Anuradha et al., Intern Med 2015, 5:3
DOI: 10.4172/2165-8048.1000193

Internal Medicine: Open Access
ISSN: 2165-8048

Research Article Open Access

Antimicrobial Resistance among Commonly Encountered Bacteria Isolated in 2013 – The ESKAPE Menace

Anuradha S De*, Baveja S, D'Souza D and Patwegar S

Department of Microbiology, L.T.M. Medical College and Hospital, Mumbai, India

Abstract

Introduction: The most serious, life-threatening infections caused by a group of drug-resistant bacteria are named as "ESKAPE" pathogens by the Infectious Diseases Society of America (IDSA), because they effectively escape the effects of antibacterial drugs.

Objectives: To find out the antibiotic susceptibility pattern of bacteria isolated from various specimens, with special reference to the ESKAPE bugs.

Methods: A retrospective study of one year was undertaken in this tertiary care hospital. Samples (pus/wound swabs, respiratory samples, blood cultures and urine samples were processed as per standard techniques and bacteria identified by standard biochemical tests.

Antibiotic susceptibility (ABS) was done by the Kirby Bauer Disc Diffusion Method on Mueller Hinton Agar, according to CLSI guidelines.

Results: Maximum growth was seen from pus swabs (51.49%), followed by respiratory samples (35.66%). Overall Gram negative bacilli (GNB) isolated was 77% and GPC 23%. MDR was mainly seen with Proteus species (50%), followed by *Acinetobacter* species (48%) and *Pseudomonas aeruginosa* (46%). *Staphylococcus aureus* was the major Gram positive isolate in pus samples and enterococci in urine samples. Imipenem susceptibility for all bacteria was more than 80%, except in some respiratory samples. Both MDR and carbapenem resistant bacteria increased in 2013, as compared to 2012. *S. aureus* showed 100% susceptibility to linezolid and 33.86% of all MRSA showed ICR. One VISA and four VRE were isolated. HLAR was seen in 23.36% enterococci.

Conclusion: Judicious use of antibiotics is the need of the day to control the spread of MDR "ESKAPE" bugs. There is also an urgent need to develop Antimicrobial Stewardship.

Keywords: ESKAPE bugs; Multidrug resistant (MDR) bacteria; IDSA

Introduction

"We're not at the point where all antibiotics are useless, that's overstating it. But there's no question we have a problem with increasing bacterial resistance to current antibiotics." - Dr. Andrew Simor.

Antimicrobial Resistance (AMR) is present in all parts of the world. New resistance mechanisms emerge and spread globally. It is an increasingly serious threat to global public health that requires action across all government sectors and society. There is a warning for India by WHO, that antimicrobial resistance is reaching critical levels [1]. AMR is a problem worldwide, but is particularly worrying in India, where hospital standards are inconsistent and antibiotics are readily available over the counter at pharmacies. Antibiotic use is unnecessary or inappropriate in as many as 50% of cases and this creates unnecessary pressure for the selection of resistant species. Moreover, overuse and misuse of antimicrobial agents in humans, food, animals, agriculture and consumer products are also responsible for increase in AMR. Inadequate infection control practices add further to this problem [2,3].

Antibiotic exposure increases the risks of resistance of Carbapenem Resistant Enterobactericeae (CRE). Carbapenems increase the risk of resistance up to 15 fold and ESBL producing organisms and cephalosporins increase the risk up to 6 to 29 fold [4].

The most serious, life-threatening infections caused by a group of drug-resistant bacteria are named as "ESKAPE" pathogens by the Infectious Diseases Society of America (IDSA), because they effectively escape the effects of antibacterial drugs. The six "ESKAPE" bacteria are Enterococcus faecium (E), *Staphylococcus aureus* (S), *Klebsiella pneumoniae* (K), *Acinetobacter baumannii* (A), *Pseudomonas aeruginosa* (P) and *Enterobacter* species/*Escherichia coli* (E). These bugs are responsible for two thirds of all health care-associated infections (HAIs) [5], prompting IDSA to raise the alarm and label this threatening situation as "Bad Bugs, No Drugs" [6]. The latter microorganisms span over a wide range of microbial species such as methicillin resistant *Staphylococcus aureus* (MRSA) being healthcare-associated (HA-MRSA) or community-associated (CA-MRSA), vancomycin-intermediate or resistant *S. aureus* (VISA or VRSA), vancomycin-resistant enterococcus (VRE), the multidrug-resistant *Acinetobacter* spp. and *Pseudomonas aeruginosa*, extendedspectrums-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* spp., and carbapenem resistant enterobacteriaceae.

(CRE) [7,8]. Thus, surveillance and revealing the antimicrobial profile as well as monitoring and determining the changing trends of resistance among these pathogens at different periods of time provides essential valuable information to the clinicians, hospital infection control committee and also to epidemiologists, for the containment of this problem [9,10].

***Corresponding author:** Anuradha S De, Professor, Department of Microbiology, L.T.M. Medical College and Hospital, Sion, Mumbai, India, Tel: +91 9892147781, E-mail: dr_anuradhade@yahoo.com

Received May 01, 2015; **Accepted** May 20, 2015; **Published** May 27, 2015

Citation: Anuradha S De, Baveja S, D'Souza D, Patwegar S (2015) Antimicrobial Resistance among Commonly Encountered Bacteria Isolated in 2013 – The ESKAPE Menace. Intern Med 5: 193. doi:10.4172/2165-8048.1000193

Therefore the present study was undertaken to reveal and reflect on antimicrobial resistance among commonly encountered bacteria recovered in this tertiary care hospital during one year period, with special reference to the ESKAPE bugs.

Materials and Methods

A retrospective study of one year (January-December 2013) was undertaken in this tertiary care hospital. Samples comprised of pus/wound swabs (6112), respiratory samples (2465), blood cultures (5931) and urine (4818). All the above samples were processed as per standard techniques and bacteria identified by standard biochemical tests [11].

Antibiotic susceptibility (ABS) was done by the Kirby Bauer Disc Diffusion Method on Mueller Hinton Agar, according to CLSI guidelines. For *Acinetobacter* species, tigecycline disc and colistin MIC strip were also put up. For *Pseudomonas aeruginosa*, colistin disc was also put up. For Streptococcus species, ABS was put up on blood agar. Vancomycin susceptibility for *S. aureus* and Streptococcus species were done by E-strip (HiMedia). For *S. aureus*, inducible clindamycin resistance (ICR) was done by D-test. For enterococci, high level aminoglycoside resistance (HLAR) detection was performed using gentamycin (120 µg) and streptomycin (300 µg) discs [12].

Results

Maximum growth was seen from pus/wound swabs, i.e. 51.49% (3147/6112), followed by 35.66% (879/2465) from respiratory samples, 14.16% (840/5931) from blood cultures and 14.43% (695/4818) from urine samples. Overall growth of Gram negative bacilli (GNB) was 77.1% and Gram positive cocci (GPC) were 22.9%. GNB in pus and respiratory samples was 78.03% and 75.43% respectively and GPC in these samples were 21.97% and 24.57% respectively. GNB was isolated maximum from urine samples to the tune of 91.08% and only 8.92% was GPC. In blood cultures, GPC was slightly more than in other samples, i.e. 37.5%, though GNB also predominated (62.5%).

Table 1 shows overall bacteria isolated from different samples. Table 2 shows type of growth from different samples taken from each specialty. Figures 1-3 show% antibiotic susceptibility pattern of GNB and Enterococcus species. Figure 4 shows prevalence of Multidrug resistant (MDR) Gram negative bacilli (GNB) in 2013. MDR-GNB was maximum seen in Proteus species (50.79%), followed by *Acinetobacter* species (48.76%) and *Pseudomonas aeruginosa* (46.14%).

Overall imipenem susceptibility was >80%, except for *Pseudomonas aeruginosa* (65.38%) and *Enterobacter* species (58%) in respiratory samples. All isolates from urine samples showed 100% susceptibility to imipenem. For blood culture isolates, imipenem susceptibility of *Acinetobacter* species and *Enterobacter* species were 96.23% and 88.89% respectively. All other GNB from blood cultures were 100% susceptibile to imipenem.

All Enterobacteriaceae from urine samples showed 100% susceptibility to netilmycin, whereas in *Acinetobacter* species and *Pseudomonas aeruginosa*, susceptibility to netilmycin was 90% and 33.33% respectively. Netilmycin susceptibility of *Acinetobacter* species and *Pseudomonas aeruginosa* in other samples varied from 33-45% and 14-43% respectively. Netilmycin susceptibility of all Enterobacteriaceae from pus samples was between 12-22%, except in *E. coli*, where it was 65.75%. In respiratory samples, the same was between 11-32% and in blood cultures it was from 5-11%.

Piperacillin-tazobactam susceptibility of *Acinetobacter* species and *Pseudomonas aeruginosa* from blood cultures was 58.5% and 64% respectively. From urine samples, the same was 50% and 27%

Bacteria (Total No.)	Pus No. (%)	Respiratory No. (%)	Blood Culture No. (%)	Urine No. (%)
Acinetobacter species (1247)	684 (54.85)	287 (23.02)	216 (17.32)	60
Pseudomonas aeruginosa (1415)	1111 (78.52)	156 (11.00)	66	82
Escherichia coli (807)	420 (52.04)	40	39	308 (38.17)
Klebsiella pneumoniae (473)	209 (44.19)	106 (22.41)	61	97 (20.51)
Enterobacter species (535)	308 (57.57)	50	104 (19.44)	73
Proteus species (189)	156 (82.54)	14	07	12
Citrobacter species (31)	10	10	10	01
Salmonella typhi (16)	-	-	16	-
Serratia marcescens (01)	01	-	-	-
Other nonfermenters (06)	-	-	06	-
Methicillin Sensitive *Staphylococcus aureus* (MSSA) (659)	414 (62.82)	27	206 (31.26)	12
Methicillin Resistant *Staphylococcus aureus* (MRSA) (436)	361 (82.80)	15	58 (13.30)	02
Enterococcus species (104)	20	10	31 (29.81)	43 (41.35)
Streptococcus species (209)	21	164 (78.47)	20	04
Coagulase negative *Staphylococcus aureus* (CONS) (01)	-	-	-	01

Table 1: Overall bacteria isolated from different samples.

Year	Gram negative bacilli (No.)	Total MDR No. (%)	Total Carbapenem resistant No. (%)
2012	Enterobacteriaceae (2951)	723 (24.50)	05 (0.17)
	Non-fermenters (3043)	1653 (54.32)	32 (1.05)
	Total (5994)	2376 (39.64)	37 (0.62)
2013	Enterobacteriaceae (2312)	719 (31.10)	59 (2.55)
	Nonfermenters (2814)	1392 (49.47)	163 (5.79)
	Total (5126)	2111 (41.18)	222 (4.33)

Table 2: Multidrug Resistant Gram negative bacilli (MDR-GNB) and Carbapenem resistant (CR) bacteria isolated in 2012 and 2013.

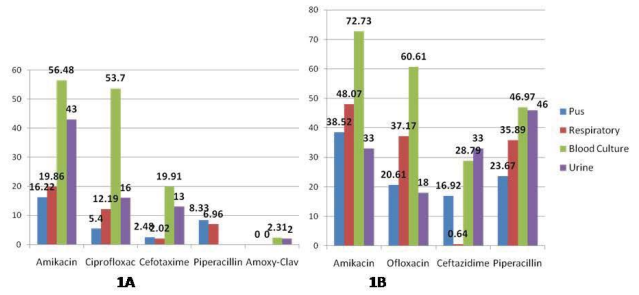

Figure 1: %Antibiotic susceptibility pattern of 1A: *Acinetobacter species* (n=1247) and 1B: *Pseudomonas aeruginosa* (n=1415).

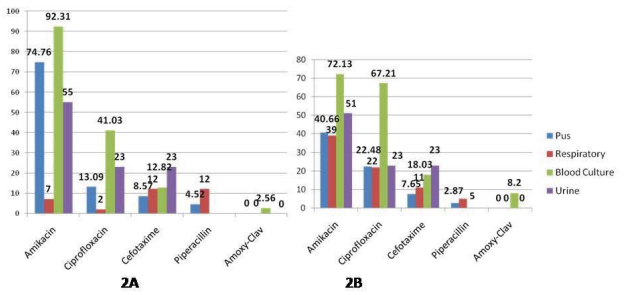

Figure 2: %Antibiotic susceptibility pattern of 2A: *Escherichia coli* (n=807) and 2B: *Klebsiella pneumoniae* (n=473).

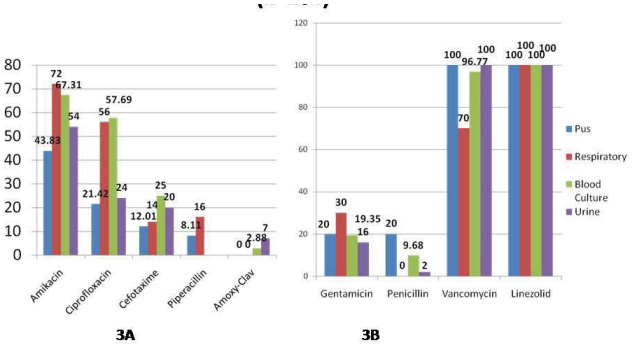

Figure 3: %Antibiotic susceptibility pattern of 3A: *Enterobacter species* (n=535) and 3B: *Enterococcus species* (n=104).

respectively. Piperacillin-tazobactam susceptibility of *Acinetobacter* species in pus and respiratory samples was only 28% and 12% respectively and that of *Pseudomonas aeruginosa* in the same samples was 24.5% and 61% respectively. All Enterobacteriaceae from pus samples showed susceptibility to piperacillin-tazobactam varying from 24.5% to 55% and from respiratory samples the same varied from 7.5% to 46%. From urine samples Enterobacteriaeceae susceptibility to piperacillin-tazobactam was within 0% to 27% and from blood cultures the same varied from 0% to 52%.

Colistin susceptibility of *Acinetobacter* species and *Pseudomonas aeruginosa* was 100%. *Acinetobacter* spp. susceptibility to tigecycline was 98%. Overall Multidrug Resistant Gram negative bacilli (MDR- GNB) isolated in 2013 was 41.18% (2111/5126), of which nonfermenting GNB

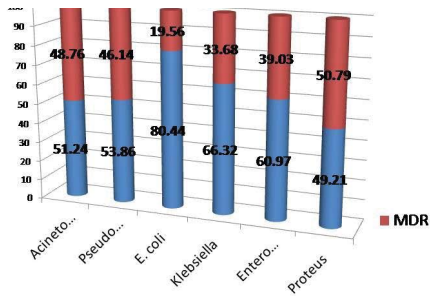

Figure 4: Prevalence of Multidrug resistant (MDR) Gram negative bacilli (GNB) in 2013.

showed more MDRs (49.47% - 1392/2814) than enterobacteriaceae (31.1% - 719/2312). Carbapenem resistant (CR) Gram negative bacilli in 2013 was 4.33% (222/5126), of which CR in nonfermenting GNB was 5.79% (163/2814) and in enterobacteriaceae CR was 2.55% (59/2312).

Figure 5 shows% antibiotic susceptibility pattern of *Staphylococcus aureus* (MSSA and MRSA). *S. aureus* showed 100% susceptibility to linezolid and only one Vancomycin Intermediate Resistant *S. aureus* (VISA) was recovered from blood culture. Netilmycin susceptibility of MRSA from urine samples and blood cultures were 100% and 88% respectively, whereas netilmycin susceptibility of MRSA from pus and respiratory samples were <66%. All Streptococcus species isolated from all sampled showed 100% susceptibility to linezolid and vancomycin.

Overall Inducible Clindamycin Resistance (ICR) in *S. aureus* was 18.57% (207/1115). ICR encountered in MRSA was 33.86% (149/440) and in MSSA it was 8.59% (58/675). Vancomycin In 2013, four (3.74%) Vancomycin Resistant Enterococci (VRE) were isolated – three from respiratory samples and one from blood culture. High Level Aminoglycoside resistance (HLAR) was seen in 23.36% enterococci (25/107) in 2013.

Discussion

In 2011, the theme of World Health Day was "Antimicrobial resistance: no action today, no cure tomorrow", and WHO published a six-point policy package to assist countries with tools to combat antimicrobial resistance. In 2014, WHO published its first global report on surveillance of antimicrobial resistance, with data provided by 114 countries [1]. The global emergence of antimicrobial resistance constitutes serious human and public health burdens, especially due to limited availability of treatment options. Such resistance poses morbid and mortal threats with challenges in the treatment of patients infected with such pathogens, as well as the infection control tolls associated with these resistant microorganisms [5,13].

Escherichia coli isolates from patients were mostly from cases of uncomplicated primary UTI. Other isolates from cases of UTI were from catheterized patients (Table 2). All the isolates were presumed pathogens in an established infectious process, as all urinary isolates with colony count $>10^5$ cfu/ml and with symptoms of UTI were selected for antibiotic susceptibility testing. Similarly, all patients with positive blood cultures were clinically diagnosed as sepsis with at least 2-3 positive biochemical markers of sepsis. All respiratory samples were endotracheal secretions from patients on ventilator in Intensive Care Units (ICUs) and sputum samples from wards (Table 2). Pus/wound

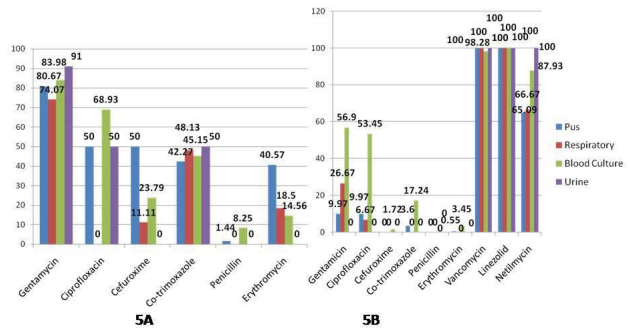

Figure 5: %Antibiotic susceptibility pattern of 5A: MSSA (n=659) and 5B: MRSA (n=436).

swabs were from patients having infection of post-surgical abdominal or thoracic wounds and also from burn patients. The infections were hospital acquired, as all the patients were admitted in this hospital for more than 48 hours.

In the present study, amongst Gram negative bacilli, maximum Proteus species was isolated from pus/wound swabs (82.54%), followed by *Pseudomonas aeruginosa* (78.52%), *Enterobacter* species (57.57%), *Acinetobacter* species (54.85%) and *Escherichia coli* (52.04%). *Escherichia coli* was predominant in urine (38.17%), followed by *Klebsiella pneumoniae* (20.51%). Amongst Gram positive cocci, maximum Enterococcus species was isolated from urine (41.35%), followed by from blood cultures (29.81%). *Staphylococcus aureus* was the major Gram positive isolate in pus/wound swabs, with MRSA being 82.8%. Streptococcus species was predominantly seen in respiratory samples (78.47%) (Table 1).

Enterococcus showed very high susceptibility to vancomycin, ranging from 96.77 to 100%, except in respiratory samples, where it was 70% (Figure 3B). Only four Vancomycin Resistant Enterococci (VRE) strains were detected in 2013. Zouin et al. have also observed 99.6% to 100% susceptibility to vancomycin and they detected seven VRE [14]. Rare and sporadic vancomycin resistant strains in enterococci are encountered. The prevalence of VRE in India, varies from 1.4 to 8% in few studies [15-18], but one study from Mumbai reported a prevalence of 23% [19].

High level aminoglycoside resistance (HLAR) detected was 23.36% in this study. Indian studies have reported a prevalence of HLAR, ranging from 7.8% to as high as 56% [20-23]. Zouin et al. detected HLAR in E. faecalis and *E. faecium* being, respectively, 19% and 39% against gentamicin and 36% and 26% against streptomycin [14].

In India, the incidence of MRSA is increasing, with prevalence rates varying from 23.6% to as high as 59.3% [24-26]. Out of total MRSA isolated in this study, 82.8% were from pus samples (Table 1). MRSA from blood cultures showed 57% and 53.5% susceptibility to gentamicin and ciprofloxacin. All other first line antibiotics showed very less susceptibility (Figure 5B). Vancomycin, which was regarded as the drug of choice for the MRSA infections, is showing early signs of emerging resistance. Hopefully, only one VISA was isolated in this study and no VRSA was encountered. Methicillin resistant *Staphylococcus aureus* (MRSA), though was relatively high in this study but vancomycin maintained uniform activity.

Penicillin and erythromycin susceptibility of MSSA were 8.25% and 14.56% in blood cultures. Gentamicin and ciprofloxacin susceptibility of MSSA were good, being >74% and >49% respectively but in respiratory samples, ciprofloxacin susceptibility was 0% (Figure 5A). Macrolide and clindamycin increasing rates of resistance is being noted in *S. pneumoniae*, group A streptococci, *S. aureus* and viridans streptococci in the recent years. Inducible Clindamycin Resistance encountered in MRSA and MSSA was 33.86% and 8.59% in the present study (Table 3).

Drug-resistant *Acinetobacter baumannii* has the distinction of simultaneously being a National Institute of Allergy and Infectious Diseases (NIAID) Category C pathogen and one of the six most dangerous MDR bacteria amongst the ESKAPE bugs. It accounts for 6% of Gram negative infections in intensive care facilities in the USA, with mortality rates as high as 54% having been reported by the IDSA [27]. In an USA study, isolation of MDR *acinetobacter* soared from 6.7% in 1993 to 29.9% by 2004, emphasizing the need for newer and better drugs [10].

The overall susceptibility of *Acinetobacter* spp. to the vast majority of antimicrobial agents is very low (Figure 1A). Since MDR *A. baumannii* is being encountered with increasing frequency in the hospitals, the use of fluoroquinolones is not advisable as a long-term treatment strategy. In this study, ciprofloxacin susceptibility of *Acinetobacter* spp. From blood cultures was 53.7% but in all other samples, ciprofloxacin susceptibility was <17% (Figure 1A). Overall imipenem susceptibility was >80% in the present study. Araj et al. have reported a remarkable resistance encountered against imipenem (increased from 1% in 2000/1 to 70% in 2010/11). The susceptibility rates against doripenem, meropenem and imipenem, were only 38.9%, 36.1% and 16.7%, respectively [28].

Tigecycline being one of the few remaining effective drugs, 98% of the *Acinetobacter* spp. analyzed by El Herte et al. during 2006-2007 were susceptible [29], and this rate is maintained till date. *Acinetobacter* spp. susceptibility to tigecycline was also 98% in this study. Colistin susceptibility was 100%.

With respect to P. aeruginosa, their susceptibilities to the different antimicrobial agents show fluctuations, generally within 46% to 72%, with susceptibility slightly higher in isolates from blood cultures (Figure 1B). Susceptibility of first line antibiotics to isolates from pus samples was <38%. Overall ceftazidime susceptibility was <34%, with only 0.64% ceftazidime susceptibility in isolates from respiratory samples (Figure 1B). Imipenem susceptibility of *Pseudomonas aeruginosa* was 65.38% in respiratory samples and 89% in pus samples, whereas in blood cultures and urine samples, imipenem susceptibility was 100% each. Araj et al. have reported susceptibility rates against doripenem, meropenem and imipenem, to be 65%, 47.5% and 27.5%, respectively [10].

E. coli isolates have been showing increasing resistance against most cephalosporins, fluoroquinolones and aminoglycosides. In this study, cefotaxime and ciprofloxacin susceptibility of *E. coli* was <24% and <42% respectively in all samples. Amikacin susceptibility was good in isolates from blood cultures (92.31%) but amikacin susceptibility of urinary isolates of *E. coli* was only 55%. In respiratory samples, susceptibility of *E. coli* to first line antibiotics was <13%. (Figure 2A). A relatively high and stable susceptibility are maintained for nitrofurantoin in urinary isolates and it was 85% in this study. Overall imipenem susceptibility was >86%, with 100% susceptibility in isolates from urine samples and blood cultures. However, piperacillin-tazobactam susceptibility of *E. coli* was <21% in all samples, except in pus samples, where it was 54.79%.

Klebsiella pneumoniae showed increasing resistance to all first line antibiotics. Amoxycillin/ clavulanic acid showed 100% resistance for *E. coli* and *Klebsiella* spp. in all samples, except in blood cultures, where susceptibility was only 8.2% and 2.56% respectively (Figure

Year	Gram positive cocci (No.)	Total ICR & VISA No. (%)	Total VRE & HLAR No. (%)
2012	MRSA (693)	50 (7.22)	-
	MSSA (1225)	55 (4.49)	-
	Enterococcus species (224)	-	2 VRE (0.89) 10 HLAR (4.46)
	Total	105/1918 (5.47)	
2013	MRSA (440)	149 (33.86)/01VISA (0.23)	-
	MSSA (675)	58 (8.59)	-
	Enterococcus (107)	-	4VRE (3.74) 25 HLAR (23.36)
	Total	207/1115 (18.57)	

Table 3: Inducible clindamycin resistance (ICR), Vancomycin Resistant Enterococci (VRE) and High Level Aminoglycoside resistance (HLAR) in 2012 and 2013.

2). Cefotaxime and ciprofloxacin susceptibility of *K. pneumoniae* was <24% and <68% respectively in all samples. Amikacin susceptibility in all samples was <52%, except in isolates from blood cultures, where it was 72% (Figure 2B). Piperacillin/tazobactam susceptibility of *K. pneumoniae* was <25% in all samples. Overall imipenem susceptibility was >82% in all samples, with 100% susceptibility in isolates from urine samples and blood cultures. Dutta et al. have reported a rise in resistance to cefotaxime (75 to 97%), piperacillin-tazobactum (55-84%) and carbapenem (2.4-52%) in *K. pneumoniae*, over a period of 10 years [30].

Nitrofurantoin susceptibility of *K. pneumoniae* in urinary isolates was 80% in this study but amikacin susceptibility was 51%, cefotaxime and ciprofloxacin susceptibility were only 23% each and amoxicillin-clavulanic acid susceptibility was 0% (Figure 2B). A study of urinary tract infections with *K. pneumoniae* in children from Pakistan has shown less than 30% susceptibility to cephalosporins and 31% to ciprofloxacin and amoxicillin-clavulanic acid. Piperacillin-tazobactam and meropenem were the most effective drugs [31].

Susceptibility of *Enterobacter* species to cefotaxime, piperacillin and amoxycillin/clavulanic acid was <26%, < 17% and <8% respectively. Even ciprofloxacin susceptibility was <58% but amikacin susceptibility was better in respiratory samples (72%) and blood cultures (67.31%) (Figure 3A). Piperacillin/tazobactam susceptibility of *Enterobacter* species was about 26% in pus and urine samples, whereas in respiratory samples and blood cultures the same was 46% and 51.85% respectively. Imipenem susceptibility of *Enterobacter* species was >88% in all samples, except in respiratory samples, where it was 58%.

Since 1989, outbreaks caused by strains of *S. typhi* resistant to chloramphenicol, ampicillin and trimethoprim/ sulfamethoxazole have been reported in many developing countries, especially Pakistan and India [32]. *S. typhi* has maintained uniform susceptibility to ampicillin, cefotaxime, ciprofloxacin and trimethoprim/ sulfamethoxazole till 2004. Thereafter, few resistant strains started to emerge with variable susceptibility to ampicillin (65% to 100%) and trimethoprim/sulfamethoxazole (43%-100%). In this study, 16 strains of *S. typhi* recovered from blood cultures were susceptible to ampicillin, cefotaxime, trimethoprim/sulfamethoxazole, nalidixic acid, ciprofloxacin and chloramphenicol. Resistance to quinolones is also being encountered in Salmonella spp. but in this study, no *S. typhi* resistance to third generation cephalosporins or fluoroquinolones was detected.

Resistance to carbapenems remains problematic in *Acinetobacter* spp. and *Pseudomonas aeruginosa*, and has also started emerging in *E. coli* and *K. pneumoniae*. Very few options remain for the treatment of these virulent organisms. Antibiotics which are currently in use to treat Carbapenem Resistant Enterobacteriaceae (CRE) infections include aminoglycosides, polymyxins, tigecycline, fosfomycin and temocillin [4]. Fortunately, overall carbapenem resistance in this study was only 4.33% but overall multidrug resistant bacteria was 41.18%. Tigecycline and colistin maintains excellent activity against most ESBL and carbapenem resistant bacteria.

One must be aware of the resistant flora which is being generated due to the rampant use of the higher generation antibiotics. Most often we fail to differentiate colonization from infection and needlessly prescribe those antibiotics, which were meant to be used as reserve drugs. The organisms that are not inhibited by the cephalosporins, consequently overgrow, with varying potential, to cause infections and the association between the cephalosporin usage and the emergence of multiple drug-resistant organisms has been proved [33].

Clinico-microbiologic cum hospital infection control committee meetings should be regularly organized in hospitals, for increasing the awareness on the local sensitivity patterns, to guide the rational use of antibiotics, especially their empirical use. Antibiotic prescriptions should be reviewed by microbiologists/infectious disease specialists before their administration to the patients [34].

This hospital has an active Hospital Infection Control Committee (HICC), which regularly takes rounds in the different wards and Intensive Care Units (ICUs) and also monthly meetings of HICC with all the committee members are held to discuss indiscriminate antibiotic use.

It has been proposed by the Directorate General Health Services of the Government of India that the sale of antibiotics Over the Counter (OTC) without proper prescriptions, should be stopped.

Practical application of the principles of the rational antibiotic therapy should be included in the medical/dental undergraduate curriculum. Most of the hospitals in India do not have a standardized antibiotic policy or a constant infection surveillance program. This institute has an effective antibiotic policy, which are reviewed from time to time according to the situation.

Conclusion

Simple measures such as hand washing and barrier precautions can significantly reduce the spread of ESKAPE bugs. As these are multidrug resistant, they might pose a therapeutic challenge to the clinicians as well as microbiologists. Timely implementation of proper infection control practices reduce, eliminate and prevent establishment of these bugs. Judicious use of antibiotics is the need of the day to control the spread of MDR "ESKAPE" bugs. Physicians should be aware of the local epidemiology of antimicrobial resistance to properly guide the initial therapy.

A strict antibiotic policy should be followed in every hospital which restricts the use of the broad spectrum agents (especially the third-generation cephalosporins). The cephalosporins should only be used as reserve drugs, in the fluoroquinolone resistant cases, with evidence based indications only. The reserve drugs such as vancomycin or those which are used against the resistance to the carbapenems, like polymyxin B and E (colistin), tigecycline and fosfomycin should never be used indiscriminately.

Most of these resistance problems are attributed to uncontrolled use of antimicrobial agents. Therefore, there is an urgent need to develop antimicrobial stewardship, to curb this threat [34].

References

1. World Health Organization. Antimicrobial resistance. From: http://www.who.
2. Raghunath D (2008) Emerging antibiotic resistance in bacteria with special reference to India. J Biosci 33: 593-603.
3. De A (2014) Detection of Drug Resistance in Bacteria. In Practical and Applied Microbiology. (5thedn). The National Book Depot, Mumbai 132-137.
4. van Duin D, Kaye KS, Neuner EA, Bonomo RA (2013) Carbapenem-resistant Enterobacteriaceae: a review of treatment and outcomes. Diagn Microbiol Infect Dis 75: 115-120.
5. Spellberg B, Guidos R, Gilbert D, Bradley J, Boucher HW, et al. (2008) The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. Clin Infect Dis 46: 155-164.
6. Peterson LR (2009) Bad bugs, no drugs: no ESCAPE revisited. Clin Infect Dis 49: 992-993.
7. Mulvey MR, Simor AE (2009) Antimicrobial resistance in hospitals: how concerned should we be? CMAJ 180: 408-415.
8. Orsi GB, Falcone M, Venditti M (2011) Surveillance and management of multidrug-resistant microorganisms. Expert Rev Anti Infect Ther 9: 653-679.
9. Araj GF, Kanj SS (2000) Current status and changing trends of antimicrobial resistance in Lebanon. J Med Liban 48: 221-226.
10. Winn W Jr., Allen S, Janda W, Koneman E, Procop G, et al. (2006) In Koneman's Color Atlas & Textbook of Diagnostic Microbiology. (6th edn). Williams & Wilkins, Lippincott. pp 75-78, 82-88, 95-103, 213-227, 313-316, 645-648, 709-718, 726-733.
11. Performance Standards for Antimicrobial Susceptibility Testing; Twenty Third Informational Supplement (2013) Clinical and Laboratory Standards Institute. M100-S23. pp 44-49, 62-67, 72-79, 84-85, 90-95
12. Okeke IN, Laxminarayan R, Bhutta ZA, Duse AG, Jenkins P, et al. (2005) Antimicrobial resistance in developing countries. Part I: recent trends and current status. Lancet Infect Dis 5: 481-493.
13. Zouain MG, Araj GF (2001) Antimicrobial resistance of Enterococci in Lebanon. Int J Antimicrob Agents 17: 209-213.
14. Ghoshal U, Garg A, Tiwari DP, Ayyagari A (2006) Emerging vancomycin resistance in enterococci in India. Indian J Pathol Microbiol 49: 620-622.
15. Taneja N, Rani P, Emmanuel R, Sharma M (2004) Significance of vancomycin resistant enterococci from urinary specimens at a tertiary care centre in northern India. Indian J Med Res 119: 72-74.
16. Kapoor L, Randhawa VS, Deb M (2005) Antimicrobial resistance of enterococcal blood isolates at a pediatric care hospital in India. Jpn J Infect Dis 58: 101-103.
17. Shah L, Mulla S, Patel KG, Rewadiwala S (2012) Prevalence of enterococci with higher resistance level in a tertiary care hospital: a matter of concern. National J Med Res 2: 25-27.
18. Karmarkar MG, Gershom ES, Mehta PR (2004) Enterococcal infections with special reference to phenotypic characterization & drug resistance. Indian J Med Res 119 Suppl: 22-25.
19. Agarwal VA, Jain YI, Pathak AA (1999) Concomitant high level resistance to penicillin and aminoglycosides in Enterococci at Nagpur, Central India. Indian J Med Microbiol 17: 85-87.
20. Randhawa VS, Kapoor L, Singh V, Mehta G (2004) Aminoglycoside resistance in enterococci isolated from paediatric septicaemia in a tertiary care hospital in north India. Indian J Med Res 119 Suppl: 77-79.
21. Adhikari L (2010) High-level Aminoglycoside Resistance and Reduced Susceptibility to Vancomycin in Nosocomial Enterococci. J Glob Infect Dis 2: 231-235.
22. Narayanaswamy A, Rajalakshmi K, Varadharajan M (2011) Speciation and antimicrobial susceptibility pattern of Enterococci from a tertiary health care center of south India. J Pharm Res 4: 989-990.
23. Majumder D, Bordoloi JS, Phukan AC, Mahanta J (2001) Antimicrobial susceptibility pattern among methicillin resistant Staphylococcus isolates in Assam. Indian J Med Microbiol 19: 138-140.
24. Tiwari HK, Sen MR (2006) Emergence of vancomycin resistant Staphylococcus aureus (VRSA) from a tertiary care hospital from northern part of India. BMC Infect Dis 6: 156.
25. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, et al. (2009) Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis 48: 1-12..
26. Lockhart SR, Abramson MA, Beekmann SE, Gallagher G, Riedel S, et al. (2007) Antimicrobial resistance among Gram-negative bacilli causing infections in intensive care unit patients in the United States between 1993 and 2004. J Clin Microbiol 45: 3352-3359.
27. El-Herte RI, Araj GF, Matar GM, Baroud M, Kanafani ZA, et al. (2012) Detection of carbapenem-resistant Escherichia coli and Klebsiella pneumoniae producing NDM-1 in Lebanon. J Infect Dev Ctries 6: 457-461.
28. Datta S, Wattal C, Goel N, Oberoi JK, Raveendran R, et al. (2012) A ten year analysis of multi-drug resistant blood stream infections caused by Escherichia coli & Klebsiella pneumoniae in a tertiary care hospital. Indian J Med Res 135: 907-912.
29. Jamil I, Zafar A, Qamar MU, Ejaz H, Akhtar J, et al. (2014) Multi-drug Resistant Klebsiella pneumoniae causing urinary tract infections in children in Pakistan. African J Microbiol Res 8: 316-319.
30. Rowe B, Ward LR, Threlfall EJ (1997) Multidrug-resistant Salmonella typhi: a worldwide epidemic. Clin Infect Dis 24 Suppl 1: S106-109.
31. Dancer SJ (2001) The problem with cephalosporins. J Antimicrob Chemother 48: 463-478.
32. Thakuria B, Lahon K (2013) The Beta Lactam Antibiotics as an Empirical Therapy in a Developing Country: An Update on Their Current Status and Recommendations to Counter the Resistance against Them. J Clin Diagn Res 7: 1207-1214.
33. Gould IM (1988) Control of antibiotic use in the United Kingdom. J Antimicrob Chemother 22: 395-397.
34. IDSA. (2014) Antimicrobial Stewardship. Antimicrobial Stewardship Policy Statement of the IDSA, SHEA and PIDS. From: http://www.idsociety.org/stewardship_policy/. Accessed November 7.