8%), ciprofloxacin (92.6%), ofloxacin (89.5%), chloramphenicol (74.6%) and cefotaxime (81.8%) where as the least effective was cloxacillin (0.0%) followed by ampicillin (11.1%) and cefixime (27.2%) in our study. The observed sensitivity pattern to amoxycillin and cloxacillin in the present study is far from our assumption. This surprising finding might be due to fewer number of this organism found in the blood isolates. For instance, only 27.0% of CoNS was reported to be resistant to cloxacillin by Shrestha et al.[15]

Among the commonly tested antibiotics, *Klebsiella sp* was shown to be most sensitive to ciprofloxacin (92.3%) followed by ofloxacin (91.6%), amikacin (61.5%), chloramphenicol (58.3%) and least sensitive to ceftazidime (21.3%) and cefotaxime (27.3%) in the present study. These isolates were found to be 100.0% resistant to cephalexin, cefixime, amoxycillin and ampicillin. Bhat et al[16] showed *Klebsiella sp* to be the most sensitive to amikacin (77.8%). The sensitivity of ampicillin, gentamycin, tobramycin to it was below 25% and cefotaxime, ceftazidime, cotromoxazole wad ciprofloxacin around 50.0%. However, another study conducted in India almost in the same period showed more than 90.0% of *Klebsiella pneumoniae* to be resistant to ampicillin, amikacin and ceftriaxone and more than 80.0% of them resistant to cefotaxime, ceforuxime, gentamycin and cotrimoxazole while imipenem was found to be 100.0% effective.[17] It shows that the sensitivity pattern changes not only over time but also differs from one institution to another in the same period. For instance, it was reported about 4 decades back by Riley HD[22] that the antibiotic resistance pattern differed by different regions significantly and similar trend was observed by Alzohairy et al[23] in a study conducted 2 years ago. It also appears that the multidrug resistant extended β-lactamase strains are on the rise. Kumar et al[17] showed the extended β-lactamase production mediated resistance to third generation cephalosporin to be 13.5% which is much higher than in the USA (5.0%) but same as in the UK and France (14 -16.0%). However, he further argues that this percentage of third generation cephalosporin resistant strains reported in their study could be much higher, because the conventional disc diffusion criteria used in the routine laboratory underestimate the incidence of these isolates.

Streptococcus species constituted 3.4% of the isolates and were found to be 100.0% sensitive to chloramphenicol and bacitracin followed by ciprofloxacin (83.3%), erythromycin (71.4%) and cotrimoxazole (66.7%) and least sensitive to optochin (20.0%) followed by ceftazidime (33.4%), ampicillin (40.0%), penicillin (45.5%) and amoxycillin (50.0%) among the commonly tested antibiotics in the present study. In the contrary, they were the second most commonly isolated organism (16.3%) after *S aureus* in a study conducted by Ladhani et al[13] and amoxiclav was the most effective antibiotic (84.0%) followed by cepalexin/cephradine (69.0%), amoxicillin (65.0%) and penicillin G (62.0%).

The findings of this study are compared with the findings of the studies conducted in Nepal as well as in other countries. The main purpose of comparison with the findings of studies conducted abroad was to see the trends of antibiotic resistance pattern in other countries as well. It was assumed that the antibiotic resistance pattern has been changing all over the world over time and it would have been interesting to see such change over time and by different locations. However, it is perceived that age group of patients and culture specimen should be matched to make such comparison more reliable and valid.

Neisseria elongata constituted 4.7% of the blood isolates in the present study. This organism is rarely being isolated in the laboratory (In a conversation with Dr. Rekha Manandhar, MD, Pathologist, March 2012) and the isolation of this organism might be due to contamination. The observation on *Neisseria elongata* is presented in this study for information sharing.

National drug policy is in existence in Nepal since 1995.[24] One of the objectives of this national drug policy in Nepal is to promote rational use of drugs and to establish a drug information system. It is also stated in the policy that the supervision and monitoring of antibiotic use at different levels of health institutions should be carried out routinely. For this reason, as per national drug policy, there are 2 committees functioning in the ministry of health and population: national antibiotic therapeutic advisory committee and national antibiotic control committee. Despite

these facts antibiotics are being used irrationally and inappropriately in our communities.[2] It is estimated that such practice ranges from 30 to 50% even in the countries with preexisting antibiotic policy.[25, 26] Such practices have been reported as high as 64 to 85.0 % by some authors. [2, 27] Such irrational practice is regarded as one of the leading causes of increasing incidence of drug resistant organisms posing a great challenge to medical personals. Antibiotic protocol for different infections for different specialties has already been drafted by the department of drug administration in collaboration with the curative division of ministry of health and population in Nepal after discussions with experts and will be finalized soon (In a conversation with Mr. PB Chhetry, M Pharma, May 2013).

Misdiagnosis is also considered as one of the reasons of antibiotic misuse.[27] It has been argued that only existence of antibiotic guidelines is not the solution for rational and appropriate prescription practice because they need a correct diagnosis in order to be effective. Therefore, health workers need to be trained continuously in diagnosing the cases. Furthermore, improvement in the diagnostic process should become a part of antibiotic policy as suggested by Pulcini et al.[27] It has also been suggested that the use of antibiotics should be adapted to the specific circumstances affecting the patient, geographical location, local epidemiology of causative bacteria and availability of specific antibiotics.[28]

This study is considered a part of local microbiological surveillance and monitoring. It is believed that it has added recent information about the bacteriological profile and their sensitivity pattern. It is also assumed that this study will help us to choose empirical antibiotics more rationally and develop local antimicrobial policies.

CONCLUSION

The most commonly isolated organisms were found to be sensitive to amikacin, chloramphenicol, ofloxacin and ciprofloxacin. However, they were highly resistant to other commonly used and available antibiotics like amoxicillin, ampicillin, cephalexin, cefixime, cloxacillin and third generation cephalosporin like cefotaxime, ceftriaxone and ceftazidime. It seems that the antibiotic sensitivity pattern is changing over time and also differs according to geographical location. This emphasizes the importance of periodic assessment of antibiotic sensitivity pattern in different parts of the country.

ACKNOWLEDGEMENT

We would like to thank all the staff of department of pathology at Kanti Children's Hospital for their kind help and cooperation to undertake this study.

REFERENCES

1. Richardson M, Lakhanpaul M. Assessment and initial management of feverish illness in children younger than 5 years: summary of NICE guidance. BMJ. 2007; 334 (7604):1163-4.
2. Palikhe N. Prescribing pattern of antibiotics in paediatric hospital of Kathmandu valley. Kathmndu Univ Med J. 2004; 2:6-12.
3. Zaidi AKM, Golmann DA. Diagnostic microbiology. In: Kliegman RM, Stanton BF, Geme III JW, Schor NF, Behrman RE, editors. Nelson Textbook of Pediatrics. 19th edition. Philadelphia: Elsevier Saunders; 2011.
4. Shrestha SD, Malla S, Adkikari BR, Shakya G, Basnyat SR, Sharma S. Antibiotic susceptibility patterns of Vibrio cholera isolates. JNMA. 2010; 49(3):232-36.
5. Sharma M, Yadav A, Yadav S, Goel N, Choudhary U. Microbial Profile of septecaemia in children. Indian J of Practising Doctor. 2008; 5:9-10.
6. Sharma M, Goel N, Choudhary U, Aggarwal R, Arora DR. Bacteremia in children. Indian J Pediatr. 2002; 69:1029-32.
7. Thapa B, Mahat K. In-vitro activity of three brands of ceftriaxone against different clinical isolates. JNMA. 2010; 49(3):225-7.
8. Makoka MH, Miller WC, Hoffman IF, Cholera R, Gilligan PH, Kamwendo D, & et. al.
9. Meremikwu MM, Nwachukwu CE, Asuquo AE, Okebe JU, Utsalo SJ. Bacterial isolates from blood culture of children with suspected septicaemia in Calabar, Nigeria. BMC Infect Dis. 2005; 5:110-14.
10. Karki S, Rai GK, Manandhar R. Bacteriological analysis and antibiotic sensitivity pattern of blood culture isolates in Kanti Children's Hospital. J. Nepal Paediatr. Soc. 2010; 30(2):94-7.
11. Sherchand JB, Joshi AR, Gauchan P, Amatya J. Distribution of serotypes and antimicrobial resistance of Streptococcus pneumoniae in a children's hospital in Nepal. J. Nepal Paediatr. Soc. 2008; 28(2):45-8.
12. Al-Zamil FA. Bacteremia in children at the University Hospital in Riyadh, Saudi Arabia. World J Pediatr. 2008; 4(2):118-122.
13. Anandan S, Thomas N, Veeraraghavan B, Jana AK. Prevalence of Extended spectrum β-lactamase Producing

Escherichia coli and Klebsiella spp in a Neonatal Intensive Care Unit. Indian Pediatrics. 2009; 46:1106-7.

14. Ladhani S, Konana OS, Mwarumba S, Emglish MC. Bacteraemia due to Staphylococcus aureus. Arch Dis Child. 2004; 89:568-571.
15. Shrestha S, Adhikari N, Shakya D, Manandhar L, Chand A, Shah S. Bacteriological profile of neonatal blood cultures at Patan Hospital. J. Nepal Paediatr. Soc. 2007; 26(1):1-4.
16. Bhat RY, Leslie E, Lewis S, Vandana KE. Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: an audit from a center in India. Italian Journal of Pediatrics. 2011; 37:32-7.
17. Kumar CS, Neelagund YF. Extended spectrum of β-lactamase mediated resistance to third generation cephaloisporins among Klebsiella pneumonia in neonatal septicaemia. Indian Pediatrics. 2004; 41: 97-8.
18. Ladisch S, Pizoo PAA. Staphylococcus aureus Sepsis in Children with Cancer. Pediatrics. 1978; 61:231-34.
19. Shrestha NJ, Subedi KU, Rai GK. Bacteriological profile of neonatal sepsis: a hospital based study. J. Nepal Paediatr. Soc. 2011; 31(1):1-5.
20. Niederman MS. Appropriate use of antimicrobial agents: changes and strategies for improvement. Critical Care Med. 2003; 3:608-16.
21. Shrestha P, Das BK, Bhatta NK, Jha DK, Das B, Setia A, Tiwari A. Clinical and bacteriological profiles of blood culture positive sepsis in newborns. J. Nepal Paediatr. Soc. 2007; 27(2):64-7.
22. Riley HD. Antimicrobial therapy in medical gastrointestinal disease. Pediat. Clin. N. Amer. 1968; 15:227-41.
23. Alzohairy M, Khadri H. Frequency and antibiotic susceptibility pattern of uro-pathogens isolated from community and hospital – acquired infections in Saudi Arabia - a prospective case study. British Journal of Medicine & Medical Research. 2011; 1(2):45-56.
24. Government of Nepal. Ministry of Health and Population. Department of drug Administration. National Drug Policy 1995.
25. Ochoa C, Eiros JM, Inglada L, Vallano A, Guerra L. Assessment of antibiotic prescription in acute respiratory infections in adults. J Infect. 2000; 41:73–83
26. Thuong M, Shortgen F, Zazempa V, Girou E, Soussy CJ, Brun-Buisson C. Appropriate use of restricted antimicrobial agents in hospitals: the importance of empirical therapy and assisted re-evaluation. J Antimicrob Chemother. 2000; 46:501–508
27. Pulcini C, Cua E, Lieuter F, Landraud L. Dellamonica P, Roger PM. Antibiotic misuse: a prospective clinical audit in a French university hospital. Eur J Clin Microbiol Infect Dis. 2007; 26:277–280.
28. Park SH, Lee DH, Cho YJ, Cho DK, Shin SK, Kim DJ et al. Causative organisms and patterns of antibiotic sensitivity of CAPD peritonitis in different dialysis centers. Korean J Med. 2003; 64(6):682-89.