Australasian Medical Journal AMJ 2010, 3, 10, 633-637

Blood Stream Infections among febrile patients attending a Teaching Hospital in Western Region of Nepal

Joshy M Easow[1], Noyal M Joseph[1], Banodita A Dhungel[2], Bipin Chapagain[3], PG Shivananda[4]

[1]Department of Microbiology, Mahatma Gandhi Medical College and Research Institute, Pondicherry, India;
[2]Department of Clinical Microbiology, Nepal Medical College Teaching Hospital, Attarkhel, Nepal;
[3]Department of Clinical Microbiology, Manipal Teaching Hospital, Pokhara, Nepal;
[4]Department of Microbiology, Kasturba Medical College, Manipal, India

RESEARCH

Please cite this paper as: Easow JM, Joseph NM, Dhungel BA, Chapagain B, Shivananda PG. Blood Stream Infections among febrile patients attending a Teaching Hospital in Western Region of Nepal. AMJ 2010, 3, 10, 633-637.
Doi 10.4066/AMJ.2010.422

Corresponding Author:
Dr. Joshy M Easow,
Associate Professor,
Department of Microbiology,
Mahatma Gandhi Medical College and Research Institute,
Pillaiyarkuppam, Pondicherry – 607 402 (India)
dr.jmeasow@gmail.com

Abstract

Background
Blood stream infections (BSIs) are important determinants for prolonged hospital stay and if uncontrolled, progress to become life-threatening. The aim of this study is to determine the common bacterial agents associated with BSI and their antimicrobial susceptibility patterns in a tertiary care teaching hospital in the Western region of Nepal.

Method
A cross-sectional study was conducted for a 20 month period from January 2006 to August 2007. All adult patients with fever (temperature ≥ 38°C) when assessed in the outpatient department or various inpatient wards were enrolled in the study.

Results
Of the 933 patients with febrile illness, only 96 were diagnosed to have BSIs. *Salmonella* spp., *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the common etiological agents of BSIs. *S*. Paratyphi A and *S*. Paratyphi B were responsible for 46.7% of the enteric fever cases. The clinical diagnosis of enteric fever was not sensitive and specific. The members of Enterobacteriaceae were frequently resistant to ampicillin, amoxicillin/ clavulanic acid and gentamicin. About one-third of the *K.pneumoniae*, *E.coli* and *Enterobacter* spp. produced extended-spectrum β-lactamases. The non-fermenters were unusually sensitive to most antibiotics.

Conclusion
Gram-negative bacteria were the predominant causes of BSIs. The occurrence of drug resistant S. Paratyphi A is of great concern for travellers, as they are not protected with an effective vaccine. Imipenem showed good activity against Pseudomonas aeruginosa indicating lack or low level of MBL activity.

Key Words
Blood stream infections; enteric fever; *Klebsiella pneumoniae*; *Escherichia coli*; *Pseudomonas aeruginosa*

Background
Blood stream infection (BSI) is an important event responsible for prolonged hospital stay. BSIs can be health-care associated or community-associated.(1) Health-care associated BSIs are a frequent form of nosocomial infection occurring in hospitalised patients.(2) BSIs continue to be a severe, often life-threatening condition. Despite the emergence of advanced life-support facilities and development of new antimicrobial agents, they are associated with a high mortality rate ranging 25 – 50% (3).

Gram-negative organisms are the leading cause of blood stream infections (4). Gram negative sepsis has been reported in an estimated 200,000 Americans every year with a mortality rate of 30 – 65%. (4). In a study from Northern India, gram-negative organisms were observed in majority of the patients with BSI (5). *Escherichia coli, Klebsiella pneumoniae, Enterobacter* spp., *Proteus* spp., *Citrobacter* spp., *Acinetobacter* spp. *and Pseudomonas* spp. are the common gram-negative organisms causing BSI (4).

In recent years gram-positive organisms are increasing in frequency and are often associated with BSIs (3, 4). *Staphylococcus aureus* is the most common gram-positive bacteria causing BSI (4). The Antimicrobial Surveillance Programme (SENTRY) of the Latin American countries

described 30.9% prevalence of methicillin-resistant Staphylococcus aureus (MRSA) bacteremia in hospitalized patients (6).

However, there are only a few studies from Nepal, which have studied the organisms involved in BSI and their susceptibility pattern. Awareness about the variations in the antimicrobial susceptibility patterns of microorganisms causing BSIs is not only an important factor in managing patients, but also for monitoring the spread of resistant organisms. We therefore conducted this study to determine the common bacterial agents associated with BSI and their antimicrobial susceptibility patterns in a tertiary care teaching hospital in the Western region of Nepal.

Method

Study design and setting

This cross sectional study was conducted over a 20-month period from January 2006 to August 2007 at Manipal Teaching Hospital (MTH), Nepal. MTH is the teaching hospital of Manipal College of Medical Sciences (MCOMS), Pokhara, situated in the western development region of Nepal. The hospital is a major healthcare provider for the region. The institution caters to the population of ten of the fifteen districts of western development region of Nepal. The population of these ten districts was approximately 2 million as per 2001 census (7). The hospital has an average daily patient load of 500 outpatients and 150 inpatients though it shows seasonal variations.

Patients

All adult patients with fever (temperature ≥ 38°C) when assessed in the outpatient department or various inpatient wards were enrolled in the study. The demographic details such as age, sex, date of admission in hospital, clinical diagnosis at presentation, presence of an indwelling medical device, details of any surgical procedure or invasive instrumentation/ incision and presence of neutropaenia (<1 ×10^9/L) due to cytotoxic therapy were noted. Paired blood samples from each of these patients were used for the study.

Specimen collection and processing

The blood samples collected in brain heart infusion (BHI) biphasic medium from patients with suspected BSIs were incubated at 37^{o}C. It was sub-cultured on blood agar and MacConkey after 24 h, 48 h and 1 week of aerobic incubation. The bacterial isolates were identified based on standard bacteriological methods especially using various biochemical tests (8). Agglutination with specific antisera was used for identification of different *Salmonella* spp.

Antibiotic susceptibility testing

Antibiotic susceptibility testing was performed by Kirby Bauer's disc diffusion method according to Clinical Laboratory Standards Institute (CLSI) guidelines (9). Ampicillin, amoxicillin-clavulanate, carbenicillin, cefazolin, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, ciprofloxacin, trimethoprim/ sulfamethoxazole, gentamicin, tobramycin, netilmicin, piperacillin and imipenem were tested for gram-negative bacteria. Penicillin, ampicillin, amoxicillin/ clavulanate, cefazolin, erythromycin, gentamicin, netilmicin, ciprofloxacin, oxacillin and vancomycin were tested for *Staphylococcus aureus*. Penicillin, ampicillin, high-level gentamicin, ciprofloxacin and vancomycin were tested for *Enterococcus* spp. Penicillin, ampicillin, ceftriaxone and vancomycin was tested for *Streptococcus* spp. All the isolates of *Klebsiella pneumoniae* and *Escherichia coli* were screened for extended-spectrum β-lactamases (ESBL) production using both ceftazidime and cefotaxime discs according to the CLSI guidelines (10). The organisms showing zones of inhibition ≤ 22 mm and ≤ 27 mm for ceftazidime and cefotaxime, respectively, were also tested in combination with clavulanic acid. The organisms were phenotypically confirmed as ESBL producers when they showed an increase in zone of inhibition by greater than or equal to 5 mm when evaluated in combination with clavulanic acid. Quality control was performed by testing *Escherichia coli* ATCC 25922.

Definitions

BSI was defined as isolation of one or more recognised pathogen from one or more blood cultures (1). Where mixed isolates are obtained with one being an accepted pathogen, the potential contaminant organism was disregarded. Isolation of the same potential contaminant from two or more blood cultures drawn on separate occasions within a 48 hour period in patients with fever (≥38^{o}C) was also considered as BSI (1). BSIs were defined as health care associated if it occurred more than 48 hours after hospital admission or was associated with the presence of an indwelling medical device or it occurred within thirty days of a surgical procedure (where the bloodstream infection was related to the surgical site infection) or an invasive instrumentation/ incision related to the bloodstream infection was performed within 48 hours before onset of the infection or was associated with neutropaenia (<1 ×10^9/L) contributed to by cytotoxic therapy (1). BSIs were defined as community-associated if it manifested within 48 hours after admission unless an organism with a long incubation period (e.g., *Salmonella* Typhi) was isolated (1).

Statistical analysis

Data were analysed using SPSS for Windows Version 16.0 (SPSS Inc, Chicago, IL, USA). Percentages were calculated for categorical variables. Two-sided P values were calculated using the chi-square test or Fisher's exact test for dichotomous and ordinal variables. P values < 0.05 were considered statistically significant. The sensitivity, specificity, positive predictive value, and negative predictive value were determined using GraphPad InStat version 3.00 for Windows 95 (GraphPad Software, San Diego, CA, USA).

Results

A total of 933 patients with fever were enrolled in the study. Of these 933 patients with febrile illness, only 96

were diagnosed to have BSIs. The demographic details of those 96 patients with BSIs are summarised in Table 1.

Table 1: Demographic details of the patients with Blood-Stream Infections

Characteristic	
Age (mean ± SD)	41.75 ± 18.44 years
Sex	
Male	55 (57.3%)
Female	41 (42.7%)
Location	
In-patient wards	77 (80.2%)
Out-patient Department	19 (19.8%)
Clinical diagnosis at presentation	
Enteric fever	29 (30.2%)
Urinary tract infection	22 (22.9%)
Lower respiratory tract infection	21 (21.9%)
Upper respiratory tract infection	9 (9.4%)
Cellulitis	5 (5.2%)
Meningitis / encephalitis	5 (5.2%)
Sepsis	2 (2.1%)
Puerperal sepsis	1 (1%)
Burns	1 (1%)
Malignancy with neutropenia	1 (1%)

The 18 to 40 year age group accounted for 52.1% of all positive cases of BSIs. The male to female ratio was 1.3:1. Enteric fever was the most common clinical diagnosis at presentation, followed by urinary tract infection and lower respiratory tract infection. Of the 96 events of BSIs, 75 (78.1%) were community-associated, while 21 (21.9%) were health care associated.

The etiological agents of BSIs in our patients are summarised in Table 2. Majority (76.0%) of the isolates were gram-negative organisms, while the remaining were gram-positive organisms. The causative agents of enteric fever such as *Salmonella* Typhi, *Salmonella* Paratyphi A and *Salmonella* Paratyphi B were isolated from 15.6% of the patients with BSIs. Of the 15 cases of enteric fever, 13 (86.7%) required hospitalisation. Of the 29 patients with a clinical diagnosis of enteric fever, only 4 (13.8%) had positive blood cultures for either *S*. Typhi or *S*. Paratyphi A. On the other hand, 11 (16.4%) patients with other diagnoses had *S*. Typhi or *S*. Paratyphi A isolated from blood. The sensitivity, specificity, positive predictive value and negative predictive value of the clinical suspicion of enteric fever was 26.7%, 69.1%, 13.8% and 83.6% respectively. The Salmonella species causing enteric fever were significantly associated with community-acquired BSIs (P value 0.0360).

Members of Enterobacteriaceae other than *Salmonella* spp. were responsible for 31.3% of BSIs. Of these pathogens, *Klebsiella* species were frequently associated with community-acquired BSIs (P value 0.0360).

Table 2: Etiological agents of Blood-Stream Infections

Etiological agent	Frequency	Percentage
Enterobacteriaceae		
Salmonella Typhi	8	8.3
Salmonella Paratyphi A	6	6.3
Salmonella Paratyphi B	1	1.0
Klebsiella pneumoniae	13	13.5
Klebsiella spp.	2	2.1
Escherichia coli	10	10.4
Enterobacter spp.	4	4.2
Serratia marcescens	1	1.0
Non-fermenters		
Pseudomonas aeruginosa	8	8.3
Pseudomonas spp.	15	15.6
Acinetobacter spp.	4	4.2
Other non-fermenters	1	1.0
Gram positive bacteria		
Staphylococcus aureus	13	13.5
Staphylococcus epidermidis	1	1.0
Streptococcus spp.	3	3.1
Streptococcus viridans	2	2.1
Group B β-hemolytic Streptococci	1	1.0
Streptococcus pneumoniae	1	1.0
Enterococcus spp.	2	2.1
Total	96	100

Non-fermentative gram-negative bacteria such as *P. aeruginosa*, *Pseudomonas* spp. and *Acinetobacter* spp. were isolated from 29.2% of our patients. The common pathogens affecting the elderly patients (≥ 60 years) were *Salmonella* Typhi, *Salmonella* Paratyphi A, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. In young individuals (≤ 40 years), *Escherichia coli* (18%) was the most common pathogen causing BSIs, followed by *Salmonella* spp. (16%), *Klebsiella pneumoniae* (12%) and *Staphylococcus aureus* (12%). *Escherichia coli* were associated with BSIs in 18% of young individuals (≤ 40 years), while only 2% of those > 40 years had BSIs caused by *Escherichia coli* (*P* value 0.0164). There was no statistically significant difference in the occurrence of BSIs due to other pathogens in young and older individuals. Even the *Salmonella* spp. causing enteric fever was equally distributed among young and older individuals.

The resistance patterns of the gram-negative bacteria isolated from blood are shown in Table 3. The eight *Salmonella* Typhi isolates were found susceptible to all the routine antibiotics tested. However, three of the six *Salmonella* Paratyphi A isolates were resistant to chloramphenicol and one isolate was resistant to ampicillin. Most of the Klebsiella pneumoniae were resistant to amoxicillin/clavulanate and gentamicin. Similarly, majority of the *Escherichia coli* were found resistant to ampicillin and amoxicillin/clavulanate. ESBL was produced by 23% and 40% of *Klebsiella pneumoniae* and *Escherichia coli* respectively.

Table 3: Resistance pattern of the Gram negative bacteria causing BSI

Etiological agent (no. of isolates)	Antibiotic resistance pattern (%)										
Enterobacteriaceae	**AMP**	**AMC**	**GEN**	**AMK**	**NET**	**CFZ**	**CTX**	**CRO**	**CXM**	**CIP**	**CHL**
Salmonella Typhi (8)	0	-	0	-	-	-	0	0	-	0	-
Salmonella Paratyphi A (6)	17	-	0	-	-	-	-	0	0	0	50
Klebsiella pneumoniae (13)	-	100	77	15	0	38	31	23	38	23	-
Escherichia coli (10)	70	100	40	0	0	40	40	40	60	30	20
Enterobacter spp. (4)	100	100	100	25	25	75	75	75	100	50	25
Non-fermenters	**CRB**	**PIP**	**GEN**	**AMK**	**TOB**	**CAZ**	**CIP**	**IPM**			
Pseudomonas aeruginosa (8)	0	25	0	13	0	13	0	0			
Pseudomonas spp. (15)	13	7	27	40	-	13	7	-			
Acinetobacter spp. (4)	50	50	25	25	-	50	25	0			

AMP – ampicillin, AMC – amoxicillin/ clavulanate, GEN – gentamicin, AMK – amikacin, NET – netilmicin, CFZ – cefazolin, CTX – cefotaxime, CRO – ceftriaxone, CXM – cefuroxime, CIP – ciprofloxacin, CHL – chloramphenicol, CRB – carbenicillin, PIP – piperacillin, TOB – tobramycin, CAZ – ceftazidime, IPM - imipenem

All our *P. aeruginosa* isolates were susceptible to gentamicin, tobramycin, ciprofloxacin, carbenicillin and imipenem. None of the non-fermenters were resistant to imipenem. Of the 13 *Staphylococcus aureus* isolates, 23% were identified as MRSA. The resistance of *Staphylococcus aureus* to erythromycin, gentamicin and ciprofloxacin was 46%, 38% and 15%, respectively. The two *Enterococcus* spp. were resistant to penicillin, while one of them was resistant to ampicillin and ciprofloxacin also. The *Streptococcus* spp. was sensitive to ampicillin, ceftriaxone and vancomycin.

Discussion

BSIs are among the most severe manifestations of bacterial disease. Patients can present to hospital with a bloodstream infection or may develop one as a result of healthcare interventions. Gram-negative bacteria are more frequent cause of BSIs than gram-positive bacteria. In our study 76.0% of the BSIs were caused by gram-negative bacteria. In a similar study from Indonesia, 68% of the isolates from BSIs were gram-negative bacteria (4). However, in a study from Australia both gram-positive and gram-negative bacteria were almost equally responsible for BSIs (11). Therefore, the relative predominance of the etiological agents of BSIs appears to vary according to the place of study and the population.

Salmonella spp., *K. pneumoniae, E. coli, Pseudomonas* spp. and *S. aureus* were the most common etiological agents of BSIs in our study. In other similar studies, *Acinetobacter* spp., *P. aeruginosa, S. aureus, K. pneumoniae* and *Enterobacter* spp. were the frequent causes of BSIs (4, 12). We isolated *Salmonella* spp. from 15.6% of the patients with BSIs, while in another recent study from Nepal they were isolated from 51.6% of the positive blood cultures of patients with BSIs (13). A remarkable finding in our study is that *S.* Paratyphi A and *S*. Paratyphi B were responsible for 46.7% of the enteric fever cases. This report may have an important implication on the vaccine strategies, as the current vaccines used in this region do not confer protection against paratyphoid fever. Although *Salmonella* species are important etiological agents of community-acquired BSIs, because of the variable signs and symptoms, the clinicians are often not able to correctly suspect enteric fever in patients with BSIs. In our study we found that the clinical suspicion of enteric fever was associated with only 26.7% sensitivity and 69.1% specificity. Similarly, in another study from Nepal, only 25% of the patients with a clinical diagnosis of enteric fever had blood culture positive for either *S*. Typhi or *S*. Paratyphi A, whereas these pathogens were detected in many patients with other diagnosis (14). Therefore, as the clinical features are not reliable, enteric fever should be suspected in all patients with community-acquired BSIs and they should be investigated appropriately to confirm the diagnosis.

In the current study, in addition to *Salmonella* spp. other members of Enterobacteriaceae such as *Escherichia coli*, *K. pneumoniae*, etc were isolated in 31.3% of the patients with BSIs. However, in two different recent studies from Nepal, they were isolated only from about 2 - 4% of the patients with positive blood cultures (13, 14). *S. aureus* was the most common gram-positive bacteria associated with BSIs in the present study. Likewise, in a study by Einsiedel LJ et al 39.8% of the BSIs were caused by *S. aureus* (11).

In this study, *S*. Typhi and *S*. Paratyphi A, which are the important cause of community-acquired BSIs, were noted to be susceptible to most of the routinely used antibiotics. In a study by Moehario et al also majority of these isolates were observed to be susceptible to all the antibiotics tested (4). However, of the six *S*. Paratyphi A isolated in our study one was found to be resistant to ampicillin, while three were resistant to chloramphenicol. Similarly, in another study from Nepal, 24% of the *S*. Paratyphi A was resistant to ampicillin and 52% were resistant to chloramphenicol (15). In developing countries, chloramphenicol and ampicillin are still the drugs of choice for treatment of enteric fever. Therefore, the occurrence of drug resistant *S*. Paratyphi A is of great concern especially for travellers visiting these countries, as they are not protected with an effective vaccine against *S*. Paratyphi A.

We observed that the members of Enterobacteriaceae such as *K. pneumoniae, Enterobacter* spp. and *E. coli* were frequently resistant to the first-line antibiotics such as

ampicillin, amoxicillin/ clavulanic acid and gentamicin. About one-third of the *K. pneumoniae, E. coli* and *Enterobacter* spp. were also resistant to extended-spectrum cephalosporins. *E. coli* and *K. pneumoniae* which were earlier susceptible to the third generation cephalosporins have developed resistance to these antibiotics mainly because of production of ESBL (16). About 23% of the *S. aureus* isolated were MRSA comparable with other studies (3, 11).

Majority of the non-fermenters such as *Pseudomonas* spp. and *Acinetobacter* spp. were sensitive to the routinely used antibiotics such as ciprofloxacin, ceftazidime, gentamicin and amikacin. Moreover, all the non-fermenters were sensitive to imipenem. This is in contrast to the high prevalence of resistance to these antibiotics observed in the neighbouring regions due to production of various β-lactamases such as AmpC β-lactamases and metallo-β-lactamases (17).

Conclusion

To conclude, gram-negative bacteria were the predominant causes of BSIs. *Salmonella* spp., *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the common etiological agents of BSIs. We observed that the clinical diagnosis of enteric fever was not sensitive and specific. The occurrence of drug resistant *S*. Paratyphi A is of great concern for travellers, as they are not protected with an effective vaccine. The members of Enterobacteriaceae were frequently resistant to the first-line antibiotics such as ampicillin, amoxicillin/ clavulanic acid and gentamicin. About one-third of the *K. pneumoniae, E.coli* and *Enterobacter* spp. were also resistant to extended-spectrum cephalosporins due to production of ESBLs. However, the non-fermenters were unusually sensitive to most antibiotics.

References

1. Australian Commission on Safety and Quality in Health Care. Blood Stream Infection (BSI) definition. Available from: http://www.agargroup.org/files/Blood%20stream%20defintions.pdf 2010 [cited 2010 May 5]
2. Malacarne P, Boccalatte D, Acquarolo A, Agostini F, Anghileri A, Giardino M, et al. Epidemiology of nosocomial infection in 125 Italian intensive care units. Minerva Anestesiol 2010; 76:13-23.
3. Ribas RM, Freitas C, Filho PG. Nosocomial methicillin-resistant *Staphylococcus aureus* bacteremia in a tertiary care hospital: Risk factors, overall mortality and antimicrobial resistance. International Journal of Medicine and Medical Sciences 2009; 1:412-7.
4. Moehario LH, Tjoa E, Kiranasari A, Ningsih I, Rosana Y, Karuniawati A. Trends in antimicrobial susceptibility of gram-negative bacteria isolated from blood in Jakarta from 2002 to 2008. J Infect Dev Ctries 2009; 3:843-8.
5. Habibi S, Wig N, Agarwal S, Sharma SK, Lodha R, Pandey RM, et al. Epidemiology of nosocomial infections in medicine intensive care unit at a tertiary care hospital in northern India. Trop Doct 2008; 38:233-5.
6. Sader HS, Jones RN, ndrade-Baiocchi S, Biedenbach DJ. Four-year evaluation of frequency of occurrence and antimicrobial susceptibility patterns of bacteria from bloodstream infections in Latin American medical centers. Diagn Microbiol Infect Dis 2002; 44:273-80.
7. Distribution of Population and Area by Development Regions and Districts, 1981, 1991 and 2001. Available from: http://www.cbs.gov.np/statistical_year_book_content.php. 2010 [cited 2010 Jun 27]
8. Mackie TJ, McCartney JE. Practical medical microbiology. 14th ed. New York: Churchill Livingstone; 1996.
9. Clinical Laboratory Standards Institute. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Approved standard, 6th ed. CLSI document M7-A6. CLSI: Wayne, PA; 2005.
10. Clinical Laboratory Standards Institute. Performance standards for antimicrobial disk susceptibility tests. Approved standard, 9th ed. CLSI document M2-A9. CLSI: Wayne, PA; 2006.
11. Einsiedel LJ, Woodman RJ. Two nations: racial disparities in bloodstream infections recorded at Alice Springs Hospital, central Australia, 2001-2005. Med J Aust 2010; 192:567-71.
12. Japoni A, Farshad S, Alborzi A, Kalani M, Rafaatpour N, Oboodi B, et al. Epidemiology and antibacterial susceptibility patterns of bloodstream infections, 2001-2004: an experience with BACTEC 9240 in Southern Iran. Pak J Biol Sci 2008; 11:422-7.
13. Sharma NP, Peacock SJ, Phumratanaprapin W, Day N, White N, Pukrittayakamee S. A hospital-based study of bloodstream infections in febrile patients in Dhulikhel Hospital Kathmandu University Teaching Hospital, Nepal. Southeast Asian J Trop Med Public Health 2006; 37:351-6.
14. Murdoch DR, Woods CW, Zimmerman MD, Dull PM, Belbase RH, Keenan AJ, et al. The etiology of febrile illness in adults presenting to Patan hospital in Kathmandu, Nepal. Am J Trop Med Hyg 2004; 70:670-5.
15. Pokharel BM, Koirala J, Dahal RK, Mishra SK, Khadga PK, Tuladhar NR. Multidrug-resistant and extended-spectrum beta-lactamase (ESBL)-producing Salmonella enterica (serotypes Typhi and Paratyphi A) from blood isolates in Nepal: surveillance of resistance and a search for newer alternatives. Int J Infect Dis 2006; 10:434-8.
16. Bradford PA. Extended-spectrum beta-lactamases in the 21st century: characterization, epidemiology, and detection of this important resistance threat. Clin Microbiol Rev 2001; 14:933-51.
17. Noyal MJ, Menezes GA, Harish BN, Sujatha S, Parija SC. Simple screening tests for detection of carbapenemases in clinical isolates of nonfermentative Gram-negative bacteria. Indian J Med Res 2009; 129:707-12.

ACKNOWLEDGEMENTS

We are grateful to the Department of Microbiology, Manipal Teaching Hospital, Nepal.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors do not have any competing interest to declare