World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF MICROORGANISMS CAUSING URINARY TRACT INFECTIONS IN A TERTIARY CARE FACILITY

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Article Received on 08/09/2022 **Article Revised on 28/09/2022** **Article Accepted on 18/10/2022**

ABSTRACT

Background: Urinary tract infection (UTI) represents one of the most common diseases encountered in medical practice today and occurring from neonate to geriatric age group. Urinary tract infection is defined as bacteriuria along with urinary symptoms. It is one of the most common bacterial infections in humans and a major cause of morbidity. UTI has become difficult to treat because of the appearance of pathogens with increasing resistance to antimicrobial agents. The objective of this study was to determine the bacteriological profile of pathogens responsible for urinary tract infection and to assess the antibiotic sensitivity pattern of the causative uropathogens. **Material and Methods:** 500 urine specimens collected from symptomatic patients were processed for isolation of pathogens and antimicrobial susceptibility by Kirby Bauer disc diffusion method as per CLSI guidelines. **Result:** Of the 500 samples received 118 yielded culture positive. *E.coli* was the predominant organism followed by *Candida* species. UTI was predominant in females. Maximum sensitivity of *E.coli* was seen with Nitrofurantoin (91.67%), followed by Fosfomycin (86.11%). *Candida* species showed highest sensitivity to Voriconazole (100%) followed by Nystatin (92.31%) Amphotericin (84.62%). **Conclusion:** *Escherichia coli* were a predominant pathogen causing urinary tract infection followed by *Candida* species. Hence, the aim of this study was to isolate the pathogenic agents involving UTI and to study the antibiotic sensitivity pattern among the samples collected from subjects with clinically suspected infection.

KEYWORDS: Antibiotic sensitivity, Bacteria, Urinary tract infection, Uropathogens.

INTRODUCTION

Urinary tract infection remains the most common infection worldwide, which can occur anytime in the life of an individual. UTI can affect both the upper and lower urinary tract. Urinary tract infection is caused mainly by normal bowel flora principally *Escherichia coli*, responsible for ≥75% of cases. Other Gram negative Enterobacteriaceae, Gram positive *Enterococcus faecalis* and *Staphylococcus saprophyticus* are responsible for the remainder of UTI.[1] UTIs are one of the most common types of infections; at least one in two women and one in 10 men will experience a UTI in their lifetime. Since women often have shorter urethras than men, they are more likely to develop UTIs. UTI infection can present with a variety of symptoms, such as burning micturition, bacteraemia, sepsis, and even death. It is also possible to relapse due to pregnancy, sexual interactions, and family history among the different etiological agents of UTI-causing bacteria. Hygiene conditions, low socio-economic status, suppressed immunity, urinary catheters, diabetes, unhygienic public toilets, birth control devices, and family history may also contribute.[2] Uncomplicated urinary tract infections, also known as cystitis or lower urinary tract infections, are bacterial infections of the bladder and associated structures. Uncomplicated urinary tract infections occur in female patients with no structural abnormality or comorbidities such as diabetes, old age, pregnancy, or immunocompromised status. Complicated urinary tract infections occur in patients with structural abnormalities or comorbidities such as diabetes, old age, pregnancy, or immunocompromised status.[3]

More than 95% of urinary tract infections are caused by a single bacterial species. *E.coli* is the most frequent infecting organism in acute infection. *Enterobacter, Staphylococci, Klebsiella, Proteus, Pseudomonas*, and *Enterococci* species are more often isolated from inpatients, whereas there is a great preponderance of *E.coli* in an outpatient population.[4]

Urinary tract pathogens are treated empirically with broad spectrum antibiotics. However, excessive and inappropriate use of antibiotics has led to the development of antibiotic resistance among uropathogens which is a major issue worldwide.[5] This increasing antimicrobial resistance complicates an uncomplicated UTI treatment by increasing patient morbidity, prolonged hospital stay, retreatment and use of broader spectrum of antibiotics. Hence, comprehensive efforts are needed to minimize the pace of resistance by studying emergent microorganisms, resistance mechanisms, and antimicrobial agents. [6]

Thus, the aim of this study was to isolate the pathogenic agents involving UTI and to study the antibiotic sensitivity pattern among the samples collected from subjects with clinically suspected infection.

MATERIAL AND METHODS

A total of 500 midstream urine samples were collected in sterile containers from patients with suspected urinary tract infection. The wet mount of all the urine samples was observed to determine the presence of pus cells, epithelial cells, yeast cells or bacteria which over significant numbers are indicators of Urinary Tract infections. Then with the help of a standard calibrated loop delivering 0.01 ml of urine was inoculated on Blood agar and MacConkey's agar and incubated aerobically at 37^0C for 18-24 hours. A urine sample containing more than 10^5colonies per ml of urine in a calibrated bacteriological loop is considered significant bacteriuria. After incubation a CFU count more than 10^5 per ml of urine the sample was considered as significant bacteriuria and such urine samples further processed for identification, isolation and determining antibiogram of bacterial pathogens causing UTIs. If the CFU is less than 10^4per ml the samples were considered as non-significant bacteriuria or negative. Identification of bacterial pathogen was made on the basis of gram staining reactions, morphology and biochemical characteristics. Isolates were tested for antimicrobial susceptibility by Kirby Bauer's disc diffusion technique according to Clinical and laboratory standards Institute (CLSI) guidelines on Mueller Hinton agar.[7] After incubation the results were interpreted by measuring zone diameter and then compared with the standard chart to determine whether the organism is sensitive, intermediate or resistant to the respective drugs.

RESULTS

Out of the 500 midstream samples collected from patients with suspected Urinary tract infections, 118 samples tested positive for significant bacteriuria with colony counts greater than 10^5 whereas the rest of the samples were negative or had a colony count less than 10^5. Eleven types of organisms were isolated, among which *Escherichia coli* was responsible for the highest number of Urinary Tract Infections (30.51%), followed by *Candida spp* (22.03%), *Klebsiellaspp* (19.49%), *Pseudomonas aeruginosa* (11.02%) followed by others. (Figure1).

In addition only a single strain of Methicillin sensitive *Staphylococcus aureus, Streptococcus* spp and Non fermenter gram negative bacilli was isolated.

The Age and Gender Distribution showed that the higher prevalence of Urinary tract infections was found in females (53.38%) than in males (42.37%).

And the highest prevalence of Urinary tract infections was found in both females and males in the age groups between 61-76 (37.2%) followed by age groups 46-60 (20.4%), 76 and above(15.9%) and 31-45 (14.2%). (Table-1 and Figure 1)

The results of the antibiotic sensitivity profile for gram negative organisms showed that maximum sensitivity of *E. coli* was seen with Nitrofurantoin (91.67%), followed by Fosfomycin (86.11%), Meropenem (86.11%), Piperacillin/Tazobactam (83.33%), Imipenem (83.33%), Amikacin (83.33%). Maximum sensitivity of *Klebsiella* spp was seen with Fosfomycin (86.96%), Meropenem (60.87%), and Imipenem (60.87%). For *Pseudomonas* spp maximum sensitivity was seen for Piperacillin/Tazobactam (76.92%) and Polymyxin-B (53.85%). For *Citrobacter koseri* maximum sensitivity was seen for Meropenem (100%), Amikacin(80.0%), Fosfomycin(80.0%),Gentamicin(80.0 %), Imipenem(80.0%), Nitrofurantoin(80.0%), Piperacillin/Tazobactum(80.0%), Tobramycin(80.0%).

For *Acinetobacter* spp maximum sensitivity was seen for Gentamicin (100%), Levofloxacin (100%), Piperacillin/Tazobactam (100%). And for *Proteus mirabilis* maximum sensitivity was seen for Gentamicin(100%), Imipenem(100%), Piperacillin/Tazobactum (100%). (Table-3)

Candida species showed highest sensitivity to Voriconazole(100%) followed by Nystatin(92.31%) Amphotericin (84.62%). (Table-3)

The results of antibiotic sensitivity profile for gram positive organisms showed that the maximum sensitivity for *Enterococcus* spp was seen for Fosfomycin (50.00%) and linezolid (50.00%). While an accurate sensitivity profile for *Staphylococcus aureus*, Streptococcus and Non-fermenter gram negative bacilli cannot be determined due to a very low number of isolates.

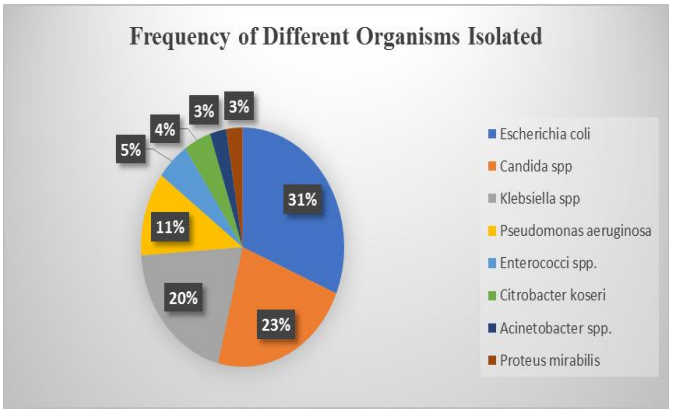

Figure 1: Frequency of different organisms isolated from urine specimens.

Table 1: Distribution of UTI as per Age and Gender.

Age	Females with UTI		Males with UTI		Total	
	Number	Percentage	Number	Percentage`	Number	Percentage`
0-15	0	0%	2	4%	2	1.8%
16-30	8	12.7%	4	8%	12	10.6%
31-45	10	15.9%	6	12%	16	14.2%
46-60	11	17.5%	12	24%	23	20.4%
61-75	26	41.3%	16	32%	42	37.2%
76 above	8	12.7%	10	20%	18	15.9%
Total	63		50		113	

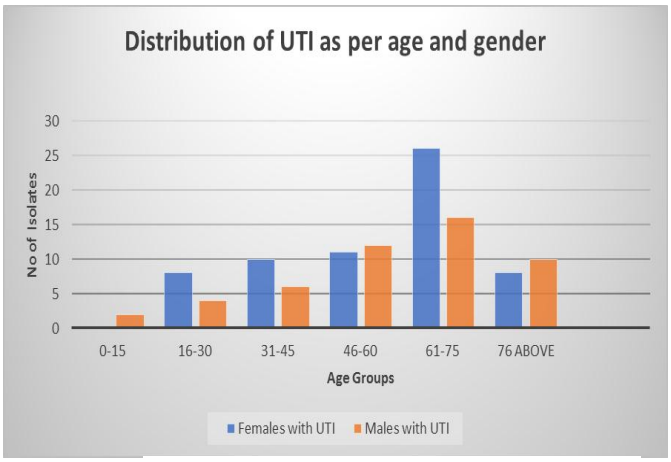

Figure 2: Distribution of UTI as per Age and Gender.

Table 2: Antibiotic sensitivity profile of Gram Positive and Gram negative organisms Isolated.

Antibiotics	E.coli (%)	Klebspp (%)	Pseudo spp(%)	Citrospp (%)	Acinetospp (%)	Proteus spp (%)	Enterococci spp (%)
Ak	83.33	56.52	15.38	80	66.67	66.67	16.67
Amc	41.67	17.39	0	20	33.33	33.33	0
Amp	11.11	0	0	0	33.33	33.33	16.67
As	55.56	39.13	0	20	66.67	66.67	16.67
At	38.89	8.7	15.38	20	33.33	0	0
Azm	5.56	4.35	0	0	0	33.33	0
Caz	52.78	39.13	7.69	40	66.67	33.33	0
Cec	50	56.52	0	20	66.67	33.33	16.67
Cip	38.89	34.78	7.69	20	33.33	33.33	16.67
Cis	25	8.7	0	40	33.33	33.33	0
Cfs	0	0	7.69	20	0	0	0
Cl	38.89	47.83	7.69	20	66.67	0	16.67
Cot	55.56	43.48	0	40	66.67	0	0

Cpz	8.33	17.39	0	0	33.33	33.33	0
Cpm	44.44	34.78	15.38	40	66.67	66.67	0
Ctx	38.89	34.78	0	20	33.33	0	0
Cx	50	43.48	0	40	0	33.33	16.67
Cxm	38.89	21.74	0	20	33.33	66.67	0
Cz	36.11	17.39	0	20	0	0	0
Fo	86.11	86.96	0	80	0	66.67	50
G	77.78	52.17	15.38	80	100	100	
Imp	83.33	60.87	7.69	80	66.67	100	16.67
Le	61.11	47.83	7.69	40	100	33.33	0
Lz	0	0	0	0	0	0	50
Mrp	86.11	60.87	15.38	100	66.67	66.67	16.67
Nit	91.67	47.83	15.38	80	0	0	33.33
P	0	0	0	0	0	0	16.67
Pit	83.33	52.17	76.92	80	100	100	0
PB	0	0	53.85	0	0	0	0
Te	22.22	26.09	0	40	33.33	0	33.33
Tob	72.22	43.48	15.38	80	66.67	66.67	0
Va	0	0	0	0	0	0	33.33
HLG	0	0	0	0	0	0	16.67
HLS	0	0	0	0	0	0	33.33
Ak- Amikacin, Amc-Amoxyclav, Amp- Ampicillin, A/S- Ampicillin/Sulbactam, At-Aztreonam, Azm-Azithromycin, Caz- Ceftazidime, Cec- Cefotaxime/Clavulanic acid, Cip- Ciprofloxacin, Cis-Ceftriaxome/Sulbactam, Cfs- Cefoperazozonel/Sulbactam, Cl-Colistin, Cot-Co-Trimoxazole(Sulpha/Trimethoprim), Cpz- Cefoperazone, Cpm-Cefepime, Ctx- Cefotaxime, Cx-Cefoxitin, Cxm-Cefuroxime, Cz- Cefazoline, Fo-Fosfomycin, G-Gentamicin, Imp-Imipenem, Le– Levofloxacīn,Lz-Linezolid, Mrp-Meropenem. Nit-Nitrofurantoin, P- P-Penicillin, Pit-Piperacillin/Tazobactum, PB- Polymyxin-B, Te-Tetracycline, Tob- Tobramycin, Va-Vancomycin, HLG-High Level Gentamicin, HLS- High Level Streptomycin							

Table 3: Antibiotic sensitivity profile for *candida* spp.

Antibiotics	Ap	Flc	It	Kt	Ns	Vrc
Candida spp (%)	84.62	46.2	73.1	73.08	92	100
Ap-Amphotericin, Flc-Fluconazole, It-Itraconazole, Kt-Ketoconazole, Ns- Nystatin, Vrc-Voriconazole						

DISCUSSION

Urinary tract infection is one of the most common illnesses that affect people of all ages and genders. A useful approach to treat UTIs is to isolate and identify the organism that is causing the infection, and then determine its antibiotic susceptibility profile to select antibiotics that will be effective against it. In this study 118 samples tested positive for significant bacteriuria out of 500 patients who were suspected of having Urinary Tract infections. The results of the study indicate that females (53.38%) have a higher prevalence of urinary tract infections than males (42.37%) which was also reported by Rezina Parveen and Ina Rahim.[1] Higher prevalence of urinary tract infections in females is due to the shorter urethra in females as well as the fact that the urethra of females is located more proximal to the anus, making coliforms more easily able to invade and cause infection.

The prevalence of Urinary Tract Infections was found to be highest in age groups 61-75 and 46-60. The reason behind this is that older adults are more vulnerable to UTIs, because of the weaker muscles in the bladder and pelvic floor that can cause urine retention or incontinence. Whenever the urine stays in the urinary tract, there's a potential for bacteria, to multiply and cause an infection to spread. Age-associated changes in immune function, exposure to nosocomial pathogens and an increasing number of comorbidities put the elderly at an increased risk for developing infection.[8]

Out of the 500 urine samples, 118 were found to be positive for bacteriuria. Isolation and identification of organisms responsible for Urinary Tract Infections revealed that *Escherichia coli* was the predominant uropathogen causing maximum number of infections which is in concordance with other studies.[9]

For Gram negative organisms that were isolated and identified maximum sensitivity was seen for the following antibiotics Nitrofurantoin, Fosfomycin, Meropenem, Piperacillin/ Tazobactam, Imipenem, Amikacin Gentamicin, Tobramycin, Levofloxacin. According to Kaushik et al, the gram negative bacteria showed maximum sensitivity to nitrofurantoin (95.5%), Amikacin(75.5%) and Gentamicin(65.5%).[10]

Candida was second predominant organism causing Urinary Tract infections. *Candida* isolation rate was 10.2% as reported by Singhal etal. [11] and is much higher than 2.27% and 1.37% as reported by two studies from Southern India by Yashavanth *etal* and Ragini *etal* respectively. [12][13] This shows a marked geographical variation in the rate of infection by *Candida* in urinary tract infections warranting a multi-centric study to establish an overall pattern of isolation. *Candida* species showed highest sensitivity to Voriconazole(100%) followed by Nystatin(92.31%) Amphotericin(84.62%). Isolation and identification of candida species from urine and their antifungal susceptibility test can help treating Candiduria.

Whereas the Grampositive organisms were highly sensitive to Linezolid, and Fosfomycin. However, as the numbers of isolates of gram positive organisms are very low, a significant antibiotic sensitivity profile cannot be determined and further study should be carried out to obtain a antibiogram.

In a study conducted by Thattil etal the gram positive organisms were highly sensitive to linezolid, vancomycin and teicoplanin[14] while in the present study sensitivity to vancomycin is very low.

Majority of isolates showed resistance to a number of antibiotics commonly used to treat urinary tract infections. Globally, antibiotic resistance is a growing problem due to the consumption of unprescribed antibiotics, incomplete antibiotic regimes, and other factors. As a result, antibiotic misuse must be stopped and antibiotic resistance must be monitored for effective UTI treatment. This pattern of resistance to commonly used antibiotics for treating UTI alerts us against indiscriminate usage of antibiotics. As drug resistance among pathogens is an evolving process, routine surveillance and monitoring studies should be conducted to provide physicians with knowledge about the most effective empirical treatment of UTIs. All efforts to minimizing the spread of resistant bacteria through appropriate infection control would be quite important and may represent a first step in resolving the issue of resistant microorganisms.[15]

CONCLUSION

Urinary tract infections are increasing day by day and are more prevalent in females in comparison to males. They are also more prevalent in older population, mostly common after the age of 60. *Escherichia coli* is the most predominant uropathogen followed by *Candida* species. The study also pointed out that most urinary tract pathogens have developed resistance to a wide range of drugs. Study of uropathogens and their antibiotic susceptibility pattern in an area is essential for providing effective therapy and control of UTI. The emergence and spread of resistance can be reduced through appropriate and careful use of antimicrobial agents and increasing awareness among the population about the hazards of inappropriate antimicrobial use through public health education campaign. Urinary tract infections are an important public health issue, and, at present, they have worsened due to an increasing prevalence of antibiotic resistance, especially in hospitalized patients. Treatment should be based on the microbiological profile of the region or of a medical facility using broad-spectrum antibiotics to manage multidrug-resistant bacteria, while reducing the constraints associated with conventional antibiotic treatments.

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