www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i5.231

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

E-Coli Sensitivity Pattern at Tertiary Hospital in Telangana and Its Clinical Significance

Authors
Dr Ajay Kumar Khandal[1], Dr D. Raghuraman[2], Dr D.C.Thirupathi Rao[3], Dr Ghiyasuddin Ahmed Masror[4]
[1]Department of Medicine, Prathima Institute of Medical Sciences
Email: *drkhandal@gmail.com*, Phone-9246918050
Address: 2-10-36, Mukarampura, Karimnagar, 505001)
[2]Consultant Physician, Member ethics committee Prathima Institute of Medical Sciences
[3]Consultant Physician, Chaitanya Hospital, Karimnagar
[4]PG Resident, Prathima Institute of Medical Sciences

ABSTRACT
Background & Objectives: *Urinary tract Infection (UTI) is a common cause of hospitalisation, with Escherichia coli (E.coli) being the commonest organism. local resistance pattern is of paramount help in treating the organism empirically, periodic study to this end is mandated to strengthen the cause of antibiotic stewardship. This study was undertaken for the aforesaid objective in the patients of tertiary care hospital of Telangana.*
Methods: *Positive Urine Culture reports were collected from microbiology department from April to October 2016 period, antibiotic susceptibility reports were conducted as in the Clinical and Laboratory Standards Institute (CLSI) guidelines. The resistance patterns were studied for clinical significance.*
Results: *A total of 41 inpatients samples were included in the study. The resistance pattern detected was as follows: floroquinolones (91%); third generation cephalosporins (85%); trimethoprim-sulphamethoxazole (TMP-SMX) (81%); aminoglycosides-gentamycin (58%); piperacillin/tazobactum (46%); amikacin (42%); nitrofurantoin (31%); carbapenem (12%). A significant number—greater than 81 percent—are harbouring multi-drug resistance as observed by resistance to 3 class of antibiotics. With well over 85 percent resistance to third generation cephalosporins, suggesting possible ESBLs.*
Conclusions: *The resistance pattern is distressing as the empirical choice of upper tract infection viz., ceftriaxone and piperacillin tazobactam, cannot be used when the resistance is as high as 85 percent and 46 percent respectively. A greater than 10 percent carbapenem resistance (CR) is more agonising as it implies a grave possibility of treatment failure in a seriously ill individual. Fortunately, this pattern might not be reflective of community acquired E.coli.*
Keywords: *UTI, ESBLs, E.COLI, MDR strains, HAI.*

INTRODUCTION

Urinary tract infections (UTI) is the commonest bacterial infection, and one of the commonest cause of hospitalisation. Moreover, UTI complicating inpatient stay is common adding to the hospital stay with associated morbidity including

escalating cost. Growing resistance to antimicrobial agents is a global phenomenon.[1,2,3] Resistance to third generation cephalosporins in E.coli is matter of particular concern, as it indicates extended spectrum β-lactamases (ESBLs) mediated resistance. Furthermore, ESBLs are associated with plasmid mediated resistance to other class of antibiotics resulting in multi drug resistance (MDR).[4,5] Besides, such MDR strains are highly prevalent in hospital setups. [4] Another concern is the growing carbapenems resistance (CR) among E.coli, as these carbapenems resistant MDR strains can be extremely difficult to treat if at all.[6]

Urinary tract infections (UTIs) is also the commonest hospital acquired infection (HAI) with catheterisation of inpatients as an important component, resulting in the nomenclature catheter associated UTI (cUTI). The Burden of HAI is substantially higher in developing countries including India. [9] cUTI is frequently caused by MDR strains, the disease burden is not known as data is limited. Furthermore, the dangers of hospitalisation needs awareness [10] such that minor ailments in elderly and other risk groups can be managed without hospitalisations and avoid dissemination of MDR strains to these at-risk individuals.

Resistance pattern varies greatly among different geographical area, great variation can be seen even between two hospitals of the same region. [15] High level of quinolone and betalactams resistance has been reported from fewIndian studies. [12, 14] Similarly, other Indian studies have noted a growing burden of MDR in UTI E.coli isolates. [15-18] Therefore, the present study is undertaken to understand the resistance pattern among E.coli at the local level, to generate contemporary data, such that it can guide the clinician for optimal antibiotic usage.

MATERIAL AND METHODS

A retrospective study was carried out, based on the records in Microbiology department of a tertiary care teaching hospital in Karimnagar— the fourth largest and rapidly growing urban territory in Telangana. The Culture and Sensitivity (C/S) reports of the inpatients (all departments included) of Prathima Hospital from February 2016 to October 2016 was analysed; only E.coli positive reports showing significant growth was included in the study. Ethical committee prior permission was taken. Microbiology Head's permission was sought forth and was granted. C/S reports of the urine samples, registered in the records register, ordered by various wards during the aforementioned study period was selected and analysed. Repeat culture reports were excluded from the study. A total of 41 E.coli reports were analysed further for pattern of resistance.

The reporting pattern at the microbiology department of PIMS follows the following method: the samples are cultured on blood agar and MacConkey agar with a standard loop followed by overnight incubation at 37°C. The isolates are then identified by gram-staining and routine biochemical screening. Susceptibility pattern for antimicrobial agents is then done by Kirby-Bauer dis diffusion method on Mueller-Hinton agar. The interpretation of the sensitivity or resistance is done according to Clinical and Laboratory Standards Institute (CLSI) guidelines. [19] Antibiotics included for sensitivity testing were the following: Betalactams (BLs): ampicilin, betalactams /betalactam inhibitors (BL/BLI): amoxyclav, piperacillin/tazobactum; aminoglycosides: amikacin, gentamycin; third generation cephalosporins: ceftriaxone, ceftazidime, cefoperazone; carbapenams: imipenem; trimethoprim-sulphamet-hoxazole (TMP-SMX); quinolones: ciprofloxacin, ofloxacin, levofloxacin, norfloxacin, nalidixic acid and nitrofurantoin. The data of the study was then analysed using Microsoft Excel 2011, tabulations and charts when necessary were added.

RESULTS

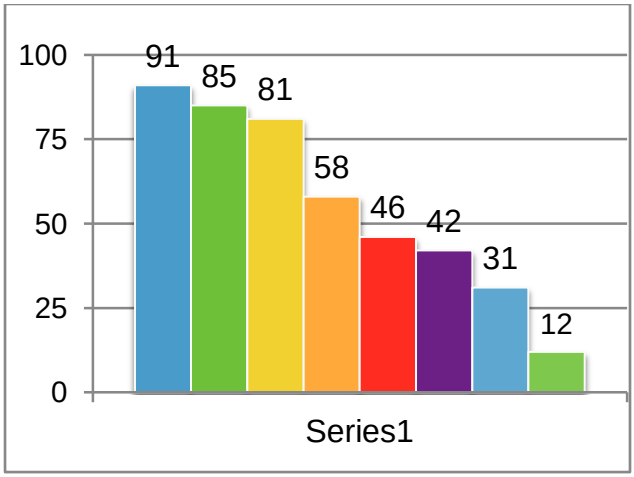
The following resistance pattern was detected in our study: floroquinolones (FQNs) (91%), third generation cephalosporins (3GC) (85%), trimethoprim-sulphamethoxazole (TMP-SMX) (81%), aminoglycosides-gentamycin (58%), piperacillin-

tazobactum (46%), amikacin (42%), nitrofurantoin (31%), carbapenem (12%).

MDR pattern, whereby the organism is resistant to three different group of antibiotics (here cephalosporins including 3GC, TMP-SMX, and FQNs), was identified in well over 80 percent of samples.

E.COLI ANTIBIOGRAM

ANTIBIOTICS	RESISTANCE IN PERCENTAGE
FQN	91
3-G-C	85
TMPSMX	81
GNTN	58
PIPTZO	46
AMKCN	42
NFTN	31
CBPNM	12



3-G-S: third generation cephalosporin, AGs: aminoglycosides, Piptazo: piperacilin/tazobactum, NFTN: nitrofurantoin, CBPNM: carbapenams, FQNs: floroquinolones, TMP-SMX: trimethoprim/sulfamethoxazole

DISCUSSION

Antimicrobial resistance is a global phenomenon challenging the health care facilities appropriate usage.[1,2,3] The clinical implications of a C/S report is less appreciated in clinical settings. A clinician applies due diligence to an ECG, similar fine reading of a C/S report is also warranted, as it has many clinical implications beyond the obvious antibiotic guidance in the index case for which the culture was requested. For example, a C/S report showing resistance pattern to only 3 isolates: ampicillin, cefoperazone-sulbactum and cefotaxime—BL, BL/BLI, 3GC—may mean that the choice of antibiotics need to be judicious, even though the other antibiotics are reportedly sensitive. As a third generation cephalosporin resistance implies ESBL mediated resistance [20, 23, 24] and along with beta-lactamases inhibitor (BLI) resistance it implies a possible AMPc [21,31] mediated resistance; moreover, ESBLs and AmpC commonly co-exist.

Fundamental to this understanding is knowing which enzymes mediates resistance to which set of antibiotics, ESBLs enzymes allow E.coli to become resistance to all beta-lactams except carbapenems, cephamycins (cefoxitin, cefotetan), clavulanic acid.[23, 24] The cephamycin sensitivity is rarely reported in antibiogram reports, hence in clinical practice the surrogate for ESBLs is third generation cephalosporin resistance. Betalactamases (BLs) enzymes on the other hand, allows the bacteria to develop resistance from penicillins upto second generation cephalosporins, further movement up in the antibiotic ladder is made possible via extended spectrum—the ESBLs. However as ESBLs principally are not resistant to betalactamases inhibitor (BLIs), [24] the presence of cefoperazone-sulbctum resistance in the above example brings in another enzyme consideration the AmpC. [21,31]

ESBLs are class A beta-lactamases, and are plasmid-mediated enzymes, and hence easily transferable between strains and between different species of gram negative enterobacteriacea. Besides plasmids harbour resistance to other class of antibiotics resulting in MDR strains. The mortality rate in a misdiagnosed ESBLs has ranged from 42-100%[25-27] emphasising the clinical importance. Hence a third generation cephalosporin (3GC) re-

sistance should be viewed skeptically. The present study demonstrated a 3GC resistance in well over 80 percent, other studies demonstrating a resistance ranging from 70% to above 80% of 77.3%, [15 -17] even an outpatient based study depicted resistance of 47%.[18]

Second clinical significance while observing a C/S report is noting the resistance to piperaillin/tazobactum as it is a betalactam/betalactam inhibitor (BL/BLI) and a carbapenem sparing choice for ESBLs. If BL/BLI resistance is widespread it implies a possibility of AmpC mediated resistance, as noted above. AmpC enzymes allows the bacteria to become resistant to susceptible antimicrobial agent during the treatment, [31] resulting in treatment failure. Moreover, AmpC and ESBLs frequently co-exist creating further challenge in the clinical setting. In the present study piperacillin/tazobactum resistance was found to be substantial at 46%, with various studies reporting resistance ranging from 20% to greater than 50%. [15-18] The immediate clinical implication being that, in a seriously ill patient with UTI a clinician can't bestow confidence on BL/BLI—an otherwise potent carbapenem sparing choice for ESBLs.

Generally beta-lactams (cell wall active agents) are not an ideal choice for urinary tract infection (both upper and lower tract) as it doesn't result in effective eradication of infection, in comparison to FQNs, TMP-SMX and aminoglycosides. [29,30] Therefore, resistance to FQNs is disturbing, as this class of drug is uniquely important, more so, in hospitalised individual with UTI where a renal failure of some degree is invariably present, restricting the use of aminoglycosides—which do not achieve therapeutic concentration in acidic environment (abscess scenario—pyelonephritis). Furthermore, TMP-SMX already has high level of resistance even in community isolates precluding its use. Notwithstanding these needs, E.coli in Indian circumstance is highly resistant to FQNs. The present study depicted a resistance to FQN at 91%, various other studies have demonstrated a resistance ranging from 60% to 80%. [14-18,28.]

Aminoglycosides are a potent choice for urinary tract infection (both upper and lower) as they have higher eradication potential of the infective organism than cell wall active agents (betalactams). Unfortunately, the growing resistance of aminoglycosides in hospital isolates remains a cause of concern, in the present study the resistance level stands at 58% and 42% respectively for amikacin and gentamicin. A resistance ranging from 26% to 67% has been reported by various studies. 14,15

Nitrofurantoin is uniformly sensitive, and hence a good choice for community acquired UTI, unfortunately its ability to reach sufficient concentration is imparted with a eGFR of <60 a common scenario in elderly patients whose baseline GFR even without raised creatinine is low, and even slight renal impairment (creatinine of 1.5-1.7) can result in inability of the drug to be concentrated in the urinary tract with resultant treatment failure. Moreover, it has no role in upper tract infection where it does not achieve therapeutic concentration. As hospitalised patients invariably have upper tract infection its role in hospitalised patients remains limited. However, the data of resistance can have implication for infection control strategies and a warning for potential spread of resistance in the community. The present study showed a resistance to nitrofurantoin over 30%, other studies have showed resistance ranging from 18-36% 15,16,18 A growing resistance to nitrofurantoin is a cause of concern as nitrofurantoin remains an important antimicrobial to treat UTI in community.

TMP-SMX resistance has been uniformly reported including this study, 14-18 although the clinical importance of this agent cannot be overemphasised as it is indispensably cheap and the urinary concentrations and tissue penetration is excellent, in individuals who are sensitive and not allergic to sulpha it remains a good choice.

Carbapenems remains the antibiotic of choice in hospitalised seriously ill individuals with UTI, unfortunately, a growing resistance, 2-12% reported in various study 14-18 including this study, is a cause of concern, and demands urgent

measures for judicious use of antibiotics including infection control measures. Moreover, AmpC producing strains can result in mutations that cause reduced influx (porin mediated) of antimicrobials or increased efflux (efflux pump activation) of antibiotics resulting in resistance31 even without carbapenemases.

LIMITATIONS

The numbers reported were on the lower side and might result in skewed representation of the data. Moreover, the clinical characterisation of resistance based on the antibiotic to which resistance is shown is not absolute, and microbiological confirmation remains gold standard for ESBLs, AmpC and other bacterial enzymes mediating antimicrobial resistance. Notwithstanding these imitations, an astute clinician can take bedside decisions promptly pending further confirmation, based upon the principles discussed above.

CONCLUSION

UTI is the commonest bacterial infection, and among the commonest cause of hospitalisations, catheter associated urinary tract infection (cUTI) is also among the commonest hospital acquired infection (HAI). The clinical significance of commonly used antibiotics needs to be understood and decisions should be based on such reasoning. Contemporary data to guide the clinician is the need of the hour, as there can be substantial variations between region and within the same regions, best practices needs to be followed when a common infectious entity is to be dealt with. Infection control measures in hospital and community needs to be strengthened.

ACKNOWLEDGEMENT

We acknowledge the cooperation of microbiology department Head, and the postgraduates and interns of medicine at PIMS. We extend our heart felt gratitude to the Professor and Head Department of Medicine Dr. P. John Israel.

REFERENCES

1. Morrissey I, Hackel M, Badal R, et al. A review of ten years of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2002 to 2011. Pharmaceuticals (Basel) 2013;6:1335–46.
2. Annual Report of the Chief Medical Officer, Volume Two, 2011, Infections and the rise of antimicrobial resistance (published on March 2013). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/138331/CMO_Annual_Report_ Volume_2_2011.pdf
3. UK Five Year Antimicrobial Resistance Strategy 2013–2018, September 2013. https://www.gov.uk/government/uploads/system/ uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_ strategy.pdf
4. Hoban DJ, Lascols C, Nicolle LE, et al. Antimicrobial susceptibility of Enterobacteriaceae, including molecular characterization of extended spectrum beta-lactamase-producing species, in urinary tract isolates from hospitalized patients in North America and Europe: results from the SMART study 2009–2010. Diagn Microbiol Infect Dis 2012;74:62–7.
5. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 2012;18: 268–81.
6. Levison ME, Kaye D. Treatment of complicated urinary tract infections with an emphasis on drug-resistant gram-negative uropathogens. Curr Infect Dis Rep 2013;15:109–15.
7. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002;113(Suppl 1A):5S–13S.

8. European Centre for Disease prevention and Control. Point prevalence survey of healthcare- associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC, 2013. http://ecdc.europa.eu/en/publications/Publications/ healthcare-associated-infections-antimicrobial-use-PPS.pdf
9. Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, Donaldson L, Pittet D. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet. 2011 Jan 15;377(9761):228-41.
10. Sensitising people about hospital- acquired infections. 09 Feb 2006 [Online]. Available from: URL: http://www.thehindu.com/2006/02/09/stories/2006020912040400.htm
11. Sarkar SK, Bhattacharyya A, Mandal SM. YnfA, a SMR family efflux pump is abundant in Escherichia coli isolates from urinary infection. Indian J Med Microbiol 2015;33(1):139-42.
12. Varughese L, Beniwal V. High quinolone resistant pattern among enteric pathogens isolated from patients with urinary tract infection. Indian J Biotechnol 2015;14:167-71.
13. Williams A, Mathai AS, Phillips AS. Antibiotic prescription patterns at admission into a tertiary level intensive care unit in Northern India. J Pharm Bioallied Sci 2011;3(4):531-6.
14. Somashekara SC, Deepalaxmi S, Jagannath N, Ramesh B, Laveesh MR, Govindadas D. Retrospective analysis of antibiotic resistance pattern to urinary pathogens in a tertiary care hospital in South India. J Basic Clin Pharm 2014;5(4):105-8.
15. Sharma N, Gupta A, Walia G, Bakhshi R. Pattern of Antimicrobial Resistance of Escherichia coli Isolates From Urinary Tract Infection Patients: A Three Year Retrospective Study. J App Pharm Sci, 2016; 6 (01): 062-065.
16. Antimicrobial resistance pattern in Escherichia coli causing urinary tract infection among inpatients Niranjan V. & Malini A. Indian J Med Res 139, June 2014, pp 945-948
17. Krishnan C, Gireeshan VK, Nimmi EJ, et al. Clinico-bacteriological profile of urinary tract infections in children and resistance pattern of uropathogens- A study from south India. J. Evid. Based Med. Healthc. 2017; 4(15), 859-863. DOI: 10.18410/jebmh/2017/164
18. Ray J, Paul R, Haldar A, Mondol S. A study on antibiotic resistance pattern of Escherichia coli isolated from urine specimens in Eastern India. Int J Med Sci Public Health 2015;4:1670-1674
19. Clinical and Laboratory Standard Institute. Performance Standards for Antimicrobial Susceptibility Informational Supplement. M100-S16. Wayne, PA: Clinical and Laboratory Standards Institute; 2006.
20. Clinical significance of extended-spectrum β-lactamasesJesús Rodríguez-Baño & Alvaro PascualExpert Rev Anti Infect Ther. 2008 Oct;6(5):671-83. doi: 10.1586/14787210.6.5.671
21. Treatment options for extended-spectrum beta-lactamase (ESBL) and AmpC-producing bacteria Ryan G. D'Angelo, Jennifer K. Johnson, Jacqueline T. Bork & Emily L. Heil Expert Opinion on Pharmacotherapy Vol. 17 , Iss. 7,2016
22. Chaudhury U, Aggarwal R. Extended spectrum beta-lactamases (ESBL)- An emerging threat to clinical therapeutics. Indian J Med Microbiol 2004;22:75–80.
23. Paterson DL, Bonomo RA: Extended spectrum β-lactamases: a clinical update. Clin Microbiol Rev 2005, 18(4):657–686.
24. Bradford PA: Extended spectrum β-lactamases in the 21st century: characteri-

zation, epidemiology, and detection of this important resistance threat. Clin Microbiol Rev 2001, 14(4):933–951.

25. Meyer KS, Urban C, Eagan JA, Berger BJ, Rahal JJ: Nosocomial outbeak of Klebsiella infection resistant to late-generation cephalosporins. Ann Intern Med 1993, 119:353–358.
26. Naumovsky L, Quinn JP, Miyashiro D, Patel M, Bush K, Singer SB, et al: Outbreak of ceftazidime resistance due to a novel extended spectrum β-lactamase in isolates from cancer patients. Antimicrob Agents Chemother 1992, 36:1991–1996.
27. Schiappa DA, Hayden MK, Matushek MG, Hashemi FN, Sullivan J, Smith KY, et al: Ceftazidime resistant Klebsiella pneumoniae and Escherichia coli blood stream infection: a case control and molecular epidemiologic investigation. J Infect Dis 1996, 174:529–536.
28. Dugal S, Purohit H. Antimicrobial susceptibility pro le and detec- tion of extended spectrum beta-lactamase production by gram negative uropathogens. Int J Pharm Pharm Sci 2013;5:434–8.
29. Warren JW, Abrutyn E, Hebel JR, et al.: Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis. 29:745-758 1999
30. Hooton TM: The current management strategies for community-acquired urinary tract infection. Infect Dis Clin North Am. 17:303-322 2003 12848472
31. AmpC -Lactamases George A. Jacoby* CLINICAL MICROBIOLOGY REVIEWS, Jan. 2009, p. 161–182 0893-8512/09/$08.00 0 doi:10.1128/CMR.00036-08.