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ORIGINAL RESEARCH

High prevalence of extended-spectrum β-lactamase-producing pathogens: results of a surveillance study in two hospitals in Ujjain, India

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Background: Recent reports of the rapid evolution of bacterial resistance in India require urgent antibiotic stewardship programs. This study aimed to define the magnitude and pattern of resistance of bacterial pathogens to guide empirical therapy.

Methods: We prospectively collected consecutive, clinically significant, and nonduplicate bacterial isolates from each patient from two hospitals in Ujjain, India. The antibiotic susceptibility of the bacteria was tested using a disc diffusion method as recommended by the Clinical and Laboratory Standards Institute.

Results: A total of 716 pathogens were isolated from 2568 patients (median age, 25 years; range, 0 days to 92 years). Gram-negative infections were predominant (62%). The isolated pathogens included *Staphylococcus aureus* (n = 221; 31%), *Escherichia coli* (n = 149; 21%), *Pseudomonas aeruginosa* (n = 127; 18%), and *Klebsiella pneumoniae* (n = 107; 15%). Common diagnoses included abscesses (56%), urinary tract infections (14%), blood stream infections (10%), pneumonia (10%), and vaginal infections (10%). In *E. coli* isolates, 69% (95% confidence interval [CI] 61.6–76.6) were extended-spectrum β-lactamase (ESBL) producers and 41% (95% CI 31.6–50.5) of *K. pneumoniae* isolates were ESBL producers. These isolates had a high resistance to fluoroquinolones and β-lactams, except for imipenem and piperacillin-tazobactam. *Salmonella typhi* remained sensitive to third-generation cephalosporins. Methicillin-resistant *S. aureus* (MRSA) constituted 30% of all *S. aureus* isolates and showed resistance to ciprofloxacin (81%), cotrimoxazole (76%), and levofloxacin (60%).

Conclusion: Our results showed a high prevalence of ESBL among Gram-negative bacterial isolates and a high prevalence of MRSA among *S. aureus* isolates. Carbapenems provided the broadest coverage for Gram-negative bacteria, while glycopeptides were the most effective against MRSA; however, both classes of drugs need to be used judiciously. This study will help in planning future antibiotic stewardship programs.

Keywords: antibiotic susceptibility, surveillance, extended-spectrum β-lactamases, India

Introduction

Antibiotic resistance is a global public health problem.[1,2] The foundation of modern medicine is built on the availability of effective antibiotics, especially in economically deprived areas of the world where the disease burden due to bacterial infections remains high. Antibiotic resistance is predominantly fueled by antibiotic use.[3] The regular introduction of new antibiotic classes over the years has partly masked the problem of increasing resistance. However, this is no longer the case today because the pipeline for newer antibiotics is nearly empty.[4] Therefore, we need to preserve the currently available antibiotics for use by future generations.[1,2] The World Health Organization

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and European Commission have recognized the importance of studying the emergence and determination of resistance and the need for control strategies. The need for strategies to control antibiotic resistance is greater in resource constraint settings because antibiotic resistance puts further strain on an already fragmented health care system in low and middle-income countries.[5]

One recent eye opener is the spread of *Enterobacteriaceae*, with resistance to carbapenem conferred by New Delhi metallo-β-lactamase 1 (NDM-1).[6] NDM-1 received extensive media coverage for two reasons, ie, the bacteria carrying the *NDM-1* gene are resistant to all antibiotics except tigecycline and colistin, and were rapidly transmitted across national borders.[6]

In India, rapid evolution of bacterial resistance may be due to a complex interaction of several factors such as higher burden of infectious disease, treatment uncertainty, lack of treatment guidelines, inadequate access to standard laboratory facilities, self-medication, prescription based on availability, government support to pharmaceutical industries, market forces, antibiotics prescribed by unqualified health professionals, less strict law enforcement, fragmented public health system, poor population-wide insurance coverage, inadequate adherence to universal hygiene and infection control measures, and to low population-wide education level.[7–12] Antibiotic stewardship programs are thus urgently needed in India.[8,10]

Antibiotic susceptibility surveillance is fundamental for creating an antibiotic stewardship program. Thus, we set up a surveillance system in two hospitals in Ujjain, India, with the aim of defining resistance magnitude and patterns of bacterial pathogens and providing locally applicable data to guide empirical therapy.

Materials and methods

This prospective study was conducted over a period of 15 months from November 2007 to February 2009 in Ujjain, India.

Study settings

The study sites were two hospitals, ie, a 570-bed teaching hospital attached to RD Gardi Medical College and a 350-bed nonteaching hospital. Both hospitals cater predominantly for rural populations from the villages surrounding Ujjain city. In both hospitals, most admissions (89%–91%) to the medical and intensive care units are made on an emergency basis, whereas admissions into surgical units are made on an elective or emergency basis.

Collection of samples and study participants

We prospectively collected consecutive, nonduplicate, single patient samples. Only "clinically significant" samples (from patients with presumed infections) were sent for culture. The following infections and corresponding samples were included in the study: abscesses (pus/secretions and swabs from skin and soft tissue infections), post-surgery or traumatic wounds, and burns, and ear discharge (in clinically proven serous otitis media), urinary tract infections (mid-stream clean catch urine or urine from a catheter), blood stream infections (in cases of clinical sepsis), pneumonia (induced sputum and/or bronchoalveolar lavage), and vaginal infections (high vaginal swab). Isolates from the screening procedures and samples for fungal, mycobacterial, and anaerobic bacterial cultures were not included in the study.

The admitting consultants were requested to send clinically relevant samples for culture from all patients suspected of having a bacterial infection. The following demographic information was collected for all the patients: age, gender, family size, education level (of adult patients or of a child patient's mother), breadwinner's occupation, reported history of antibiotics received in the past two weeks, and reported hospitalizations in the past two weeks.

Participating departments in both hospitals included pediatrics, general medicine, general surgery, obstetrics and gynecology, ear, nose and throat, orthopedics, chest medicine, adult medicine intensive care unit, and neonatal intensive care unit.

Identification, antibiotic susceptibility testing, and definitions of resistance

Within four hours of receipt at the laboratory, all the samples were plated on blood agar and MacConkey agar medium (HiMedia Laboratories Pvt, Ltd, Mumbai, India). Pathogenic bacteria were identified using standard conventional microbiological methods.[13] Antibiotic sensitivity testing was performed using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar plates. The disc strengths were as recommended by the Clinical and Laboratory Standards Institute (CLSI) at the time of the study. CLSI interpretive criteria for susceptibility and resistance were followed.[14] Antibiotic sensitivity testing quality control was performed using the following reference strains: *Escherichia coli* ATCC (American Type Culture Collection) 25922, *Klebsiella pneumoniae* ATCC 70063, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, and *Staphylococcus aureus* ATCC 29213. Intermediate sensitive

isolates of Gram-negative bacteria were counted as resistant in the calculations.

Extended-spectrum β-lactamase (ESBL) production was detected using a double-disc synergy test.[15] The presence of ESBL was assayed using the following antibiotic discs: cefotaxime 30 µg, cefotaxime/clavulanic acid 30/10 µg, ceftazidime 30 µg, and ceftazidime/clavulanic acid 30/10 µg (HiMedia Laboratories Pvt, Ltd, Mumbai, India). According to the CLSI criteria for ESBL detection, each isolate with an inhibition zone diameter of ≤22 mm for ceftazidime or ≤27 mm for cefotaxime was considered to be a potential ESBL producer or screen positive. A zone diameter increase of ≥5 mm for either antimicrobial agent when tested in combination with clavulanic acid versus when tested alone was considered as an ESBL-producing organism. *K. pneumoniae* ATCC700603 (positive control) and *E. coli* ATCC25922 (negative control) were used for quality control in the ESBL tests.[14]

For *S. aureus* isolates, screening for methicillin resistance was performed using a cefoxitin disc screen test and 6 g/mL oxacillin in Mueller-Hinton agar supplemented with NaCl (4% w/v; 0.68 mol/L) according to the CLSI guidelines.[14] Multidrug-resistant isolates were defined as isolates having coresistance to at least three antibiotic groups.[16] The ethics committee of RD Gardi Medical College approved the study (approval number 41/2007). The cultures were performed without any cost to the patients, and the results were made available to each patient's physician.

Statistical analysis

The data were entered in EpiData Entry (version 3.1) software and then transferred to Stata 10.0 for further analysis (Stata Corporation, College Station, TX). Descriptive statistics were used.

Results

Patient demographics and distribution within departments or wards

The main characteristics of patients enrolled in the study are shown in Table 1. A total of 716 pathogens were isolated from 2568 patients. Thus, the culture positivity rate was 28% (95% confidence interval [CI] 26.1–29.6). The median patient age was 25 (range, from 0 days to 92 years), and the median age of men and women was 23 and 26 years, respectively. Most samples (95%) were sent from wards while the remaining samples were sent from intensive care units. The most common diagnoses (Table 2) were abscesses (56%), urinary tract infections (14%), blood stream infections (10%), pneumonia (10%), and vaginal infections (10%).

Table 1 Demographic characteristics of the 901 pediatric and 1667 adult patients from whom 716 pathogenic bacteria were isolated in Ujjain, India

Patient characteristics	Pediatrics (0–12 years)	Adults	Total (%)
	n = 901 (35%)	n = 1667 (65%)	n = 2568 (100%)
Gender			
Male	569 (63)	868 (52)	1437 (56)
Female	332 (37)	799 (48)	1131 (44)
Family size			
≤4	356 (40)	742 (44)	1098 (43)
5–10	502 (55)	778 (47)	1280 (50)
>10	43 (5)	147 (9)	190 (7)
Hospital			
Nonteaching	552 (58)	608 (36)	1130 (44)
Teaching	379 (42)	1059 (64)	1438 (56)
Hospital ward			
Pediatrics	686 (76)	–	686 (27)
Medicine	–	243 (14)	243 (9)
Obstetrics and gynecology	14 (2)	378 (23)	392 (15)
Surgery	38 (4)	661 (40)	699 (27)
Orthopedics	10 (1)	37 (2)	47 (2)
ENT	69 (8)	150 (9)	219 (7.5)
Chest medicine	7 (0.7)	103 (6)	110 (4)
NICU	62 (7)	–	62 (2)
PICU	12 (1)	–	12 (0.5)
ICU	–	46 (3)	46 (2)
Others	3 (0.3)	49	52 (2)
Source of infection			
Abscesses	151 (17)	770 (46)	921 (36)
Pneumonia	480 (53)	257 (15)	737 (29)
UTI	75 (8)	331 (20)	406 (16)
BSI	182 (20)	72 (4)	254 (10)
Vaginal infections	13 (1)	237 (14)	250 (10)
Gram-negative bacteria grown	88 (53)	359 (65)	447 (62)
Gram-positive bacteria grown	77 (47)	192 (35)	269 (38)

Abbreviations: ENT, ear nose and throat; NICU, neonatal intensive care unit; PICU, pediatric intensive care unit; ICU, intensive cardiac care unit; UTI, urinary tract infection; BSI, blood stream infection.

Most common pathogens

The distribution of the four most common pathogens by infection site is shown in Table 2. Details of site of infection and proportion of different bacteria (n = 393) isolated from abscesses are shown in Figure 1. Gram-negative infections were predominant (62%). However, the most commonly isolated pathogen was *S. aureus* (n = 221; 31%), followed by *E. coli* (n = 149; 21%), *P. aeruginosa* (n = 127; 18%), and *K. pneumoniae* (n = 107; 15%). *S. typhi* was isolated most frequently from blood stream infections (21%). *E. coli* constituted 66% of the urinary tract infection isolates. In pneumonia, *P. aeruginosa* was the most commonly isolated organism (n = 22; 30%),

Table 2 Distribution of commonest four pathogens per site of infection in surveillance study in two hospitals, Ujjain, India

Site of infection	n	% of total	Rank
Abscess[a]			
Staphylococcus aureus	185	47	1
Pseudomonas aeruginosa	84	21	2
Klebsiella pneumoniae	44	11	3
Escherichia coli	43	11	4
Others	37	10	–
Total	393	100	
UTI[b]			
Escherichia coli	61	60	1
Klebsiella pneumoniae	25	24	2
Pseudomonas aeruginosa	6	5	3
Bacillus spp.	3	3	4
Others	8	8	–
Total	103	100	
BSI[c]			
Salmonella typhi	21	28	1
CoNS	20	27	2
Staphylococcus aureus	10	13	3
Pseudomonas aeruginosa	6	8	4
Others (*Escherichia coli*, 8 isolates)	18	24	–
Total	75	100	
Pneumonia[d]			
Pseudomonas aeruginosa	22	30	1
Klebsiella pneumoniae	21	28	2
Staphylococcus aureus	10	14	3
Escherichia coli	8	8	4
Others	15	20	–
Total	74	100	
Vaginal infections[e]			
Escherichia coli	32	45	1
Staphylococcus aureus	14	20	2
Klebsiella pneumoniae	12	17	3
Pseudomonas aeruginosa	9	13	4
Others	4	5	–
Total	71	100	

Notes: [a]Including pus/secretions and swabs from skin and soft tissue infections, post-surgery or traumatic wounds, burns, ear discharge (clinically confirmed otitis media), empyema, breast abscess and intra-abdominal abscess (See Figure 1 for details); [b]UTI urinary tract infection; most (91%) samples were mid-stream clean catch and the rest urine from catheter; [c]BSI blood stream infections; samples sent in cases of clinical sepsis; [d]pneumonia samples were induced sputum and bronchioalveolar lavage; [e]vaginal infection samples were high-vaginal swabs.

Abbreviations: BSI, blood stream infection; CoNS, coagulase-negative staphylococci; UTI, urinary tract infection.

followed by *K. pneumoniae* (n = 21; 28%) and *S. aureus* (n = 10; 14%). Gram-negative organisms were isolated from the bronchoalveolar lavage samples from adults or from the pneumonia with sepsis samples from neonates. Gram-negative *E. coli*, *K. pneumoniae*, and *P. aeruginosa* constituted 75% of the organisms isolated from vaginal infection.

Antibiotic susceptibility testing of common Gram-negative bacteria

A total of 447 Gram-negative pathogens were isolated. The in vitro antibiotic susceptibility of the common Gram-negative bacteria is shown in Table 3. Remarkably high resistance for β-lactam antibiotics (range 72%–97%) and fluoroquinolones (range 51%–95%) was observed for the three most common Gram-negative bacteria, ie, *E. coli*, *P. aeruginosa*, and *Klebsiella. E. coli* showed the highest susceptibility (98%) to imipenem followed by piperacillin-tazobactam (85%). The same antibiotics were also active against other *Enterobacteriaceae*, *Klebsiella*, *Pseudomonas*, and *Proteus* species. *S. typhi* showed good sensitivity to the third-generation cephalosporins, ie, ceftriaxone (86%) and ceftazidime (88%), as compared with fluoroquinolones, ie, ciprofloxacin (31%) and ofloxacin (28%, Table 3).

The ESBL rates were 69% (95% CI 61.6–76.6) for *E. coli* and 41% (95% CI 31.6–50.5) for *K. pneumoniae.* Among *E. coli*, *P. aeruginosa*, and *Klebsiella*, coresistance to cephalosporins and fluoroquinolones was 51.2% (95% CI 44.8–58.3). The multidrug-resistant rate among Gram-negative bacteria was 17.6% (95% CI 14.1–21.2). The multidrug-resistant rates were highest for *E. coli* (21%; 95% CI 14.8–28.1), followed by *K. pneumoniae* (19%; 95% CI 11.1–26.1) and *P. aeruginosa* (17%; 95% CI 9.9–23.0). There were three pan-resistant isolates (for the tested antimicrobial drugs), one each for *E. coli*, *P. aeruginosa*, and *K. pneumoniae*.

Antibiotic susceptibility testing of common Gram-positive bacteria

The in vitro antibiotic susceptibility pattern of 154 methicillin-sensitive *S. aureus* (MSSA) isolates is shown in Table 4. Resistance to commonly used oral antibiotics, including ampicillin (86%), amoxicillin-clavulanate (50%), cotrimoxazole (38%), ciprofloxacin (49%), and erythromycin (9%) was noted in MSSA isolates. Because physicians commonly coprescribe amikacin in our study setting to treat serious *S. aureus* infections, we studied coresistance of *S. aureus* to a combination of amikacin with different classes of antibiotics. Coresistance for amikacin was observed for ampicillin (6%), amoxicillin-clavulanate (5%), ciprofloxacin (4%), ceftriaxone (1%), and chloramphenicol (1%). Coresistance to ciprofloxacin and erythromycin was 7%.

MSSA isolates did not show resistance to vancomycin, teicoplanin, linezolid, or clarithomycin. However, high susceptibility was also noted for cefoxitin (93%), amikacin (94%), clindamycin (92%), gentamicin (90%), and chloramphenicol (86%).

MRSA constituted 30% of all *S. aureus* isolates. The antibiotic susceptibility pattern of the 67 MRSA isolates is shown in Table 4. The MRSA isolates showed resistance

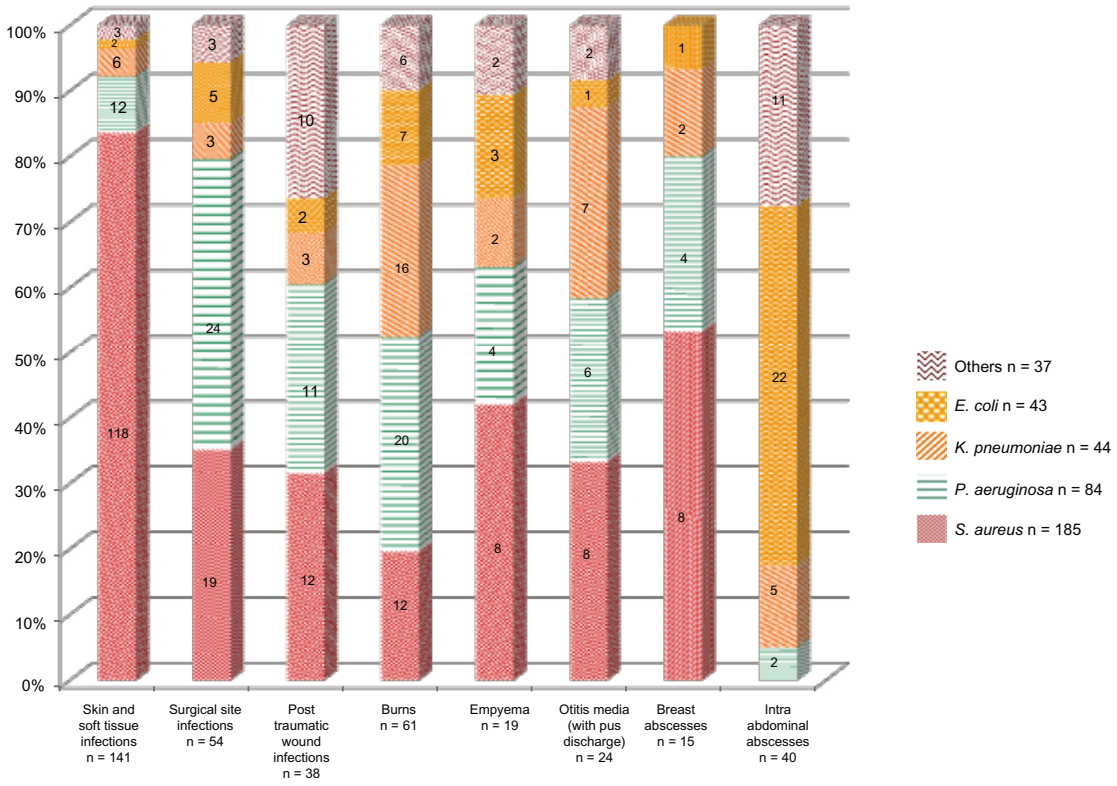

Figure 1 Details of site of infection and proportion of different bacteria (n = 393) isolated from abscesses in two hospitals in Ujjain, India.

to ciprofloxacin (81%), cotrimoxazole (76%), levofloxacin (60%), erythromycin (28%), and doxycycline (27%). Moreover, MRSA showed coresistance to levofloxacin and amikacin (27%), doxycycline and levofloxacin (27%), ciprofloxacin and amikacin (24%), ciprofloxacin and erythromycin (22%), doxycycline and amikacin (16%), and chloramphenicol with amikacin (9%). No resistance was noted for clindamycin and amikacin.

Coagulase-negative staphylococci (n = 20) were regarded as pathogens after considering the clinical condition of a patient and when cultured in paired blood samples. Methicillin resistance was 89%. A high proportion of resistance was observed for chloramphenicol (88%), cotrimoxazole (82), tetracycline (76%), doxycycline (68%), and clindamycin (54%).

Discussion

To the best of our knowledge, this is the first surveillance study that examined the antimicrobial susceptibilities of common pathogens in a rural resource-poor setting in central India. In India, most populations reside in and seek health care in similar settings. However, previously reported studies have been performed in larger metropolitan cities.[11,12] The present study showed that the common pathogens were *S. aureus* (31%), *E. coli* (21%), *P. aeruginosa* (18%), and *K. pneumoniae* (15%). The ESBL rate of *E. coli* was 69% (95% CI 61.6–76.6), while that of *K. pneumoniae* was 41% (95% CI 31.6–50.5). MRSA constituted 30% of all *S. aureus* isolates. To improve the clinical outcome of patients in resource-poor settings, treatment guidelines for empirical therapy need to be formulated. These guidelines should ideally be aligned with local susceptibility patterns. Availability of this information will help clinicians select appropriate and effective therapy and reduce the incidence of drug-resistant bacteria.

In this study, abscesses, pneumonia, and urinary tract infection were responsible for 80% of all the culture-positive infections. *E. coli*, *P. aeruginosa*, *K. pneumoniae*, and *S. aureus* were responsible for 85% of culture-positive infections. Similar patterns of bacterial isolates are noted from other resource-constrained countries,[17,18] including India.[11,12] The SENTRY Antimicrobial Surveillance Program in the Asia-Pacific also reported *S. aureus* as the most common organism, followed by *P. aeruginosa* and *E. coli*.[19,20]

P. aeruginosa was the most common organism isolated from pneumonia and the second most common organism isolated from abscesses. It remains the leading cause of health care-associated infections worldwide, especially

Table 3 Spectrum of activity of 20 antimicrobials against five most prevalent causes of Gram-negative infections in a surveillance study in two hospitals, Ujjain, India

Antimicrobial class/agent tested	Resistance by organism (number tested) R (%)				
	E. coli (149)	*P. aeruginosa* (127)	*K. pneumoniae* (107)	*S. typhi* (21)	*Proteus* spp. (20)
Penicillin					
Ampicillin	89		97	87	80
Amoxicillin/clavulanate	82		90		79
Piperacillin/tazobactam	15	17	21		12
Cephalosporins					
Cefuroxime	80		93		76
Ceftriaxone	72		79	14	74
Cefixime	79				72
Cefpodoxime	79		75		75
Ceftazidime	73	87	82		74
Other β lactam					
Imipenem	2	2	2	0	0
Quinolones					
Nalidixic acid	92		93	83	82
Ciprofloxacin	83	63	65	69	71
Norfloxacin	85		74	–	70
Ofloxacin	80	55	55	72	68
Gatifloxacin	79	64	53		67
Sparfloxacin	80	61	51		72
Aminoglycosides					
Gentamicin	59	69	69		33
Amikacin	33	38	32		20
Others					
Chloramphenicol	33			2	50
Tetracycline	92				100
Cotrimoxazole	83		94	87	58
Nitrofurantoin	12	–	–	–	–

Abbreviation: R, resistance.

in patients admitted to intensive care units. The organism is ranked second only to *S. aureus* as the most common cause of health care-associated infections in most European intensive care units.[21] A single tertiary care center reported a three-fold increase in the number of *P. aeruginosa* isolates in India during the study period of 2007–2008 along with decreasing sensitivity to meropenem (from 64% in 2007 to 35% in 2008).[11] Decreasing sensitivity to third-generation cephalosporins and fluoroquinolones is also well established in India.[11,12] Most of the isolates of *P. aeruginosa* in the present study could be from health care-associated infections. The susceptibility rates found in the present study (13% for ceftazidime, 37% for ciprofloxacin) are similar to those observed in other studies from India.[22,23] Varghese et al[12] reported 70% resistance to fluoroquinolones and other second-line antipseudomonal drugs such as piperacillin/tazobactam (42%), cefoperazone/sulbactam (40%), and cefpirome (54%).

The third generation cephalosporins effective against *Pseudomonas aeruginosa* are ceftazidime and cefaperazone. Nearly 87% of the isolates in this study are resistant to Ceftazidime. This may be a local phenomenon.

Carbapenems, colistin, polymyxin B, or a combination of ceftazidime and an aminoglycoside can be used for the empirical treatment of *Pseudomonas* infections.[11,24] Increasing carbapenem resistance is a global challenge,[20] but, fortunately, the phenomenon is rare in our setting.

Widespread resistance of *S. typhi* to commonly used oral antibiotics is a serious clinical and a public health challenge. In the present study, *S. typhi* showed high resistance to ampicillin, cotrimoxazole, and ciprofloxacin. This phenomenon has been reported in other studies, discussed in a recent review,[25] which suggested that fluoroquinolones and third-generation cephalosporins are equally effective treatment options for *Salmonella* infections.[25] In the present study, however, the sensitivity to third-generation cephalosporins remained high (86%–88%), indicating that they are a better treatment option than fluoroquinolones. However, minimum inhibitory concentrations for

Table 4 Spectrum of activity of 25 antimicrobials against three most prevalent causes of Gram-positive infections in surveillance study in two hospitals, Ujjain, India

Antimicrobial class/agent tested	Activity by organism (number tested)								
	MSSA (154)			MRSA (67)			CoNS (20)		
	R (%)	IR (%)	S (%)	R (%)	IR (%)	S (%)	R (%)	IR (%)	S (%)
Penicillin									
Oxacillin	–	–	100	100	–	–	89	–	11
Ampicillin	86	–	14	–	–	–	–	–	–
Amoxicillin/clavulanate	50	2	48	–	–	–	42	–	58
Cephalosporins									
Cefoxitin	4	3	93	*	*	*	*	*	*
Ceftriaxone	3	3	94						
Cefixime	32	3	65						
Cefoperazone	49	8	43						
Quinolone									
Ciprofloxacin	49	3	48	81	1	18	58	3	49
Ofloxacin	34	2	64	63	6	31	–	–	–
Gatifloxacin	22	4	74	58	13	29	–	–	–
Sparfloxacin	30	3	67	60	3	37	–	–	–
Levofloxacin	29	6	65	60	6	34	60	2	48
Lomefloxacin	38	2	60	67	–	33	–	–	–
Macrolides-lincosamides									
Erythromycin	9	10	81	28	16	56	68	2	32
Clarithromycin	–	–	100	9	–	91	–	–	–
Clindamycin	4	4	92	21	7	72	56	–	44
Glycopeptides									
Vancomycin	–	–	100	2	–	98	–	–	100
Teicoplanin	–	–	100	–	–	100	–	–	100
Aminoglycosides									
Gentamicin	8	1	91	34	2	64	–	–	–
Amikacin	6	2	92	24	2	74	38	–	62
Other classes									
Lenezolid	–	–	100	–	–	100	50	–	50
Chloramphenicol	13	1	86	15	5	80	88	–	12
Tetracycline	21	4	75	30	4	66	76	–	24
Doxycycline	18	4	78	27	2	71	68	2	30
Cotrimoxazole	38	4	58	76	1	23	82	1	17

Notes: CoNS were considered only in the blood stream infections if the clinical condition of the patient merited it, Resistant (R) and susceptible (S) percentage as per CLSI criteria 2006. *See the oxacillin results for rates of susceptibilty.

Abbreviations: IR, Intermediate resistant; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; CLSI, Clinical and Laboratory Standards Institute; CoNS, coagulase-negative *Staphylococcus aureus*; R, resistance.

fluroquinolones and third-generation cephlosporins would better guide therapy.

It is widely accepted that the first-line empirical treatment for uncomplicated urinary tract infection should be cotrimoxazole if resistance rates of urinary *E. coli* to cotrimoxazole are <20%. If cotrimoxazole resistance is >20%, fluoroquinolone, nitrofurantoin, or fosfomycin are recommended.[26] In the present study, resistance to cotrimoxazole was documented to be >80%, which is in accordance with the high-resistance rates recorded in other Indian studies.[27] Most patients at the two study sites were treated with norfloxacin in outpatient clinics.[28] Because quinolones select more antibiotic-resistant strains and nitrofurantoin shows good activity against *E. coli*, nitrofurantoin would serve as better alternative first-line drug for the treatment of uncomplicated urinary tract infection in this setting. However, nitrofurantoin is not aggressively marketed and has supply-related problems. Treatment options for complicated urinary tract infection need to be individualized based on culture reports.

ESBL production was 69% in *E. coli* isolates and 41% in *K. pneumoniae* isolates. The above pattern of resistance is a clue toward other possible mechanisms of resistance, including AmpC production. Studies performed in India have shown that plasmid-borne and chromosomally mediated AmpC- and cephalosporinase-producing pathogens are common in resistant *E. coli* and *K. pneumoniae* isolates.[22,29] The reported prevalence of ESBL-producing Gram-negative isolates in various hospitals in India is in the range of 19%–60%.[22]

Prevalence of ESBL-producing Gram-negative isolates in various hospitals in India is in the range of 19%–60%. Cabapenem resistance is reported to be 5.3%–59% in various metropolitan tertiary care hospitals[22]

A study performed in a tertiary care hospital in Hyderabad by Subbalaxmi et al[11] showed that only 8% *E. coli* isolates were sensitive to ceftriaxone, a frequently used empirical antibiotic. Sensitivity to a combination of β-lactam β-lactamase inhibitors like cefaperazone/sulbactam and piperacillin/tazobactam was 59% and 61%, respectively. This study showed a high prevalence of ESBL in an urban set-up.[11] A high prescribing rate of fluroquinolones was documented in an outpatient study on antibiotic prescribing linked with diagnosis in the same settings.[28] The rate of fluoroquinolone use determines the resistance rates for both fluoroquinolones and third-generation cephalosporins.[30] This finding might explain the high rate of coresistance (51.2%) to third-generation cephalosporins and ciprofloxacin documented in the present study.

Among the Gram-positive organisms, *S. aureus* and coagulase-negative staphylococci were the most common organisms. MRSA constituted 30% of all *S. aureus* isolates. The antibiotic susceptibility pattern of MRSA showed resistance to commonly used antibiotics, which has been documented in Southeast Asia[17,18] and India.[11,12] Varghese et al[12] in an Indian study performed at a tertiary care center in Manipal reported a MRSA rate of 35%. Increased resistance of MRSA isolates to almost all antibiotics over a one-year period was observed in this study.[12] They reported a high proportion of resistance of MRSA isolates to the commonly used first-line antibiotics, such as cotrimoxazole (96%), ciprofloxacin (85%), erythromycin (83%), and tetracyclines (72%). Our results showed better susceptibility to the above antibiotics except ciprofloxacin. These differences in the results could be due to the differences in geographical areas and settings. The resistance rates for ciprofloxacin in the two studies are quite similar (81% in our study versus 85% in the referenced study).[12] This finding could be because of high outpatient use of quinolones in our settings.[28] Other hospitals (predominantly urban) in India have reported MRSA rates of 8%–71%.[22]

The main strength of this survey is that it provides much needed data for evidence-based discussion on prudent antibiotic prescribing in India. The data have links to clinical infections, information that is usually minimal or absent in laboratory-based studies. Our study has limitations. Because of the limited sample size, we were unable to detect uncommon forms of resistance, such as carbapenem resistance and vancomycin-resistant enterococci. The "gold standard" for antibiotic susceptibility reporting is minimum inhibitory concentration testing; this was not performed because we wanted to perform the tests that are normally available in this type of setting. Hospitalization durations were not recorded; thus, it was not possible to distinguish between health care-associated infections and community-acquired infections. The likelihood that the isolated organism is a colonizing bacterium should be considered in such studies. However, in the present study, because the inclusion criterion was a patient with a suspected infection, this possibility was minimized.

Conclusion

In conclusion, this is the first surveillance study of antimicrobial susceptibility performed in a rural resource-poor setting in central India. The results define the occurrence of pathogens and suggest the leading antimicrobial resistance mechanisms. Carbapenems provide the broadest coverage for Gram-negative bacteria and glycopeptides are most effective against MRSA; however, both these classes of drugs need to be used judiciously. Antimicrobial resistance surveillance is necessary for both day-to-day clinical decisions and to reflect local, regional, and national trends. Comprehensive surveillance programs linked to antimicrobial prescription need to be prioritized to set up effective infection control measures. The data from this study will be useful for planning antibiotic stewardship programs in India.

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Disclosure

The authors declare no conflict of interest in relation to this paper.

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