Evaluation of antimicrobial resistance in urinary isolates of member of enterobacteriaceae among woman attending Tertiary Care Hospital

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Abstract

Introduction: 1. Urinary Tract Infections (UTIs) are one of the most common urogenital infections and affects all age groups including men, women and children worldwide.
2. Urinary tract infections are a major public health problem in terms of morbidity and financial cost and incur the highest total health care cost among urological diseases.
3. UTI represents one of the most common disease/syndrome encountered in medical practice today with an estimated 150 million UTIs per annum worldwide.

Materials and Method: A total of 300 mid-stream urine specimen from woman patient received in the department after collection in a sterile container were received processed by semi quantitative culture technique using a standard calibrated loop (diameter 0.04mm) on blood agar (BA) and MacConkey agar (MA). After 24hr of aerobic incubation at 37°C, culture growth showing significant bacteriuria were included in the study for further processing. Standard biochemical test of identification were used to identify bacterial isolates. Antimicrobial susceptibility was determined by Kirby-Bauer disk diffusion method as per CLSI Recommendations.

Result: Out of 300 urine samples received Significant Growth was seen in 134 (44.67%) samples, whereas 166 (55.33%) samples showed either Insignificant Growth (polymicrobial) or showed no Growth.

Conclusion: The restricted use of antibiotics can lead to the withdrawal of selective pressure and the resistant bacteria will no longer have a survival advantage against these antibiotics. Hence, there is a need to formulate strategies to detect and prevent the emergence of resistance for an effective treatment of the urinary tract infection.

Keywords: Urinary Tract Infections, Member of enterobacteriaceae, E. coil, Klebsiella spp., Staphylococcus spp., Enterobacter spp.

Introduction

Urinary Tract Infections (UTIs) are one of the most common urogenital infections and affects all age groups including men, women and children worldwide.(1)

Urinary tract infections are a major public health problem in terms of morbidity and financial cost and incur the highest total health care cost among urological diseases.(2) UTI represents one of the most common disease/syndrome encountered in medical practice today with an estimated 150 million UTIs per annum worldwide.(3)

Although UTIs occur in all age groups including men and women, clinical studies suggest that the overall prevalence of UTI is higher in women. An estimated 50% of women experience at least one episode of UTI at some point of their lifetime and between 20% and 40% of women can have recurrent episodes.(4,5) Approximately 20% of all UTIs occur in men.(6)

Member of enerobaceriaceae are commonly isolated from cases of UTI. More than 95% of urinary tract infections are caused by a single bacterial species. *E. coil* is the most frequent infecting organism.(7,8) *Klebsiella spp., Staphylococcus spp., Enterobacter spp., Proteus spp., Pseudomonas spp., Acinetobacter spp., Citrobacter spp.* and *Enterococci species* are more often isolated from inpatients, whereas there is a greater preponderance of *E. coli* among outpatient population.(7,9)

Though antibiotics are the mainstay treatment for all UTIs, the increasing trend of resistance in bacterial pathogens is of worldwide concern that can vary according to geographical and regional locations.(10)

Urinary pathogens also behave in similar manner like others for their existence inside urinary tract and have similar mechanisms for development of antibiotic resistance. They shows common form of antibiotic resistance is either through lack of drug penetration (i.e., outer membrane protein, mutations and efflux pumps), hyper production of an AmpC type β - lactamase, and/or carbapenem-hydrolyzing β-lactamases.(11)

Many of the second and third generation penicillins and cephalosporins were specifically designed to resist the hydrolytic action of major β lactamases. However, new β lactamases emerged against each of the new classes of β lactams that were introduced and caused resistance.(12) The incidence of these β lactamases ranges from 1.8% to 74% worldwide. The prevalence in India ranges from 6.6% to 68%.(13) This emerging trend of resistance may lead to disastrous consequences, as in years to come no antibiotics may remain effective. This

may lead to profound mortality and morbidity in patients. Steps need to be taken at many levels and one important step could be regular monitoring of these organisms for drug resistance.[14]

Since the initiation of antimicrobial therapy in UTI is empirical, a huge need demand for antimicrobial resistance exists at local, national and international levels.[15] Knowledge on the antimicrobial resistance patterns of common uropathogens and the subsequent treatment are thus required to minimize urinary diseases.[16] Along these lines, the present study was designed to identify the microbiological agents causing urinary tract infections and to know their antimicrobial susceptibility pattern.

Materials and Method

The prospective study was carried out at department of microbiology L.N. Medical College & Research Centre Bhopal (M.P.).

A total of 300 mid-stream urine specimen from woman patient received in the department after collection in a sterile container were received over a period of 2 year (October 2013 to September 2015), processed by semi quantitative culture technique using a standard calibrated loop (diameter 0.04mm) on blood agar (BA) and MacConkey agar (MA). After 24hr of aerobic incubation at 37°C, culture growth showing significant bacteriuria were included in the study for further processing. Standard biochemical test of identification were used to identify bacterial isolates. Antimicrobial susceptibility was determined by Kirby-Bauer disk diffusion method as per CLSI Recommendations.[6]

Result

Out of 300 urine samples received Significant Growth was seen in 134 (44.67%) samples, whereas 166 (55.33%) samples showed either Insignificant Growth (polymicrobial) or showed no Growth. Out of 134 clinical isolates 52 were from OPD and 21 from IPD as shown in Table 1.

Table 1: Distribution of clinical isolates from OPD and IPD (n=134)

Sr. No.	Organism	OPD n=52 (%)	IPD n=21 (%)
1	*E. coli*	26 (50)	11 (52.38)
2	*K. pneumoniae*	11 (21.15)	04 (19.04)
3	*K. oxytoca*	07 (13.46)	01 (4.76)
4	*C. koseri*	01 (1.92)	00 (0.00)
5	*C. freundii*	01 (1.92)	01 (4.76)
6	*Pr. Mirabilis*	02 (3.84)	02 (9.52)
7	*Enterobacter spp*	03 (5.76)	02 (9.52)
8	*Serratia marsescens*	01 (1.92)	00 (0.00)

Table 2: Antibiotic resistance pattern of Members of family Enterobacteriaceae - OPD(n=52)

Drugs	*E.coli* n=26	*K. pneumonia* n=11	*K. oxytoca* n=07	*C. koseri* n=01	*C. freundii* n=01	*Pr. mirabilis* n=02	*Enterobacter spp* n=03	*Serratia spp.* n=01	Total n=52
NX	20 (76.92)	8 (72.72)	6(85.71)	1(100)	1(100)	2(100)	2(66.66)	1(100)	41
NIT	3(11.53)	1(9.09)	1(14.28)	0(0)	0(0)	-	1(33.33)	-	6
AMP	25(96.15)	11(100)	07(100)	1(100)	1(100)	2(100)	3(100)	-	49
AMC	21(80.76)	9(81.81)	6(85.71)	0(0)	1(100)	2(100)	2(66.66)	-	41
CZ	24(92.30)	11(100)	7(100)	1(100)	1(100)	2(100)	3(100)	-	49
CX	9(34.61)	4(36.36)	2(28.57)	0(0)	0(0)	1(50)	3(100)	-	19
CXM	19(73.07)	8(72.72)	4(57.14)	1(100)	1(100)	1(50)	2(66.66)	1(100)	37
CAZ	15(57.69)	5(45.45)	4(57.14)	1(100)	1(100)	2(100)	1(33.33)	-	29
CTX	16(61.53)	7(63.63)	4(57.14)	1(100)	1(100)	2(100)	1(33.33)	-	32
CPM	14(53.84)	6(54.54)	3(42.85)	0(0)	0(0)	1(50)	1(33.33)	0(0)	25
PI	15(57.69)	8(72.72)	4(57.14)	1(100)	1(100)	2(100)	1(33.33)	0(0)	32
P/T	11(42.30)	5(45.45)	3(42.85)	0(0)	0(0)	1(50)	0(0)	0(0)	20
AT	13(50.00)	3(27.27)	3(42.85)	0(0)	0(0)	0(0)	0(0)	0(0)	19
IPM	2(7.69)	2(18.18)	00(0)	0(0)	0(0)	0(0)	0(0)	0(0)	4
GEN	11(42.30)	4(36.36)	2(28.57)	0(0)	0(0)	1(50)	2(66.66)	0(0)	20
AMK	5(19.23)	2(18.18)	1(14.28)	0(0)	0(0)	0(0)	1(33.33)	0(0)	9
TOB	6(23.07)	3(27.27)	3(42.85)	0(0)	0(0)	1(50)	2(66.66)	0(0)	15
NET	5(19.23)	2(18.18)	3(42.85)	0(0)	0(0)	0(0)	1(33.33)	0(0)	11
TET	18(69.23)	6(54.54)	5(71.42)	1(100)	1(100)	-	2(66.66)	-	33

COT	13(50.00)	6(54.54)	5(71.42)	1(100)	1(100)	1(50)	3(100)	1(100)	31

Table 3: Antibiotic resistance pattern of Members of family Enterobacteriaceae - IPD(n=21)

Drugs	*E.coli* n=11	*K. pneumonia* n=04	*K. oxytoca* n=01	*C. freundii* n=01	*Pr. mirabilis* n=02	*Enterobacter spp* n=02	Total n=21
NX	9 (81.81)	3(75)	1(100)	1(100)	2(100)	2(100)	18
NIT	2(18.18)	1(25)	0(0)	0(0)	-	1(100)	4
AMP	11(100)	4(100)	1(100)	1(100)	2(100)	2(100)	21
AMC	9(81.81)	3(75)	1(100)	1(100)	2(100)	2(100)	18
CZ	11(100)	4(100)	1(100)	1(100)	2(100)	2(100)	21
CX	3(27.27)	2(50)	0(0)	0(0)	0(0)	2(100)	7
CXM	7(63.63)	3(75)	1(100)	1(100)	1(50)	2(100)	15
CAZ	6(54.54)	2(50)	1(100)	1(100)	1(50)	1(50)	12
CTX	6(54.54)	2(50)	1(100)	1(100)	1(50)	1(50)	12
CPM	6(54.54)	2(50)	0(0)	0(0)	1(50)	1(50)	10
PI	6(54.54)	2(50)	1(100)	1(100)	2(100)	1(50)	13
P/T	3(27.27)	2(50)	0(0)	0(0)	1(50)	0(0)	6
AT	5(45.45)	1(25)	0(0)	0(0)	0(0)	0(0)	6
IPM	0(0)	1(25)	0(0)	0(0)	0(0)	0(0)	1
GEN	4(36.36)	1(25)	0(0)	0(0)	1(50)	1(50)	7
AMK	2(18.18)	1(25)	0(0)	0(0)	0(0)	0(0)	3
TOB	3(27.27)	1(25)	0(0)	0(0)	1(50)	1(50)	6
NET	1(9.09)	1(25)	0(0)	0(0)	1(50)	0(0)	3
TET	6(54.54)	2(50)	1(100)	1(100)	-	2(100)	12
COT	5(45.45)	2(50)	1(100)	1(100)	2(100)	2(100)	13

Discussion

The present study was carried out to determine the prevalent uropathogens in our area and their antibiotic sensitivity pattern to commonly used antibiotics. Our study was carried out in 300 clinically diagnosed female patients with urinary tract infection. Among them 134 patients were found to have significant growth in culture.

In the present study, E.coli isolates were found sensitive to Imipenem (94.6%) followed by Nitrofurantoin (86.49%), Netillmicin (83.79%), Amikacin (81.09%). Maximum resistance was seen to Ampicillin (97.29%), cefazolin (94.16%). Noor et al[17] reported that *E.coli* was 92.8% sensitive to Imipenem and 78.5% to Amikacin. 98.5%, 84.3% and 50% resistant to Ampicillin, Cefotaxime, and Nitrofurantoin respectively. They showed 60-75% resistance range to Cotrimoxazole over the study period.

Iregbu et al[18] showed 89% sensitivity of E.coli to Imipenem, 98% to Amikacin, 79% to Nitrofurantoin,67% to ceftriaxone. Gentamicin and Amoxyclav showed 57% and 73% resistant. Ampicillin was 99% resistant. Biswas et al[19] found 100% sensitivity of E.coli to Imipenem, Meropenem, Amikacin and Nitrofurantoin followed by Gentamicin(94.1%) with good Susceptibility (88.2%) to cefimime, Ceftriaxone, Cefepime.

In the present study, Klebsiella spp. isolates were 84.40% sensitive to Imipenem, Nitrofurantoin 78.8% sensitive followed by to Amikacin & Netillmicin 73.68%. Isolates were 100% resistant to Amplicilline and Cefazolin, 81.1% to Amoxiclav and 74.8% to Norfloxacin. Mandal et al[20] found Klebsiella spp. sensitive to Meropenem (81.8%) and Amikacin (71.4%). Resistance rates for Ceftazidime (56.4%), Ceftriaxone (56.3%), Nitrofurantoin (58.6%), Gentamicin (61.1%).

Sensitivity testing of Klebsiella isolates by Iregbu et al[18] showed 97% susceptibility to Imipenem followed by Amikacin (65%), Ceftazidime (55%), Ceftriaxone (48%), Nitrofurantoin (40%), Gentamicin (39%), Amoxyclav (25%). However, Swetha et al[21] found 37% sensitivity to imipenem in their study.

Some strains have now developed very effective ways to deal with the carbapenems, which could explain the decreased susceptibility reported to carbapenems now-a-days. There are various mechanisms by which these organisms achieve such feat, by Producing β lactamases which destroy the antibiotics, by blocking the entry of these antibiotics, or by efflux pumps which actively pump out these antibiotics.[22]

In our study, Citrobacter spp was 100% sensitive to Imipenem, gentamicin, nitrofurantoin, Amikacin and Netilimicin, Maximum resistance to Ampicillin, Cefazolin and Cefuroxime. Acharya et al[23] found Citrobacter spp. 90.9% sensitive to Nitrofurantoin, Amikacin, Gentamicin, Norfloxacin with resistance to Ampicillin (63.3%) and Ceftriaxone (54.5%). Nerurkar et al[24] reported lower susceptibility to Nitrofurantoin

(58.4%), Norfloxacin (48.4%), Amikacin (54%), Gentamicin (33.5%), Ampicillin (34.6%), Cotrimoxazole (31.6%).

In the present study, 100% of Proteus mirabilis isolates were sensitive to Amikacin, Netilimicin and Imipenem. 100% isolates were resistant to Ampicillin and Cefazolin. Barate et al[17] in their study showed high resistance of Proteus spp. to Ampicillin (84%), Amoxyclav (65%), Cephalexin (66%), but good sensitivity to Tetracycline (75%), Ciprofloxacin (71 %), Norfloxacin (70%), Gentamicin (65%). Biswas et al[19] found 100% sensitivity of Proteus spp. to Gentamicin, lmipenem, Meropenem, cefepime, followed by Amikadn (80%), ciprofloxacin(70%) with 100% resistant to AmoxyclIlin and NItrofurantoin.

Enterobacter spp. Isolated In our study were 100% sensitive to Imipenem, Amikacin, Netillmicin, Aztreonam, Nitrefurantoin and 100% resistant to Ampicillin and Cefazollin.

In our study, we found single isolates of Serratia spp, which showed 100% sensitivity to aminoglycosides, Aztreonam, Cefepime, Imipenem, piperacillin- tazobactam, and resistant to norfloxacin, cefuroxime. Akoacnere et al[25] reported susceptibility of *S.marcescens* in own community to Gentamicin (100%), Ampicillin (50%), Nitrofurantoin (50%), cefriaxone(50%), cotrimoxazole (0%). Wasnik et al[26] showed that Serratia Marscences was 50% resistant to 4-5 antibiotics and 100% resistance to Penicillin With their MAR index 0.076.

The majority of the isolates showed resistance to drugs commonly used to treat UTIs. Imipenem was found most sensitive drug, followed by amikacin, and these are not drugs often deployed as first line in the treatment of uncomplicated UTI. Although different studies in different parts of the world and in different parts of the same country found different resistance rates to different drugs over time. It is important that emphasis be paid to local resistance patterns as these have the greatest impact on care. These variations in susceptibility may be due to the prescription habits in different localities as inappropriate exposure to antibiotics drives development of resistance. From the results of this study it is certain that choosing drugs for empiric treatment will be challenging as no single common drug can conveniently be recommends for UTI. This reinforces the need for mandatory urine culture for all suspected UTIs to properly guide therapy.[18]

Conclusion

The restricted use of antibiotics can lead to the withdrawal of selective pressure and the resistant bacteria will no longer have a survival advantage against these antibiotics. Hence, there is a need to formulate strategies to detect and prevent the emergence of resistance for an effective treatment of the urinary tract infection.

It is certain that choosing drugs for empiric treatment of UTI will be challenging as no single common drug can conveniently be recommended for that. Therefore, we suggest urine culture and antimicrobial susceptibility testing for clinically diagnosed UTI cases.

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