COMMON ORGANISMS AND ANTIBIOTIC SENSITIVITY OF E COLI IN URINARY TRACT INFECTION, IN A TERTIARY CARE TEACHING HOSPITAL, NORTHERN KERALA

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ABSTRACT

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Urinary tract infection (UTI) includes a spectrum of Asymptomatic Bacteruria (ABU), Cystitis, Prostitis and Pyelonephritis. Except in ABU, UTI is represented by symptomatic disease that warrants antimicrobial therapy.[1] Many of the studies have shown increasing antibiotic resistance to these agents. This study consists of a retrospective observational study of culture and sensitivity of 150 urinary samples, collected from patients who presented with symptoms of UTI, in a tertiary care teaching hospital, Northern Kerala, irrespective of their age and sex for a period of six months from June 2015 to November 2015. These results are then analyzed to find common organisms causing UTI in different age groups in either sex and their respective antibiotic resistance are noted. Out of 150 urinary samples 69.34% were sterile, while 30.66% were culture positive. Among the culture positive patients sex distribution was almost equal, with a slight female predominance, having a contribution of 54.35% females and 45.65% males. The most common organism was found to be E.coli, which contributed more than 50 per cent of total culture positivity (54.35%). Others include Staphylococci, Klebsiella Pnuemoniae, Proteus species, Pseudomonas, Enterococci, Candida Albicans etc. Collateral damage is an ecological adverse effect that resist the use of a highly efficacious drug to be considered as first line agent. Our study shows that drugs causing minimal collateral damages like Nitrofurantoin and Fosfomycin can be used as first line agent for treatment of UTI.

KEYWORDS

Urinary Tract Infection, Asymptomatic Bacteruria, E. Coli, Collateral Damage, Antibiotic Resistance.

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INTRODUCTION: UTI encompasses a variety of clinical entities including ABU, Cystitis, Prostitis and Pyelonephritis.[1] In infants and elderly UTI occurs more among males than females, while between 1 and 50 years it is more common among the latter group. High incidence of congenital urinary tract abnormality among male infants and high incidence of prostatic hypertrophy among elderly males are the cause of increased prevalence of UTI among these groups.[1] While the major reason for high incidence of UTI in young sexually active females are due to sexual activity, which has got a direct relation to it.[2] Presence of a short urethra, closer to the anus also increases the risk of UTI in females.

The most common symptoms are burning micturition and urinary incontinence, which can vary from mild to severe form.[2,3] New onset urinary incontinence should rise suspicion of UTI in children.[4] In elderly, typical symptoms of UTI are usually not seen, instead they present with urinary incontinence, mental status changes or fatiguability.[5,6] Presence of pre-existing Dementia and Incontinence may interfere with the diagnosis of UTI in them[5]. Use of spermicides and diaphragm as contraceptive measures are also associated with increased incidence of UTI, while use of condoms and birth control pills do not increase the risk of UTI.[2,7] As a result of decrease in estrogen in post menopausal women and resulting loss of protective vaginal flora stands for the increased incidence of UTI in this group of patients.[8] Use of aseptic technique and maintenance of unobstructed closed drainage of the catheter can decrease the risk of UTI associated with catheterization.[9,10]

The prevalence of ABU is 5% among women between 20 and 40 years. ABU during pregnancy is associated with preterm birth and perinatal mortality for the fetus and pyelonephritis of mother. A cochrane meta-analysis found that treatment of ABU in pregnant women decreased the risk of pyelonephritis by 75%. Hence in pregnant women ABU has clinical consequences and both screening for and treatment of this condition are indicated.[11]

The pathogen causing UTI are usually gram negative rods that have migrated to the urinary tract. In acute uncomplicated Cystitis E.coli accounts for 75-90% of isolates

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and Staphylococcus Saprophyticus 5-15%. Klebsiella, Proteus, Enterococcus and Citrobacter species and others contribute 5-10%.[11]

UTI can complicate to form Pyelonephritis in which milder form can present with fever with or without lower-back or costovertebral-angle pain, while severe form present with fever, rigors, nausea, vomiting and flank and/or loin pain. High spiking "picket-fence" pattern of fever is typical of pyelonephritis which distinguish it from acute cystitis. Pathologically there are Emphysematous Pyelonephritis (severe form) and Xanthogranulomatous Pyelonephrirtis.[11]

In 1999, TMP-SMX was recommended as the first line agent for treatment of uncomplicated UTI in the published guidelines of the Infectious Disease society of America. The available data demonstrate a world-wide increase in the resistance of E.coli to antibiotics commonly used to treat UTI.[11]

Adverse ecological effect of antimicrobial therapy including killing of the normal flora and selection of drug-resistant organism is called collateral damage. It indicates that a drug that is highly efficacious for the treatment of UTI is not necessarily the optimal first-line agent, if it also has pronounced secondary effect on the normal flora or is likely to change the resistance pattern.[11]

AIM OF THE STUDY: The aim of the study is to find the common organisms associated with urinary tract infection in different age groups and to find their antibiotic sensitivity in a tertiary care teaching hospital, Northern Kerala. Also the study aims to assist the use of antibiotic based treatment of UTI in this part of country based on their sensitivity pattern, side-effects, cost-effectiveness and collateral damage.

METHODS: This is a retrospective observational study, conducted in the department of microbiology and department of internal medicine, in a tertiary care, teaching, hospital (KMCT Medical College, Mukkom, Calicut). In this study, culture and sensitivity of urine samples of 150 patients presented with symptoms of UTI, during a period of 6 months from June 2015 to November 2015 are collected from the Department of Microbiology. This data are later analyzed based on their age group, sex and culture and sensitivity results. After identifying drugs with good efficacy, they are again compared based on their cost effectiveness, route of administration, side-effects and collateral damage to find out the first line agents for UTI.

Antibiotic sensitivity test was done using Muller-Hinton agar by modified Kirby-Bauer disc diffusion method according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. The antibiotic discs used were Ampicillin, Nitrofurantoin, Ceftriaxone, Cefazoline, Amikacin, Gentamicin, Ciprofloxacin, Ofloxacin, Cotrimoxazole, Cefipime, Meropenem, Nalidixic acid and Fosfomycin.

RESULTS: Out of the total urinary samples 69.34% were sterile, while 30.66% were culture positive. Among the sterile culture female patients boasted an impressive 70.2%, while male contribution was slightly below one-third (29.8%). When considering the age group, nearly six out of ten sterile culture reported among those age from 12 to 60. Those less than 12 years and more than 60 years made an equal contribution of 20.2%.

Total Specimen		**Male (%)**	**Female (%)**
STERILE	69.34	29.8	70.2
CULTURE POSITIVE	30.66	29.8	70.2

Table 1: Sex distribution of sterile culture in patients with UTI

Among the culture positive patients sex distribution was almost equal, with a slight female predominance, having a contribution of 54.35% female and 45.65% male. Considering the age group of culture positive patients, half of the contribution was made by older people (age more than 60). Those between 12 and 60 years and below 12 years contributed nearly two-thirds and one third of total culture positivity (32.6% and 17.4%) respectively.

Culture Positive	
Male	45.65
Female	54.35

Table 2: Sex distribution of culture positivity in patients with UTI

The most common organism was found to be E. COLI, which contributed more than 60 per cent of total culture positivity (62.5%). Staphylococci including Staphylococcus Saprophyticus, MRSA and Coagulase negative staphylococcus togetherly contributed 12.5%. It was followed by K. Pneumoniae, Pseudomonas, Proteus and Enterococci having a contribution of 5-10%. In older patients (age more than 60) presented with UTI, fungi (Candida albicans) made a significant contribution which was less than that of E.coli but much higher than other bacteria (13.4%). A positive fungal culture was noted only among older people.

CULTURE POSITIVE	
E. Coli	62.5
K.pneumoniae	10
Psuedomonas	5
Proteus	5
Enterococci	5
Fungus	13.04
Staphylococci	12.5

Table 3: Distribution of common organisms associated with UTI

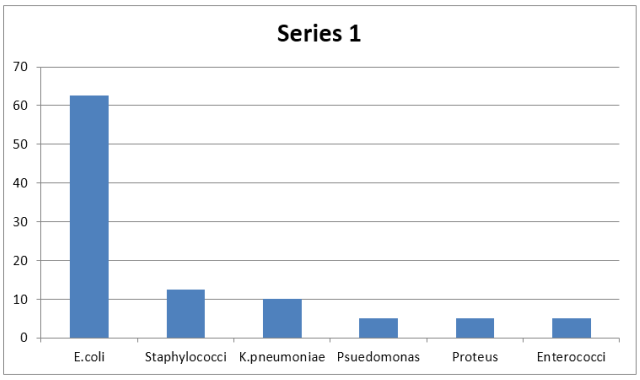

Figure 1. Distribution of common organisms associated with UTI

Out of the total patients presented with symptoms of UTI, nearly one-fifth (19.33%) were of paediatric age group. Out of this 27.6% showed a positive culture result. The most common organsism in this age group was found to be E. Coli, which was slightly below three-fourth (72.4%) of the total positivity. The K. Pneumoniae and Enterobacteriacea were the second most common bacteriae in this age group, together contributing nearly one-fourth of total positivity.

Out of the total patients presented with symptoms of UTI, the majority were of the age between 12 to 60 years, which was 51.33%. Out of this nearly one-fifth (19.5%) showed a positive culture result. The most common organism in this age group was E. COLI, that made a significant contribution of 73.3%. The second most common organism was K.pneumoniae, which was 13.3%. It was followed by pseudomonas (6.7%). The other organisms include Proteus, MRSA and Coagulase negative Staphylococci.

Out of the total, older patients' (more than 60 years) contribution was 29.33%. Out of which more than half (52.3%) were culture positive. The most common organism in this age group was E. COLI, which was higher than one-third (34.8%) of total. Proteus and coagulase negative staphylococcus made the second highest bacterial contribution (8.7%). It was followed by equal positive results by pseudomonas and klebsiella (4.35%).

Fungi, especially Candida, was the second most common organism causing UTI in elderly patients (26.1%). Fungal culture positivity was common in older patients with DM or other terminal illnesses.

Age Group	Total Samples	Culture Positive
<12	19.33	27.6
12-60	51.33	19.5
>60	29.33	52.3

Table 4: Age distribution of culture positivity in patients with UTI

Irrespective of the age and sex, the most common organism was found to be E. COLI, which contributed more than 60 per cent of total culture positivity (62.5%). When considering the sex distribution of E.coli, female patients contributed much higher than male patients, which was 64% and 36% respectively. When considering the age group, those with the age between 12 to 60 years made maximum contribution (44%). It was followed by older patients and paediatric patients respectively (32% and 24%).

CULTURE POSITIVE	
E.coli	62.5
K.pneumoniae	10
Psuedomonas	5
Proteus	5
Enterococci	5
Fungus	13.04
Staphylococci	12.5

Table 5: Distribution of common organisms in UTI

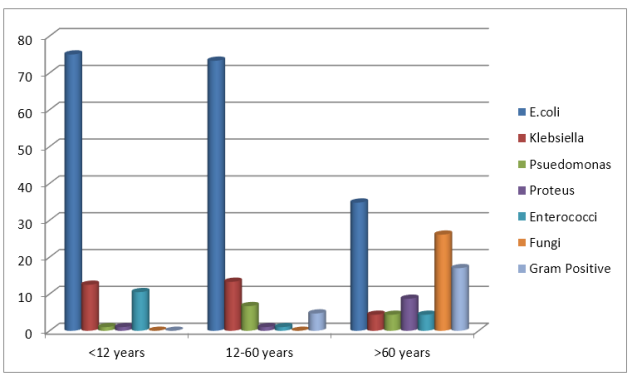

Figure 2. Distribution of common organisms in UTI

It was found that E. COLI is most sensitive to Fosfomycin (99%). Nitrofurantoin, Gentamicin and Amikacin are the second most efficacious drugs against E. COLI with a sensitivity of 92%. Ampicillin and Cefazolin are the drugs showing maximum resistance to E. COLI, with a figure of 92% and 80% respectively.

Antibiotic	Sensitivity(%)	Resistance(%)
Ampicillin	8	92
Nitrofurantoin	92	8
Cefazolin	20	80
Cotrimoxazole	48	52
Ceftriaxone	32	68
Cefipime	32	68
Gentamicin	92	8
Amikacin	92	8
Ciprofloxacin	56	44
Norfloxacin	56	44
Nalidixic acid	22	78
Meropenem	68	32
Fosfomycin	99	1

Table 6: Antibiotic Sensitivity Pattern of E. COLI

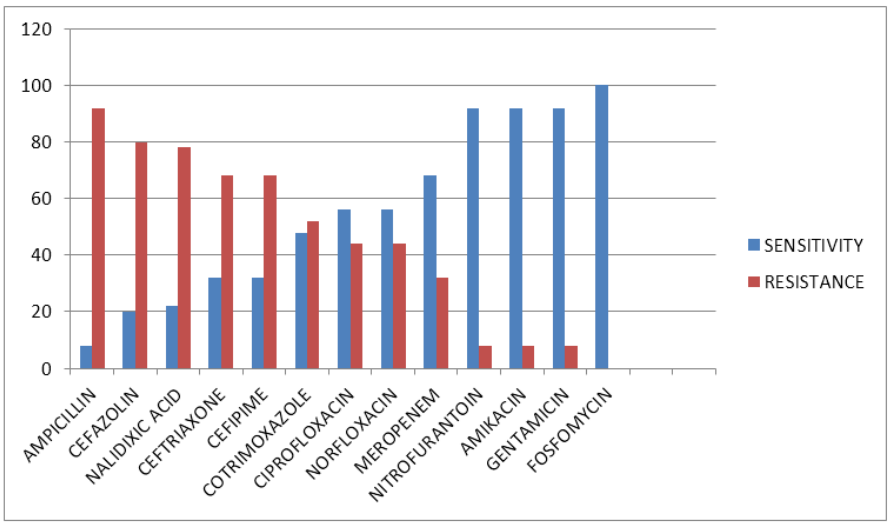

Figure 3. Antibiotic sensitivity pattern of E.coli

No.	Antibiotic	Sensitivity	Resistance	Route of Administartion	Total Cost for 7 Days (Rupees)	Side Effect
1	Fosfomycin	100	0	ORAL	858	MODERATE
				IV		
2	Nitrofurantoin	92	8	ORAL	159	MODERATE
3	Amikacin	92	8	IV	1274	MODERATE
4	Gentamicin	92	8	IV	67	MODERATE
5	Meropenem	68	32	IV	10500	MODERATE
6	Norfloxacin	56	44	ORAL	34	MODERATE
				IV		
7	Ciprofloxacin	56	44	ORAL	59	MODERATE
				IV	252	

Table 7: Cost effectiveness of different drugs aginst E.coli

DISCUSSION: This study was performed to identify the common organisms associated with UTI and to find the antibiotic susceptibility of E. COLI in patients presented with symptoms of UTI, towards 13 antibiotics, in a tertiary centre, KMCTMC, and to report the evolving antibiotic resistance by this bacteria in this part of the country.

The prevalence of culture positive UTI in this study is 30.66% which is only slightly higher when compared to a previous study conducted by Ahmad. S, et al (27%)[12] in India. This slight change may be due to difference in the study population and difference in size of the study population.

Moreover prevalence of UTI was found to be higher in females (54.35%), when compared to males (45.65%). These values are comparable with almost all previous studies on the sex distribution of UTI.[12] This increased incidence can be explained by the presence of a short urethra, which is closer to anus and due to sexual activity in females.

Incidence of culture positive UTI was found to be maximum in older individuals (52.3%), irrespective of their sex, compared to other age groups. This result is comparable with the study conducted by Iregbu KC, et al.[13] This is attributable to high incidence of prostatic hypertrophy, diabetes mellitus, ambulation and urinary tract interventions among elderly people.[1,9]

In paediatric age group the most common organism was found to be E.COLI making 72.4% of total culture positive UTI. It was followed by K. Pneumoniae and Enterococci togetherly contributing nearly 25% of the UTI in this age group.

The most common organism causing UTI in young individuals was again found to be E. COLI with a figure of 73.3%. It was followed by K. Pneumoniae and staphylococci making 13.3% and 12.5% of its contribution. Other organisms include proteus and pseudomonas.

Even though E. COLI is the most common organism causing UTI in elderly individuals its contribution is reduced to 34.8%. Fungi became the second most common organism causing UTI with a figure of 26.1%. It is important to notice that fungal culture positivity was noted only among elderly patients admitted in ICU. Second most common bacterial cause was found to be Coagulase negative Staphylococci and Proteus. It was followed by Klebsiella and Pseudomonas.

It was amazing to notice that E.coli is 99% sensitive to Fosfomycin. This value is much higher when compared with another study conducted by Rodrigo Batista Souza, et al.[14] This high sensitivity is because, this agent is not commonly

used by physicians in this part of country. Non judicious use of this agent may increase the resistance towards this drug. So it is recommended that this drug should be preserved to treat only highly resistant E. COLI.

Also it is highly sensitive to drugs like Nitrofurantoin, Amikacin and Gentamicn having more than 90% sensitivity. Sensitivity of E.COLI towards Nitrofurantoin is much higher in this part of country, while sensitivity towards aminoglycosides are almost comparable with the study conducted by Iregbu KC, et al.[13]

It is disturbing to notice that E. COLI shows significant resistance towards meropenem (32%). This value is much higher when compared with the study conducted by Iregbu KC, et al.[13] Developing high resistance to broad spectrum antibiotics like carbapenems highlight unscientific use of this drug in this part of country. So we should avoid prescribing carbapenems in the absence of a culture and sensitivity result that shows E. COLI not sensitive to narrow spectrum antibiotics and only sensitive to broad spectrum agents like carabapenems. This action may hinder the progress of antimicrobial resistance towards these agents.

This gram negative rods also show more than 50% sensitivity to quinolones like Ciprofloxacin and Ofloxacin (56%).This is highly comparable to the study conducted by Iregbu, KC et al.[13]

E. COLI is highly resistant to ampicillin (92%), Cefazolin (80%), Nalidixic acid (78%), Ceftriaxone (68%) and Cefipime (68%). Resistance towards Ampicillin and Ceftriaxone is much higher when compared with the study conducted by Iregbu KC, et al.[14] Wide spread use of these agents for treating UTI, in this part of country might be the reason for this spike in antibiotic resistance towards these agents. And this is time to stop prescribing Ampicillin for the empirical treatment of UTI in pregnant women in the absence of a proper culture and sensitivity result. We may have to consider Nitrofurantoin as first line agent for treating UTI in this group.

When considering their side-effect profile all of them show moderate side-effects to the patients. Since oral preparations are available for two highly sensitive drugs, Fosfomycin and Nitrofurantoin, they should be preferred over other drugs where only 4 preparations are available. Also drugs that are used in the UTI that has minimal effect on the normal flora include Fosfomycin and Nitrofurantoin. In contrast Trimethoprim, TPM-SMX, Quinolones and Ampicillin affect the faecal flora more significantly.[15] Also rising resistance level have been noted for this agents.[15] Nitrfutantoin is more cost effective than Fosfomycin, as a result Nitrofurantoin should be considered as first line agent for the UTI associated with E. COLI.

Highly efficacious drugs against UTI having 4 preparations include Gentamicin, Amikacin, Fosfomycin and Meropenem. Considering the cost effectiveness, Aminoglycosides, especially gentamicin, should be preferred over other drugs for in patient management of UTI. Even though Fosfomycin is highly sensitive to E. COLI, it cannot be considered as first line agent due its high cost.

CONCLUSION: The study concludes that E.coli is the most common uropathogen in community acquired UTI, irrespective of the age and sex. Prevalance of UTI is very high among females especially young females. It is attributed to the sexual activity and the presence of a short urethra which is more proximal to the gastrointestinal outlet. UTI is reported maximum in elderly individuals, irrespective of their sex, which is due to high incidence of prostatic hypertrophy, diabetes mellitus and urinary tract intervention among this age group. Also positive fungal culture was reported only among elderly individuals admitted in ICU.

E. COLI is most sensitive to Fosfomycin (99%). It is followed by Nitrofurantoin, Amikacin and Gentamicin having more than 90% sensitivity. considering the collateral damage, route of administration, cost effectiveness and side-effect profile Nitrofurantoin is preferred over Fosfomycin for out patient treatment and Aminoglycosides especially Gentamicin is preferred for in patient treatment.

Even though Fosfomycin is a highly efficacious drug with less collateral damage, it is recommended that it should be preserved for highly resistant E. COLI not responding to other antimicrobial agents and for chronic and recurrent UTI. Non-judicious use of Fosfomycin can result in the generation of highly resistant E.coli making this drug less effective.

Since E.coli shows significant resistance towards Ampicillin (92%), which is very commonly used for the empirical treatment of UTI during pregnancy, it is time to think about a new antimicrobial agent safe during pregnancy.

Also E. Coli is becoming more and more resistant to Carbapenems, in this part of country. So as to hinder the progress of resistance it is suggested to avoid routine usage of this drug unless there is a culture sensitivity report showing E. COLI only sensitive to this agent. In all other situations drugs having good sensitivity but narrow spectrum should be preferred.

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