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Extended-spectrum β-lactamase and AmpC β-lactamase Production among Gram-negative Bacilli Isolates Obtained from Urinary Tract Infections and Wound Infections

POTTAHIL SHINU*, RAJESH BAREJA*, MANOJ GOYAL†, VARSHA A SINGH*, PRIYA MEHRISHI*, MONIKA BANSAL‡, VINOD KUMAR NARANG*, PREM SINGH GROVER*, VIRENDRA SINGH*, SHAILESH YADAV†, AHMED NABEEL#

ABSTRACT

Extended-spectrum β-lactamases (ESBLs) and AmpC β-lactamases continue to be a major problem in healthcare settings. Due to the scarcity of information regarding the antibiotic susceptibility patterns particularly from urinary tract infection (UTI) and wound infections, the current study was carried out to assist the clinicians to prescribe appropriate antibiotics against Gram-negative clinical isolates. In the current study, urine (n = 620) and pus (n = 228) samples were collected from different sites (at various clinical departments) and subjected to direct microscopic examination, culture and antibiotic susceptibility testing (AST). In the AST testings, the isolates that exhibited reduced zone of inhibition to one or more of the antibiotics such as cefotaxime (≤27 mm), ceftriaxone (≤25 mm), ceftazidime (≤22 mm), cefpodoxime (≤17 mm) and aztreonam (≤27 mm) were considered as potential ESBL producers and the ESBL production was confirmed using phenotypic screening test (double-disk synergy test) and phenotypic confirmatory test (combined-disk test). However, isolates showing resistance or decreased sensitivity to cefoxitin, cefotaxime, ceftriaxone, ceftazidime, cefpodoxime or aztreonam and sensitive to cefepime were considered as a screen positive AmpC producer and subjected to AmpC disk tests. The current study concluded that 72.41% and 21.76% of ESBL and AmpC producers were detected, respectively in our hospital. It was also observed that the double-disk synergy and combined-disk tests were equally effective for ESBL detection. Further, AmpC disk test is simple, easy to perform and interpret, requiring less expertise for the rapid detection of AmpC isolates.

Keywords: Extended-spectrum β-lactamases, AmpC β-lactamases, Gram-negative isolates, antibiotic susceptibility testing

A novel class of enzymes imparting resistance to β-lactam antibiotics has emerged over the last few decades, mostly owing to the antibiotic selection pressure and most alarming are the extended-spectrum β-lactamases (ESBLs) produced by *Enterobacteriaceae* that have spread worldwide since the first report in 1983.[1] ESBLs are the enzymes produced by Gram-negative bacilli that have the potential to hydrolyze β-lactam antibiotics containing an oxyimino group (third-generation cephalosporins and aztreonam) and are inhibited by β-lactamase inhibitors such as clavulanic acid, sulbactam and tazobactam. Cephamycins (e.g., cefoxitin) or carbapenems (e.g., imipenem, meropenem and ertapenem) are not affected by these enzymes.[2] ESBL production has been reported in a variety of organisms including the members of *Enterobacteriaceae* and other nonenteric bacilli as well.[3,4] Currently, a majority of the clinical laboratories test for production of ESBLs; however, the testing of clinical isolates for the production of plasmid-mediated AmpC β-lactamases is usually ignored. Like ESBLs, AmpC β-lactamases have a broad-substrate profile including penicillins, cephalosporins (apart from zwitterionic cephalosporins) and monobactams. In addition, it hydrolyzes cephamycins and is not inhibited by commercially available β-lactamase inhibitors. Generally, AmpC

*Assistant Professor, Dept. of Microbiology
†Dept. of Pharmacology
‡Dept. of Physiology
#Dept. of Community Medicine
MM Institute of Medical Sciences and Research, Mullana, Ambala, Haryana
Address for correspondence
Dr Pottathil Shinu
Assistant Professor
Dept. of Microbiology
MM Institute of Medical Sciences and Research, MM University,
Mullana, Ambala, Haryana
E-mail: shinup1983@gmail.com

β-lactamases are associated with multiple antimicrobial resistance, limiting the therapeutic regimens.[5,6]AmpC β-lactamase production has been reported in *Escherichia coli*, *Klebsiella pneumoniae*, Salmonella spp., *Citrobacter freundii*, *Enterobacter aerogenes* and *Proteus mirabilis*.[7]

Recently, the incidence of ESBL and AmpC β-lactamase-producing strains among Gram-negative bacilli isolates has considerably increased resulting in the limitation of therapeutic alternatives.[8,9] Further, various outbreaks of infections associated with ESBL and AmpC β-lactamases have been reported across the globe in the last decades.[10,11] Furthermore, geographical distribution of ESBL producers may vary from countries to countries and even between institutions to institutions.[12-15] Various investigators reported the prevalence of ESBL and AmpC β-lactamase production in India with considerable variation between different hospitals and even between various sites of infections such as urinary tract infections (UTIs) and wound infections.[11,16-19] Due to the scarcity of information regarding the antibiotic susceptibility patterns particularly from UTI and wound infections, the clinicians may likely prescribe inappropriate antibiotics for empirical treatments. Considering these issues, the present study was designed to assess the current levels of resistance to antibiotics that are commonly used in our hospital and also to review the prevalence of ESBL and AmpC β-lactamase production among Gram-negative bacterial isolates obtained from wound infections and UTI.

MATERIAL AND METHODS

Study Design

The study was conducted among all the patients (suspected to be having UTI and wound infections) who were examined by all the clinical departments of MM Institute of Medical Sciences and Research, Ambala, India (a 750 bedded tertiary healthcare teaching hospital). During the study period, (between March, 2012 and February, 2013), urine (n = 620) and pus (n = 228) samples were collected from different sites (at various clinical departments) and were immediately transported to the Dept. of Microbiology. Immediately after receipt, specimens were subjected to direct microscopic examination (wet mount examination for uncentrifuged urine and Gram-staining for pus specimens), culture and antibiotic susceptibility testing.

Bacterial Strains and Antibiotic Susceptibility Testing

All the pus samples were cultured on blood agar and MacConkey agar. However, the urine specimens were inoculated on Cysteine Lactose Electrolytes Deficient (CLED) agar and incubated at 37°C for 18-24 hours. After incubation, the bacterial isolates were identified by standard laboratory protocols.[20]

The antibiotic susceptibility testing of Gram-negative bacilli was performed on Mueller-Hinton agar by modified Kirby-Bauer disk diffusion method as recommended by the Clinical Laboratory Standards Institute (CLSI) using ampicillin (10 μg), amoxicillin-clavulanic acid (20 + 10 μg), piperacillin-tazobactam (100 + 10 μg), piperacillin (100 μg), cinoxacin (100 μg), carbenicillin (100 μg), ceftriaxone (30 μg), cefepime (30 μg), ceftazidime (30 μg), cefoxitin (10 μg), cefpodoxime (30 μg), cefotaxime (30 μg), ceftizoxime (30 μg), aztreonam (30 μg), imipenem (10 μg), gentamicin (10 μg), amikacin (30 μg), tobramycin (10 μg), tetracycline (30 μg), cotrimoxazole (1.25/23.75 μg), ciprofloxacin (5 μg), lomefloxacin (10 μg), nitrofurantoin (300 μg), gatifloxacin (5 μg), norfloxacin (10 μg). The inoculated AST plates were incubated at 37°C for 16-18 hours and the results were interpreted as per CLSI guidelines.[21]

Screening Test for ESBL and AmpC β-lactamases

Isolates that exhibited reduced zone of inhibition to one or more of the antibiotics such as cefotaxime (≤27 mm), ceftriaxone (≤25 mm), ceftazidime (≤22 mm), cefpodoxime (≤17 mm) and aztreonam (≤27 mm) were considered as potential ESBL producers.[22] However, isolates showing resistance or decreased sensitivity to cefoxitin, cefotaxime, ceftriaxone, ceftazidime, cefpodoxime or aztreonam and were sensitive to cefepime were considered as a screen positive AmpC producer and subjected to AmpC disk test.[23]

Phenotypic Screening Test

This test for ESBL producers (double-disk synergy test) was performed as suggested by Jarlier et al, wherein an enhancement in the zone of inhibition between a β-lactam disk and one containing the β-lactamase inhibitor was indicative of the presence of ESBL.[24]

Phenotypic Confirmatory Test (Combined-disk Test)

This test was carried as per CLSI recommendations, briefly; ceftazidime (30 μg) versus ceftazidime/clavulanic acid (30 μg/10 μg), (HiMedia, Mumbai, India), used as a phenotypic confirmatory test wherein a >5 mm increase in the zone diameter for the antimicrobial agent tested in combination with β-lactamase inhibitor versus its zone when tested alone indicates ESBL production.[21] AmpC disk test was carried out as recommended by Black et al, briefly; a sterile disk (6 mm) moistened

with sterile saline (20 μL) and inoculated with several colonies of test organism was placed beside a cefoxitin disk (almost touching) on the Mueller-Hinton agar (MHA) plate lawned with a culture of *E. coli* ATCC 25922 and incubated overnight at 35°C. A positive test appeared as a flattening or indentation of the cefoxitin inhibition zone in the vicinity of the test disk and a negative test had an undistorted zone.[23]

Quality Control

Every new batch of culture media was incubated at 37°C overnight to ensure the sterility. *E. coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as quality control strains for antimicrobial susceptibility testing. However, a non-ESBL-producing organism *E. coli* ATCC 25922 and an ESBL-producing organism *K. pneumoniae* ATCC 700603 were used while testing ESBL screening and phenotypic confirmatory tests.

Statistical Analysis

Significance between the resistance level of various drugs in ESBL and non-ESBL, AmpC and non-AmpC isolates was performed using the Fisher's exact test (Graphpad Prism online version).

RESULTS

Table 1 demonstrates the distribution of all Gram-negative bacilli isolates obtained from wound infections and UTIs. Of the 848 nonrepetitive specimens processed (urine [n = 620] and pus [n = 228]), a total of 269 bacterial isolates were obtained. Out of the 269 (31.72%) nonrepetitive isolates (urine [n = 182] and pus (n = 87]), 30 isolates were *Staphylococcus aureus*, *Staphylococcus epidermidis* (n = 5) and *Staphylococcus epidermidis* (n = 7), respectively. After exclusion of these Gram-positive organisms, a total of 227 Gram-negative isolates were subjected to further analysis. Of the 227 Gram-negative bacilli isolates, 96 (40.85%) showed resistance or decreased sensitivity to any one of the 3GCs (third-generation cephalosporins??) such as cefotaxime (≤27 mm), ceftriaxone (≤25 mm), ceftazidime (≤22 mm), cefpodoxime (≤17 mm), aztreonam (≤27 mm) and isolates were further screened for ESBL production using double-disk synergy test (DDST) and confirmed using combined-disk synergy test (CDST) (Phenotypic confirmatory test). Of these 96 isolates, 80 (80/96) isolates were confirmed for ESBL production using CDST. Interestingly, it was observed that both DDST and CDST independently detected all the ESBL producers. Of these, 24 isolates were *E. coli*, *K. pneumoniae* (n = 16), *P. aeruginosa* (n = 10), *P. mirabilis* (n = 7), *Morganella morganii* (n = 6) and *C. freundii*, respectivley. Table 2 summarizes the detection of ESBL and AmpC β-lactamases among Gram-negative isolates as indicated by various detection methods.

Interestingly, we have also noticed the co-existence phenotype of both ESBLs and AmpC in 11.68% isolates of which 7 (7/227) and 6 (6/227) isolates were *E. coli* and Klebsiella spp., respectively. Table 3 illustrates the

Table 1. Distribution of All Gram-negative Bacilli Isolates Obtained from Wound Infections and UTIs

Gram-negative isolates obtained	Specimens	
	Pus (%)	Urine (%)
E. coli (77)	16 (20.7)	61 (79.22)
P. aeruginosa (38)	22 (57.8)	16 (42.11)
K. pneumoniae (34)	3 (8.82)	31 (91.18)
P. mirabilis (19)	3 (15.78)	16 (84.21)
K. oxytoca (19)	4 (21.05)	15 (78.95)
C. freundii (11)	4 (36.36)	7 (63.64)
E. aerogenes (7)	3 (42.86)	4 (57.14)
M. morganii (14)	2 (14.29)	12 (85.71)
A. lwoffii (8)	8 (100)	-
Total (227)	**65 (28.63)**	**162 (27.31)**

distribution of antibiotic resistance among ESBL and non-ESBL producers. Further, it is evident from Table 3 that a significant number of ESBL-producing strains were found to be resistant to antimicrobial agents. However, in non-ESBL-producing isolates resistance was found to be relatively low. It is also evident from Table 3 that ceftazidime is the most effective indicator of ESBL production among the 3GCs.

Table 4 demonstrates the distribution of antibiotic resistance among Amp C (n = 26) and non-Amp C (n = 201) β-lactamase producers. Of the 227, Gram-negative isolates, 49 isolates showed resistance or decreased sensitivity to cefoxitin, cefotaxime, ceftriaxone, ceftazidime, cefpodoxime, aztreonam and were sensitive for cefepime. Of theses, 26 (26/49) isolates were confirmed for AmpC β-lactamase production using AmpC disk test method. Out of the 26 AmpC β-lactamase confirmed cases, 7 and 17 isolates were *E. coli* and Klebsiella spp., respectively.

ESBL-producing isolates were resistant to more antimicrobial agents than non-ESBL-producing isolates. Multidrug resistance was seen in 56 (73.75%) ESBL-positive isolates and 35 (23.81%) non-ESBL isolates. This difference was highly significant ($p < 0.01$). On the other hand, AmpC β-lactamase-producing isolates were resistant to more antimicrobial agents than non-AmpC-producing isolates. Multidrug resistance was seen in 18/26 (69.23%) AmpC-positive isolates and 39/201 (19.4%) non-AmpC isolates. This difference was highly significant ($p < 0.01$).

Table 2. Detection of ESBL and AmpC β-lactamases among Gram-negative Isolates as Indicated by Various Detection Methods

Microorganism	Screening test (Positive)				Confirmatory test (Positive)				Combined ESBL and AmpC β-lactamase production	
	ESBL		AmpC		ESBL		AmpC		ESBL and AmpC production	
	Pus (n = 65)	Urine (n = 162)	Pus (n = 65)	Urine (n = 162)	Pus (n = 65)	Urine (n = 162)	Pus (n = 65)	Urine (n = 162)	Pus (n = 65)	Urine (n = 162)
E. coli (n = 77)	5 (7.69%)	23 (14.19%)	2 (3.07%)	22 (13.58)	4 (6.16%)	20 (12.35%)	2 (3.07%)	13 (8%)	2 (3.07%)	5 (3.08%)
P. aeruginosa (n = 38)	14 (21.54%)	5 (3.09%)	3 (4.62%)	1 (0.62)	12 (18.4%)	4 (2.47%)	2 (3.07%)	-	-	-
K. pneumoniae sub. sp. (n = 34)	1 (1.53%)	14 (8.64%)	2 (3.07%)	14 (8.64)	1 (1.53%)	9 (5.55%)	1 (1.53%)	6 (3.7%)	1 (1.53)	4 (2.47%)
P. mirabilis (n = 19)	1 (1.53%)	6 (3.7%)	-	-	-	5 (3.08%)	-	-	-	-
K. oxytoca (n = 19)	3 (4.62%)	5 (3.08%)	2 (3.07%)	1 (0.62)	2 (3.07%)	5 (3.08%)	1 (1.53%)	-	1 (1.53%)	-
C. freundii (n = 11)	3 (4.62%)	3 (1.8%)	-	-	3 (4.62%)	3 (1.85%)	-	-	-	-
E. aerogenes (n = 7)	2 (3.08%)	4 (2.46%)	-	-	1 (1.54%)	4 (2.46%)	-	-	-	-
M. morganii (n = 14)	2 (3.08%)	5 (3.08%)	-	-	2 (3.07%)	5 (3.08%)	-	-	-	-
A. lwoffii (n = 8)	-	-	2 (3.07%)	-	-	-	1 (1.53%)	-	-	-
Total = 227	**31 (47.69%)**	**65 (40.12%)**	**11 (16.9%)**	**38 (23.4%)**	**25 (38.4%)**	**55 (33.9%)**	**7 (10.7%)**	**19 (11%)**	**4 (6.15%)**	**9 (5.5%)**

Table 3. Distribution of Antibiotic Resistance among ESBL (n = 80) and Non-ESBL (n = 147) Producers

Antibiotics	ESBL producers n = 80 (%)	Non-ESBL producers n = 147 (%)	P value
Ampicillin	80 (100)	124 (84.35)	0.0001
Amoxicillin-clavulanic acid	42 (52.5)	36 (24.45)	0.0001
Piperacillin-tazobactam	30 (37.5)	25 (17)	0.001
Piperacillin	56 (70)	31 (21.08)	0.0001
Cinoxacin*	78 (97.4)	89 (60.55)	0.0001
Carbenicillin*	79 (98.75)	72 (48.98)	0.0001
Ceftriaxone	78 (97.4)	39 (26.53)	0.0001
Cefepime	78 (97.5)	34 (23.13)	0.0001
Ceftazidime	80 (100)	36 (24.49)	0.0001
Cefoxitin	28 (35)	45 (30.61)	0.0001
Cefpodoxime	79 (98.74)	32 (21.77)	0.0001
Cefotaxime	76 (95)	38 (25.85)	0.0001
Ceftizoxime*	76 (95)	34 (23.13)	0.0001
Aztreonam	77 (96.25)	34 (23.13)	0.0001
Imipenem	0	0	0
Gentamicin	41 (51.23)	38 (25.85)	0.0002
Amikacin	18 (22.5)	24 (16.32)	0.2846
Tobramycin	15 (18.75)	30 (20.41)	0.0001
Tetracycline	59 (73.75)	42 (28.57)	0.0001
Cotrimoxazole	62 (77.7)	40 (27.21)	0.0001
Ciprofloxacin	43 (53.75)	28 (19.04)	0.0001
Lomefloxacin*	49 (61.23)	26 (17.68)	0.0001
Nitrofurantoin*	2 (2.4)	1 (0.68)	0.2842
Gatifloxacin**	38 (47.5)	24 (16.32)	0.0001
Norfloxacin*	34 (42.5)	27 (18.36)	0.0001

*Tested for urinary isolates only; **Tested for both wound infections and urinary tract infections.

DISCUSSION

ESBL-producing Gram-negative bacteria are emerging worldwide, challenging the clinicians, public health professionals and hospital infection-control teams.[12] ESBLs are the enzymes produced by Gram-negative bacilli that have the potential to hydrolyze β-lactam antibiotics containing an oxyimino group (3GCs and aztreonam) and are inhibited by β-lactamase inhibitors such as clavulanic acid, sulbactam and tazobactam. However, cephamycins (e.g., cefoxitin) or carbapenems (e.g., imipenem, meropenem and ertapenem) are not affected by these enzymes.[2] Like ESBLs, AmpC β-lactamases, a group of β-lactamases, are capable of hydrolyzing penicillins, cephalosporins (apart from zwitterionic cephalosporins) and monobactams. In addition, it hydrolyzes cephamycins and is not inhibited by commercially available β-lactamase inhibitors. Further, AmpC β-lactamases are associated with multiple antimicrobial resistance, limiting the therapeutic regimens.[5,6] Furthermore, the incidence of ESBL and AmpC β-lactamase-producing strains

Table 4. Distribution of Antibiotic Resistance among Amp C (n = 26) and Non-Amp C (n = 201) β-lactamase Producers

Antibiotics	AmpC producers n = 26 (%)	Non-AmpC producers n = 201 (%)	P value
Ampicillin	26 (100)	183 (91.04)	0.2368
Amoxicillin-clavulanic acid	26 (100)	49 (24.38)	0.0001
Piperacillin-tazobactam	26 (100)	37 (18.41)	0.0001
Piperacillin	26 (100)	43 (21.39)	0.0001
Cinoxacin*	24 (92.31)	122 (60.7)	0.0009
Carbenicillin*	25 (96.15)	102 (50.74)	0.0001
Ceftriaxone	24 (92.31)	61 (30.34)	0.0001
Cefepime	79 (26.92)	59 (29.35)	0.0001
Ceftazidime	25 (96.15)	57 (28.36)	0.0001
Cefoxitin	25 (96.15)	58 (28.86)	0.0001
Cefpodoxime	22 (84.62)	52 (25.87)	0.0001
Cefotaxime	24 (92.31)	61 (30.35)	0.0001
Ceftizoxime*	24 (92.31)	55 (27.36)	0.0001
Aztreonam	25 (96.16)	51 (25.37)	0.0001
Imipenem	0	0	0
Gentamicin	21 (80.77)	54 (26.87)	0.0001
Amikacin	18 (69.23)	29 (14.43)	0.0001
Tobramycin	16 (61.54)	42 (20.9)	0.0001
Tetracycline	19 (73.08)	62 (30.85)	0.0001
Cotrimoxazole	20 (76.92)	59 (29.35)	0.0001
Ciprofloxacin	13 (50)	39 (19.4)	0.0001
Lomefloxacin*	12 (46.15)	34 (16.91)	0.0014
Nitrofurantoin*	1 (3.85)	1 (0.5)	0.2164
Gatifloxacin**	9 (34.62)	34 (16.92)	0.0579
Norfloxacin*	10 (38.46)	41 (20.4)	0.0469

*Tested for urinary isolates only; **Tested for both wound infections and urinary tract infections.

among Gram-negative bacilli isolates has considerably increased resulting in the limitation of therapeutic alternatives.[8,9] In India, the prevalence of ESBL and AmpC β-lactamase producers vary among various hospitals and even between various sites of infections such as UTIs and wound infections. However, most of the hospitals in India are lacking accessibility to prevailing antimicrobial susceptibility patterns. This may circuitously result in the inappropriate prescription of antibiotics for empirical treatments.[11,16-19] In view of these issues, the present study was designed to assess the current levels of resistance to antibiotics that are commonly used in our hospital and also to review the prevalence of ESBL and AmpC β-lactamase production among Gram-negative bacterial isolates obtained from wound infections and UTIs. In the current study, the incidence of ESBL-producing organisms was found to be 72.41%. However, this incidence rate is much lower than the previous investigations carried out in other regions of the country.[25-27] This reduced ESBL

production among the Gram-negative isolates could be attributed to the rational use of extended-spectrum cephalosporins and appropriate infection-control measures adopted in our hospital. However, the rate of AmpC β-lactamases (21.76%) production was relatively higher than that of Singhal et al (8%) and Hemalatha et al (9.2%) but was lower than the various documented figures in India.[9,28-31] Interestingly, we have also observed the co-existence of ESBL and AmpC production among 6.15% *E. coli* and 5.53% of Klebsiella spp. These co-existent phenotypes could be due to the transfer of plasmids (encoding both AmpC and ESBL enzyme-producing genes) between members of the family *Enterobacteriaceae*.[5,6]

Various phenotypic and genotypic tests have been proposed to detect ESBL and AmpC production.

However, phenotypic methods are less expensive, easy to perform and to interpret. The phenotypic methods include screening and confirmatory tests.[21] In the current study, among the 3GCs, ceftazidime demonstrated resistance to all the phenotypically confirmed ESBL producers, indicating the potential of ceftazidime to detect ESBL production more effectively than other 3GCs. This data was in consistence with previous reports as well.[32,33] However, among the phenotypic ESBL detection methods, the DDST demonstrated 100% concordance with phenotypic combined confirmatory disk test for ESBL detection and this data was comparable with Tsering et al.[33] But among the AmpC β-lactamase producers, cefoxitin resistance was found to be a good indicator (detected 96.15% cases) as reported by previous investigators.[34,35]

Multidrug-resistant strains of bacteria possess resistance to two or more antimicrobials.[36] Multidrug-resistant strains are expected to be more common among organisms harboring genes for ESBL and AmpC β-lactamases.[5] This study also reveals that the incidence of multidrug-resistant strains is significantly ($p < 0.05$) higher in ESBL and AmpC β-lactamase producers than non-ESBL and non-AmpC producers.

It is evident from Tables 3 and 4 that most of the ESBL-producing strains were resistant to 3GC and 4GC. In addition, it was observed that the resistance to amikacin (22.5% and 69.23%), ciprofloxacin (53.75% and 50%), gatifloxacin (47.5% and 34.62%) and cotrimoxazole (77.7% and 76.92%) among ESBL and AmpC producers, respectively (Tables 3 and 4). This increased incidence of multidrug resistance is attributed to the plasmid-mediated drug resistance, which is often acquired by transfer of genetic information from one organism to another. Such transferable plasmid also codes for resistance to other antimicrobial agents as well.

Therefore, multidrug resistance is expected to be more common in ESBL-producing organisms.[37] However, all the ESBL and AmpC-producing isolates were sensitive to imipenem, indicating the potential of continued efficacy of carbapenems as the first-line agents for treatment of organisms producing ESBL and AmpC β-lactamases.

CONCLUSION

In conclusion, 72.41% and 21.76% of ESBL and AmpC producers were detected, respectively in our hospital. It was also observed that the DDSTs and CDSTs were equally effective for ESBL detection. Further, AmpC disk test is simple, easy to perform and interpret, requiring less expertise for the rapid detection of AmpC isolates. In addition, imipenem was found to be the most sensitive antibiotic for treatment of ESBL and AmpC β-lactamases- producing Gram-negative isolates.

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■■■■

Exposure to Nature During COVID-19 Lockdown Benefits Mental Health: Study

According to a new study, exposure to natural spaces during the first COVID-19 lockdown last year was found to be beneficial for the mental health of people in Spain and Portugal.

In Portugal, during the first lockdown, people who maintained or increased exposure to natural public spaces, such as parks or coastal areas or those who could observe these spaces from their homes, had lower levels of stress, psychological distress and psychosomatic symptoms. Additionally, in Spain, people who maintained or increased exposure to private natural spaces, like indoor plants, exhibited lower levels of stress and psychosomatic symptoms.

The study was conducted by the Institute of Environmental Science and Technology of the Universitat Autonoma de Barcelona (ICTA-UAB) and the Instituto de SaudePublica of the University of Porto (ISPUP), and has been published in *Environment International*… (*HT – ANI*)

Bariatric Surgery Tied to Better Cardiovascular Function in Pregnancy

According to a new study presented at the Royal College of Obstetricians and Gynecologists 2021 Virtual World Congress, pregnant women who have undergone bariatric surgery tend to have better cardiovascular adaptation to pregnancy in comparison with women who have similar early-pregnancy body mass index (BMI) but have not undergone weight loss surgery.

Deesha Patel, Specialist Registrar, Chelsea and Westminster Hospital, London, United Kingdom, stated that pregnant women who have had bariatric surgery exhibit better cardiovascular adaptation via lower blood pressure, heart rate and cardiac output. The study assessed 41 women who had a history of bariatric surgery and 41 women who had no history of such surgery. Blood pressure through the three trimesters was found to be consistently lower in the women who had undergone bariatric surgery compared to those who had not undergone surgery. Heart rate and cardiac output were also lower across the three trimesters in the bariatric surgery group. There appeared to be no difference in stroke volume between the two groups studied… (*Medscape*)

FDA Issues EUA for Tocilizumab for Treatment of COVID-19

The US FDA has issued an EUA for the use of tocilizumab to treat hospitalized adults and children, aged 2 years and above, who are being given systemic corticosteroids and need supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

The drug is not authorized for use in outpatients. Clinical trials conducted among hospitalized COVID-19 patients revealed that the use of tocilizumab, along with routine care for treatment of COVID-19, including corticosteroid therapy, led to a reduction in the risk of death through 28 days of follow-up. It also reduced the duration of hospital stay.

Tocilizumab is a monoclonal antibody that works by decreasing inflammation as it blocks IL-6 receptor… (*FDA*)

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