Section: Microbiology

Original Research Article

EMERGING ESBL RESISTANCE IN ESCHERICHIA COLI: A TERTIARY CARE HOSPITAL'S PERSPECTIVE ON PREVALENCE, PATTERNS, AND IMPLICATIONS

Rajni Thapar[1], Aruna Aggarwal[2], Bimla Devi[3]

[1]Assistant Professor, Department of Microbiology, Pt. Jawahar Lal Nehru Govt. Medical College and Hospital, Chamba, Himachal Pradesh, India
[2]Consultant Microbiologist, Om Prakash Eye Hospital, Amritsar, Punjab, India
[3]Professor and Head, Department of Microbiology, Pt. Jawahar Lal Nehru Govt. Medical College and Hospital, Chamba, Himachal Pradesh, India

Received : *29/09/2023*
Received in revised form : *05/12/2023*
Accepted : *20/12/2023*

Keywords:
OPD, Urinary, Esch coli, ESBL producers, Gram-negative bacteria.

Corresponding Author:
Dr. Rajni Thapar,
Email: rajni_2912@yahoo.co.in

DOI: 10.47009/jamp.2023.5.6.308

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (6); 1498-1503

Abstract

Background: The emergence and spread of antibiotic resistance pose a global threat to healthcare. Extended Spectrum Beta-lactamase (ESBL) production in gram-negative bacteria, such as Escherichia coli (Esch coli), is of particular concern. Tertiary care hospitals, known for their specialized services and high-risk patient populations, face significant challenges in managing ESBL-producing Esch coli infections. ESBL resistance limits treatment options, often necessitating the use of last-resort antibiotics like carbapenems. This not only escalates healthcare costs but also increases the risk of promoting further antibiotic resistance. This study aimed to characterize ESBL resistance in Esch coli at tertiary care hospitals, providing essential insights for informed treatment and infection control strategies. **Materials and Methods:** This cross-sectional study, conducted at the Department of Microbiology, Government Medical College, Amritsar, over two years from July 2001 to May 2003, included 300 Escherichia coli isolates from clinical specimens. Specimens were collected aseptically and processed before incubation on MacConkey agar and blood agar plates at 37°C. Microbiological identification confirmed Esch coli strains. Antibiotic susceptibility testing was performed using the Kirby-Bauer disc diffusion method. Extended Spectrum Beta-lactamase (ESBL) production was detected through a combination of cephalosporins and beta-lactam inhibitors. Data were analyzed using SPSS version 20.0. **Result:** Of the 300 Escherichia coli isolates, 166 (53.33%) were from male patients and 134 (44.66%) from females. The highest prevalence (41.33%) was observed in the 21-40 age group, followed by 27% in the 41-60 age group. Urine samples accounted for the most isolates, with 205 (68.33%) originating from hospitalized patients. Ceftazidime exhibited the highest resistance among third-generation cephalosporins at 80.68%. The sulbactam-cefoperazone combination was the most effective with a sensitivity rate of 53.55%. Of the strains, 64.66% tested positive for beta-lactamase production. High significance was found between inpatients and outpatients. **Conclusion:** The results highlight the need for prudent antibiotic use, the consideration of beta-lactamase production, and the importance of tailoring treatment approaches based on demographic and clinical factors.

INTRODUCTION

Antibiotics have long been hailed as one of the most transformative medical advancements in human history, significantly reducing mortality rates associated with bacterial infections.[1] However, this remarkable success story is now being threatened by the emergence and dissemination of antibiotic resistance, a phenomenon that has escalated into a global crisis. Among the multitude of antibiotic resistance mechanisms, Extended Spectrum Beta-lactamase (ESBL) production by bacteria has become a subject of profound concern.[2]

ESBLs are enzymes produced by certain gram-negative bacteria, including Escherichia coli (Esch coli), that confer resistance to a wide range of beta-lactam antibiotics, such as penicillins and cephalosporins.[3] This resistance mechanism is particularly problematic, as it limits the therapeutic options available to clinicians, leaving them with few effective choices to combat infections caused by

ISSN (O): 2687-5365; ISSN (P): 2753-6556

ESBL-producing bacteria. Among these, Esch coli is of particular significance due to its ubiquity as a commensal organism in the human gastrointestinal tract and its potential to cause a wide array of infections, from urinary tract infections to bloodstream infections.[4]

Tertiary care hospitals, often referred to as referral or teaching hospitals, play a pivotal role in healthcare systems, offering specialized services, advanced medical procedures, and critical care for the most complex and severely ill patients.[5] These facilities are the cornerstone of medical education and research, and they frequently attract patients with a history of prolonged hospitalizations, comorbid conditions, and exposure to a broad spectrum of antibiotics. Consequently, tertiary care hospitals are particularly vulnerable to the challenges posed by ESBL-producing Esch coli.[6]

The increasing prevalence of ESBL resistance among Esch coli in tertiary care hospital settings has dire clinical implications.[7] It necessitates the use of more potent, often broader-spectrum antibiotics, such as carbapenems, which come with their own set of concerns, including the risk of promoting carbapenem-resistant strains of bacteria. Furthermore, the consequences of ESBL resistance extend beyond the realm of individual patient care to encompass the broader healthcare system, where increased healthcare costs, prolonged hospital stays, and compromised patient outcomes are significant concerns.[8]

In this context, understanding the dynamics of ESBL resistance among Esch coli at tertiary care hospitals is critical.[9] This resistance pattern does not only affect clinical treatment decisions but also demands a multifaceted approach encompassing infection control strategies, prudent antibiotic use, surveillance, and research to confront this multifaceted challenge effectively.[10,11] It is within this backdrop that this study aims to isolate, identify, and characterize Escherichia coli from clinical samples, conduct antimicrobial susceptibility testing using the Kirby Bauer disc diffusion method to inform treatment decisions, and detect the presence of Extended Spectrum Beta-lactamase (ESBL) production specifically in Esch coli through the double disc potentiation technique, providing insights into Esch coli-specific antibiotic resistance patterns and enabling targeted infection control and treatment strategies.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional study was conducted under the department of Microbiology of Govt. Medical College, Amritsar. The study was carried out over a 2 years period from July 2001 to May 2003. The present study comprised of 300 isolates of Esch coli from clinical specimens received in the Department of Microbiology.

Sample Collection and Processing: Specimens were collected with all aseptic precautions before administering any antimicrobial therapy. The specimens were sputum, throat swabs, blood, urine, pus, vaginal and cervical swabs, body fluids as CSF, pleural, peritoneal, ascetic and synovial fluid. These were inoculated on the Mac Conkey agar, blood agar plates and incubated aerobically at 37°C for 18-24 hours.

Microbiological Identification: After 24 hours of incubation, the plates were observed for bacterial growth. Colonies were examined with naked eye and magnifying lens, colony characters like size, shape, surface, edge, colour, opacity, consistency, emulsifiable and haemolysis on blood agar were noted. From these cultures, lactose fermenting colonies were selected. Morphology and staining characters of lactose fermenting colonies on MacConkey's agar was studied by Gram's staining method. The identity of the isolated bacteria was confirmed as being Escherichia coli species by studying their motility (hanging drop method or by growing them in semisolid agar medium) and by subjecting them to various biochemical test. Esch coli was identified as gram -ve, non-capsulated, bacilli measuring 1-3 µm in size and motile with peritrichous flagella. Catalase and nitrate reduction test, indole, MR test, was positive and negative for VP reaction, citrate utilization, PPA, gelatin liquefaction and urease test. On TSI agar medium, acid and gas were produced both butt and slant without H2S production. Identified strains of Eschierchia coli species were tested for their antibiotic susceptibility and beta-lactamase production by NCCLS reference method, 2000.

Antibiotic susceptibility Testing: The antibiotic sensitivity pattern of Esch coli species, tested by Kirby Bauer's disc diffusion method. Plates of Mueller-Hinton agar was prepared and stored at 4 degrees Celsius. Before use, these plates were dried and inoculated within 15 minutes of the preparation of the test inoculums. Sterile, non-toxic cotton swabs were soaked in the inoculums and, with firm pressure, rotated several times on the inside wall of the tube to remove excess fluid. Dried Mueller-Hinton agar plates were inoculated using the lawn culture technique. Antibiotic discs were applied over the plates, and these were incubated for 16-18 hours at 37°C. For precision and accuracy, a parallel set of control strains of Esch coli (ATCC 25922) was set up. The zones of inhibition were measured using calipers or a transparent plastic ruler in millimeters across the disc. The diameter of the disc was included in this measurement. Results were interpreted according to the zone size in the Kirby–Bauer disc diffusion method. Three grades of sensitivity were recorded: Susceptible, Moderately susceptible, and Resistant.

Extended Spectrum Beta-lactamase Detection: The clinical isolates were tested against third-generation cephalosporins, namely cefotaxime, ceftazidime, and cefoperazone, as well as a

ISSN (O): 2687-5365; ISSN (P): 2753-6556

combination of third-generation cephalosporins with beta-lactam inhibitors (sulbactam + cefoperazone) using Magnex discs. The confirmation of ESBL production by a particular organism was based on a ≥ 3-5 mm increase in zone diameter when comparing the single disc to the combination disc. Interpretive criteria were defined for the 75µg/30µg (sulbactam/cefoperazone) susceptibility discs, following the US NCCLS disc method (National Committee for Clinical Laboratory Standards Performance Standards for Antimicrobial Disk Susceptibility Tests, 2000). The categories were defined based on zone diameter measurements as follows: Susceptible (>20 mm), Intermediate (16-20 mm), Resistant (<16 mm).

Data Analysis: Data analysis was done using SPSS 20.0 version.

RESULTS

Out of 300 isolates of Escherichia coli, 166 (53.33%) strains were from male patients, and 134 (44.66%) were from female patients. The majority, 124 (41.33%) of the strains, were isolated from patients in the 21-40-year age group, followed by 81 (27%), 33 (11%), 17 (5.66%), and 15 (5%) from the age groups of 41-60, 13-20, 0-5, 6-12, and >60 years, respectively [Table 1].

The data shows that the maximum number of Escherichia coli strains were isolated from urine samples, followed by pus samples, bile, blood culture, throat swab, and sputum samples of the patients. Among the 300 strains of Escherichia coli, 205 (68.33%) were isolated from hospitalized patients, while the remaining 95 (31.66%) were from outpatient (or outdoor) patients [Table 2].

The highest resistance among third-generation cephalosporins was observed against ceftazidime (80.68%), followed by cefoperazone (77.33%), cephalexin (65%), and cefotaxime (49.66%). Piperacillin exhibited a resistance rate of 71%, while generation had a resistance rate of 48.66%, and the sulbactam-cefoperazone combination showed a resistance rate of 39.66%. Among cephalosporins, cefotaxime was found to be the most effective drug, with a sensitivity rate of 46%. The sulbactam-cefoperazone combination exhibited a sensitivity rate of 53.55%, and gentamycin showed a sensitivity rate of 37.33% [Table 3].

194 (64.66%) of the strains were positive for beta-lactamse production by NCCLS (2000) reference method and 106 (35.33%) were Negative results for beta-lactamase production. [Figure 1].

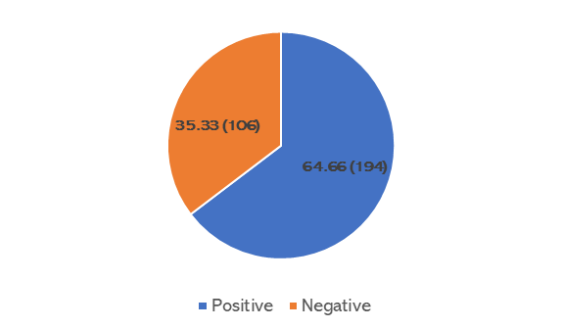

Figure 1: Incidence of beta lactamase production in 300 isolates of Esch coli.

Beta-lactamase-positive strains were most sensitive to sulbactam-cefoperazone (53.66%) and gentamycin (34.93%) but least sensitive to piperacillin (7.65%). Statistical analysis revealed a highly significant difference ($p < 0.001$) in susceptibility to each of the beta-lactamase antibiotics between beta-lactamase-producing and non-producing strains of Escherichia coli [Table 4].

The highest number of beta-lactamase positive strains, specifically 75 (25%), were observed in the 41-60 years age group. Among the beta-lactamase-positive strains, 121 (72.89%) were found in males and 73 (54.47%) in females. Statistical analysis revealed a significant difference ($p < 0.05$) in beta-lactamase production between male and female patients. Furthermore, 154 (75.12%) of the beta-lactamase-producing strains were observed in hospitalized patients, while 40 (42.10%) were among the outpatient population. Statistical analysis indicated a highly significant difference ($p < 0.001$) in beta-lactamase production between outpatients and inpatients [Table 5].

Table 1: Distribution of 300 isolates of Esch coli in relation to age and sex of patients.

Age in Years	Frequency		Total	
	Male	Female	Frequency	%
0-5	12	18	30	10.0
6-12	9	8	17	5.66
13-20	13	20	33	11.0
21-40	64	60	124	41.33
41-60	56	25	81	27.0
>60	12	3	15	5.0
Total	166	134	300	100.0

Table 2: Distribution of Esch coli isolates among the clinical samples of the patients.

Variable	Number	%
Sample		
Urine	150	50.0
Pus	139	46.33
Bile	4	1.33

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Throat swab	2	0.66
Sputum	2	0.66
Blood culture	3	1.0
OPD/IPD		
Outpatients (OPD)	95	31.66
Inpatients (IPD)	205	68.33

Table 3: Antibiogram of 300 strains of Esch coli.

Drug	Disc content (µg/disc)	Susceptable		Moderately susceptible		Resistant	
		Number	%	Number	%	Number	%
Piperacillin	10	72	24.0	15	5.0	213	71.0
Cephalexin	30	96	32.0	9	3.0	195	65.0
Cefotaxime	30	138	46.0	13	4.33	149	49.66
Ceftazidme	30	47	15.66	11	3.66	242	80.68
Cefoperazone	30	55	18.66	13	4.33	232	77.33
Sulbactam- cefoperazone	75/30	161	53.55	20	6.66	119	39.66
Gentamycin	10	112	37.33	42	14.0	146	48.66

Table 4: Esch coli isolates showing sensitivity pattern against beta-lactamase producers and nonproducers.

Antibiotics	Beta- lactamase Positive Sensitivity (%)	Beta – lactamase Negative Sensitivity (%)
Piperacillin	7.65	64.0
Gentamycin	34.93	73.0
Cephalexin	15.66	66.0
Cefotaxime	26.0	100.0
Ceftazidime	12.33	100.0
Ceforperazone	18.66	100.0
Sulbactam-ceforperazone	53.66	100.0

Table 5: Age, Sex, and OPD/IPD based distribution of beta lactamase producing Esch Coli stains.

Variables	Beta-lactamase positive strains	
	Number	%
Age group in years		
0-15	15	5.0
6-12	12	4.0
13-20	18	6.0
21-40	58	19.33
41-60	75	25.0
>60	16	5.33
Sex		
Male	121	72.89
Female	73	54.47
Group		
Outpatient	40	42.10
Inpatient	154	75.12

DISCUSSION

In our study, 194 (64.66%) of the strains were positive for beta-lactamse production by NCCLS (2000) reference method, which was similar to Goyal et al., study who reported a prevalence of 63.6%, Shridhar Rao et al., study who reported a prevalence of 62.9%, and Gupta et al.[12-14] study who reported a prevalence of 63.8%. Whereas Manoharan et al., reported a higher prevalence of 78%, Hawser et al., reported a prevalence of 79%, and highest prevalence was reported by Mohamudha et al., at 87.1%.[15-17] The lower prevalence was reported by Kumar et al., at 24.8%, by Agarwal et al., at 30% and Tsering et al., at 26.15%, Varaiya et al., reported a prevalence of 27.77%, Shoorashetty et al., found a prevalence of 41%, Bajpai et al., reported a prevalence of 41.6%, Babypadmini et al., reported a prevalence of 41%, Sharma et al., recorded a prevalence of 52.49%, Wani et al., reported 52.94%, and Manchanda et al., found a prevalence of 55%.[18-27]

The study results provide valuable insights into the epidemiology and antibiotic resistance profiles of Escherichia coli (Esch coli) strains in a clinical setting. The demographic distribution of Esch coli isolates demonstrated that male patients accounted for 53.33% of the strains, while female patients represented 44.66% of the total, indicating a slight predominance of male cases. Within different age groups, the majority of Esch coli strains were isolated from patients in the 21-40-year age group (41.33%), followed by 27% in the 41-60-year age group. These findings suggest that individuals between 21 and 60 years of age are more susceptible to Esch coli infections. However, it is noteworthy that Esch coli strains were observed across various age groups, indicating the wide-ranging impact of Esch coli infections on the population. A similar trend was observed in the studies by Gupta et al., Agarwal et al., and Varaiya et al.[14,19,21]

The study also investigated the distribution of Esch coli isolates among different clinical samples. Notably, the highest number of isolates were

ISSN (O): 2687-5365; ISSN (P): 2753-6556

obtained from urine samples (50%), followed by pus samples (46.33%), emphasizing the significance of urinary tract and wound infections. Similarly, in the studies by Wani et al., and Babypadmini et al., the highest number of isolates were obtained from urine samples, followed by pus samples.[24,26] Furthermore, the distribution of isolates between inpatients and outpatients revealed that the majority of isolates (68.33%) were obtained from hospitalized patients, underscoring the importance of monitoring and managing Esch coli infections within healthcare facilities. In the studies by Manoharan et al., and Hawser et al., majority of isolates were obtained from hospitalized patients.[15,16]

The study further revealed that a significant proportion of Esch coli strains were positive for beta-lactamase production (64.66%). These strains exhibited varying levels of sensitivity to different antibiotics, with sulbactam-cefoperazone (53.66%) and gentamycin (34.93%) displaying higher sensitivity rates, while piperacillin (7.65%) demonstrated the lowest sensitivity among beta-lactamase-positive strains. The results emphasize the importance of considering beta-lactamase production in treatment decisions for Esch coli infections. Khanduri et al., reported resistance rates for amikacin (83.3%), gentamicin (27.4%), netilmicin (73.0%), tetracycline (17.2%), ceftriaxone (50.5%), ciprofloxacin (8.1%), ofloxacin (8.1%), and sulfamethoxazole-trimethoprim (SXT) (89.4%), with the highest resistance observed in amikacin and SXT.[28] Agarwal et al., reported resistance rates for gentamicin (44%), netilmicin (31%), tetracycline (50%), ceftriaxone (44%), ciprofloxacin (60%), and sulfamethoxazole-trimethoprim (SXT) (54%), with the highest resistance seen in ciprofloxacin.[19] Wani et al., observed resistance in amikacin (78.2%), gentamicin (34.8%), ceftriaxone (91.5%), and ofloxacin (69.1%), while Babypadmini et al., found the highest resistance in amikacin (86%), netilmicin (25%), and SXT (89%).[24,26] Tsering et al., reported resistance rates for gentamicin (45.5%), netilmicin (21.5%), tetracycline (25.3%), and ofloxacin (48.1%).[20] Mohanty et al., found varying resistance rates across different antibiotics, with the highest resistance observed for amikacin (52.8%) and netilmicin (52.8%), while ciprofloxacin exhibited a resistance rate of 27.1%.[29]

The association between age, sex, and outpatient (OPD) or inpatient (IPD) status and beta-lactamase production revealed significant differences in beta-lactamase production among different groups. Notably, the highest number of beta-lactamase-positive strains was observed in the 41-60 years age group (25%). A similar trend was observed in the studies by Gupta et al., Agarwal et al., and Varaiya et al.[14,19,21] A significant difference in beta-lactamase production was also observed between male and female patients ($p < 0.05$), was similar to the studies by Sharma et al., and Manchanda et al.[25,27] Additionally, beta-lactamase production significantly varied between outpatients and inpatients ($p < 0.001$), and was similar to the studies by Manoharan et al., and Hawser et al.[15,16] These findings underscore the importance of considering demographic and clinical factors when assessing antibiotic resistance and guiding treatment strategies for Esch coli infections.

CONCLUSION

In conclusion, this study provides a comprehensive overview of the epidemiology and antibiotic resistance patterns of Esch coli in a clinical context. The results highlight the need for prudent antibiotic use, the consideration of beta-lactamase production, and the importance of tailoring treatment approaches based on demographic and clinical factors. These findings contribute to the ongoing efforts to address antibiotic resistance and optimize patient care in the context of Esch coli infections.

REFERENCES

1. Lai CC, Wang CY, Chu CC, et al. Correlation between antibiotic consumption and resistance of Gram-negative bacteria causing healthcare-associated infections at a university hospital in Taiwan from 2000 to 2009. J Antimicrob Chemother. 2011;66(6):1374–82.
2. Kołpa M, Wałaszek M, Gniadek A, Wolak Z, Dobroś W. Incidence, microbiological profile, and risk factors of healthcare-associated infections in intensive care units: a 10-year observation in a provincial hospital in Southern Poland. Int J Environ Res Public Health. 2018;15(1):112.
3. Khan HA, Baig FK, Mehboob R. Nosocomial infections: epidemiology, prevention, control and surveillance. Asian Pac J Trop Biomed. 2017;7(5):478–82.
4. Agaba P, Tumukunde J, Tindimwebwa JV, Kwizera A. Nosocomial bacterial infections and their antimicrobial susceptibility patterns among patients in Ugandan intensive care units: a cross-sectional study. BMC Res Notes. 2017;10(1):349.
5. Akhtar N. Hospital-acquired infections in a medical intensive care unit. J Coll Physicians Surg Pak. 2010;20(6):386–90.
6. Dereli N, Ozayar E, Degerli S, Sahin S, Koç F. Three-year evaluation of nosocomial infection rates of the ICU. Rev Bras Anestesiol. 2013;63(1):79–84.
7. Siddique SG, Bhalchandra MH, Wyawahare AS, Bansal VP, Mishra JK, Naik SD. Prevalence of MRSA, ESBL, and Carbapenemase producing isolates obtained from endotracheal and tracheal tubes secretions of ICU patient at tertiary care centre. Int J Curr Microbiol App Sci. 2017;6(4):288–299.
8. Kayastha K, Dhunge B, Karki S, et al. Extended-Spectrum β-Lactamase-producing Escherichia coli and Klebsiella Species in pediatric patients visiting international friendship children's Hospital, Kathmandu, Nepal. Infect Dis Res Treat. 2020;13:1–7.
9. Gupta R, Malik A, Rizvi M, Ahmed M. Presence of metallo-beta-lactamases (MBL), extended-spectrum beta-lactamase (ESBL) & AmpC positive non-fermenting Gram-negative bacilli among Intensive Care Unit patients with special reference to molecular detection of blaCTX-M & bla AmpC genes. Indian J Med Res. 2016;144(2):271.
10. Uc-Cachón AH, Gracida-Osorno C, Luna-Chi IG, Jiménez-Guillermo JG, Molina-Salinas GM. High prevalence of antimicrobial resistance among Gram-negative isolated bacilli in Intensive Care Units at a Tertiary-Care Hospital in Yucatán Mexico. Med. 2019;55(9):588.
11. Bajpai T, Pandey M, Varma M, Bhatambare GS. Prevalence of TEM, SHV, and CTX-M Beta-Lactamase genes in the urinary isolates of a tertiary care hospital. Avicenna J Med. 2017;7(1):12-6.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Goyal A, Prasad K, Prasad A, Gupta S, Ghoshal U, Ayyagari A. Extended spectrum beta-lactamases in Escherichia coli & Klebsiella pneumoniae & associated risk factors. Indian J Med Res. 2009;129(6):695-700.
13. Sridhar Rao P, Basavarajappa K, Krishna G. Detection of extended spectrum beta-lactamase from clinical isolates in Davangere. Indian J Pathol Microbiol. 2008;51(4):497-9.
14. Gupta V. Detection of ESBLs using third and fourth generation cephalosporins in double disc synergy test. Indian J Med Res. 2007;126:486-7.
15. Manoharan A, Premalatha K, Chatterjee S, Mathai D. Correlation of TEM, SHV and CTX-M extended-spectrum beta-lactamases among Enterobacteriaceae with their in vitro antimicrobial susceptibility. Indian J Med Microbiol. 2011;29(2):161-4.
16. Hawser SP, Bouchillon SK, Hoban DJ, Badal RE, Hsueh P-R, Paterson DL. Emergence of High Levels of Extended-Spectrum-{beta}-Lactamase-Producing Gram-Negative Bacilli in the Asia-Pacific Region: Data from the Study for Monitoring Antimicrobial Resistance Trends (SMART) Program, 2007. Antimicrob Agents Chemother. 2009;53(8):3280-4.
17. Mohamudha PR, Harish BN, Parija SC. Molecular description of plasmid-mediated AmpC beta-lactamases among nosocomial isolates of Escherichia coli & Klebsiella pneumoniae from six different hospitals in India. Indian J Med Res. 2012;135:114-9.
18. Kumar M, lakshmi V, Rajagopalan R. Occurrence of extended spectrum beta-lactamases among Enterobacteriaceae spp. isolated at a tertiary care institute. Indian J Med Microbiol. 2006;24(3):208-11.
19. Agrawal P, Ghosh A, Kumar S, Basu B, Kapila K. Prevalence of extended-spectrum b-lactamases among Escherichia coli and Klebsiella pneumoniae isolates in a tertiary care hospital. Indian J Pathol Microbiol. 2008;51(1):139-42.
20. Tsering D, Das S, Adhiakari L, Pal R, Singh T. Extended spectrum beta-lactamase detection in gram-negative bacilli of nosocomial origin. J Glob Infect Dis. 2009;1(2):87-92.
21. Varaiya A, Dogra J, Kulkarni M, Bhalekar P. Extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in diabetic foot infections. Indian J Pathol Microbiol. 2008;51(3):370-2.
22. Shoorashetty RM, Nagarathnamma T, Prathibha J. Comparison of the boronic acid disk potentiation test and cefepime-clavulanic acid method for the detection of ESBL among AmpC-producing Enterobacteriaceae. Indian J Med Microbiol. 2011;29(3):297-301.
23. Bajpai T, Pandey M, Varma M, Bhatambare G. Prevalence of extended spectrum beta-lactamase producing uropathogens and their antibiotic resistance profile in patients visiting a tertiary care hospital in central India: Implications on empiric therapy. Indian J Pathol Microbiol. 2014;57(3):407-12.
24. Babypadmini S, Appalaraju B. Extended spectrum - lactamases in urinary isolates of Escherichia coli and Klebsiella pneumoniae - prevalence and susceptibility pattern in a tertiary care hospital. Indian J Med Microbiol. 2004;22(3):172-4.
25. Sharma M, Pathak S, Srivastava P. Prevalence and antibiogram of extended spectrum β-lactamase (ESBL) producing Gram negative bacilli and further molecular characterization of ESBL producing Escherichia coli and klebsiella spp. J Clin Diag Res. 2013;7(10):2173-77.
26. Wani K, Thakur M, Siraj FA, Fomdia B, Gulnaz B, Maroof P. Extended Spectrum -Lactamase Mediated Resistance in Escherichia Coli in a Tertiary Care. International J Health Sci. 2009;3(2):155-63.
27. Manchanda V, Singh NP. Occurrence and detection of AmpC {beta}-lactamases among Gram-negative clinical isolates using a modified three-dimensional test at Guru Tegh Bahadur Hospital, Delhi, India. J Antimicrob Chemother. 2003;51(2):415-8.
28. Khanduri A, Thakuria B, Gupta P. Effectiveness of Combination Drugs In Extended Spectrum Beta Lactamases Producing Gram Negative Isolates- Experience In A Tertiary Care Hospital of Uttarakhand. Int J Pharm Bio Sci. 2012;3(3):251-60.
29. Mohanty S, Singhal R, Sood S, Dhawan B, Das B, Kapil A. Comparative in vitro activity of beta-lactam/beta-lactamase inhibitor combinations against gram negative bacteria. Indian J Med Res. 2005;122(5):425-8.

ISSN (O): 2687-5365; ISSN (P): 2753-6556