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PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF UROPATHOGENS IN PATIENTS ATTENDING IN A TERTIARY CARE HOSPITAL

Microbiology

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ABSTRACT

Background: Urinary tract infection (UTI) remains the most common infection worldwide that may occur in any age of an individual. It has been evaluated that symptomatic UTI occurs in around in 7 million patients visiting to emergency units and 100,000 hospitalized per annum worldwide. Urinary Tract Infections are more common in females, in reproductive age group (15-49) than in males. Mostly *Enterobacteriacea* members, particularly uropathogenic strains of *Esch. coli* and *Enterobacter* species are primary causative microorganism of UTIs.

Material And Methods: Total 750 mid stream urine samples were collected from all groups of patients with clinically suspected to UTI. Patient urine samples were aseptically collected in sterile containers. In case of catheterized patients, it collected directly from catheter. Samples were inoculated on CLED agar, Blood agar and MacConkey agar plates by using standard loop. The organisms were identified by colony morphology as well as biochemical test and Antibiotic sensitivity test performed using standard microbiological procedure.

Result: Total 750 urine samples were processed from outdoor and indoor patient out of which 298 (39.73%) were found to be culture positive and 452 (60.61%) are negative.

Conclusion: The conclusion recommended the need for regular screening for the occurrence of symptomatic or asymptomatic bacteriuria for populations and constant monitoring of susceptibility to commonly used anti-microbial agents.

KEYWORDS

Urinary tract infections, CLED Agar, Antibiotic susceptibility.

INTRODUCTION

Urinary tract infections (UTI) are most frequent disease in children. At least 8% of girls and 2% of boys are affected with UTI in childhood and between 30% and 40% will have another episode within two years.[1,2] Microorganisms invade the genitourinary tract and causes urinary tract infection. In anatomically abnormal urinary tract complication urinary tract infection occurs due to the inflammation of the urothelium is common condition that occurs in male and female.

It has been evaluated that symptomatic UTI occurs in around 7 million patients visiting to emergency units and 100,000 hospitalized patients per annum. UTI is the most common cause of infection in hospitalized patients which is responsible for 40% of hospital acquired infections.[2,3] UTI is more common in females than in males as female urethra structurally found less effective for preventing the bacterial entry. It may be due to the proximity of the genital tract and urethra.[4,5]

The other main factors which make females more prone to UTI are pregnancy and sexual activity. In pregnancy, the physiological increase in plasma volume and decrease in urine concentration develop glycosuria in up to 70% women which ultimately leads to bacterial growth in urine. [6,7]

The most commonly encountered organisms are gram negative bacteria including *Escherichia coli, Enterobacter aerogenes, Citrobacter spp., Proteus vulgaris, Pseudomonas aerogenosa, Acinetobacter, Serratia, Klebsiella species* and the common gram positive pathogenic bacteria include *Staphylococcus saprophyticus, Staphylococcus epidermidis* and *Enterococcus species* results in urinary tract infection colonization of the vagina and perianal skin. [8] *Gardenella vaginalis, Mycoplasma* species and *Ureaplasma urealyticum* organisms which may cause infection in patients with irregular catheters. [9]

Klebsiella, Staphylococci, Enterobacter,Proteus, Pseudomonas, and *Enterococci* species are more often isolated from inpatients, whereas there is a greater preponderance of E. coli in an outpatient population. [10] It is required to identify the causative agent of UTI and spectrum of its antimicrobial susceptibility in order to treat UTI. The aims of this study were isolation of pathogenic organism which involving urinary tract infection and determination of their antibiotics susceptibility pattern in patients.

MATERIAL AND METHODS:

This study was conducted in a tertiary care hospital over a period of 12 months from 2018 October to 2019 march. Total 750 mid stream urine samples were collected from both OPD and IPD patient suspected of UTI. Both male and female patients of age group 5-55 years were included in the study.. Samples were collected prior to administering the antibiotic in sterile wide mouthed screw-capped universal container. In case of catheterized patients, it collected directly from catheter. The specimens were labeled and transported to the laboratory and analyzed within 6 hours. If delay than samples are refrigerated a 4 ^{0}C. Each specimen was subjected to direct microscopy, culture by the semi quantitative standard loop technique on CLED agar, Blood agar and MacConkey agar. A calibrated sterile nichrome wire loop used for the plating and it has a 4.0 mm diameter loop which collected 0.01 ml of sample. After inoculation the plates were incubated aerobically at 37 ^{0}C for overnight or 24 hours. The plates were examined and the bacterial colonies were counted and multiplied by 100 to give an estimate of the number of bacteria present per ml of urine. Significant growth was determined as ≥105 colony-forming units (CFU)/mL of midstream urine and bag urine samples, and ≥102 CFU/mL of a catheter specimen. Isolates were identified by Gram staining and conventional biochemical methods (11).

Antimicrobial Susceptibility Testing:

Isolates were tested for antimicrobial susceptibility testing by the modified Kirby Bauer disc diffusion method following the clinical laboratory standards institute (CLSI) guidelines.[12]

All Enterobacteriaceae were tested against first line agents: ampicillin (10µg), cephalexin (30µg), gentamicin (10µg), nitrofurantoin (300µg), trimethoprim-sulphamethoxazole (co- trimoxazole) (1.25-23.75µg), norfloxacin (10µg) and ofloxacin (5µg); Enterococcus spp. against ampicillin (10µg), vancomycin (30µg), nitrofurantoin (300µg), ciprofloxacin (5µg), norfloxacin(10µg) and high level gentamicin (120µg); Pseudomonas aeruginosa agains piperacillin (10µg), amikacin (30µg), gentamicin (10µg), ceftazidime (30µg) ofloxacin (5µg) and ciprofloxacin (5µg). Acinetobacter spp against gentamicin (10µg), ceftazidime (30µg), levofloxacin (5µg), ciprofloxacin (5µg), imipenem (10µg) and meropenem (10µg).

Second line antibiotics were tested only for organisms in those isolates resistant to all 1st line antimicrobials or on request by the physician.

These included amikacin (30µg), imipenem (10µg), ertapenem (10µg), cefoperazone- sulbactam (75µg), cefepime (30µg) and piperacillin tazobactam (100/10µg) for all Enterobacteriaceae; imipenem (10µg), meropenem (10µg), cefepime (30µg) and piperacillin tazobactam (100/10µg) for *P.aeruginosa.E.coli* ATCC 25922, *E.coli* ATCC 35218, *Staphlococcus aureus* ATCC 2523 and *P.aeruginosa* ATCC 27853 were used as controls.

RESULT

Total 750 urine samples were processed from outdoor and indoor patient out of which 298 (39.73%) were found to be culture positive and 452 (60.61%) are negative.

Table 1: Sex Wise Distribution

Sex	Total processed samples	Positive cases (%)	Negative cases (%)
Male	365	74 (24.83%)	291(64.38%)
Female	385	224(75.16%)	161(35.61%)
Total	750	298	452

Table 1 and figure 1 shows out of 750 urine specimens of patients 298 (39.73%) samples were positive out of these one fourth 74 (24.83%) are male and nearly two third 22 (75.16%) are female. This shows a female predominance over male.

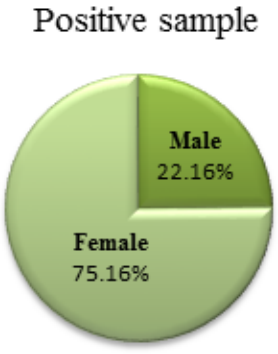

Figure 1: Sex Wise Distribution

Table II and Figure II shows the distribution of pathogenic bacteria. Out of 298 positive cases 54 (18.12%) were gram positive organisms and gram negative organisms were 244 (81.8%). Thus gram negative organisms are more common affecting the younger females. Out of gram negative organism *E coli* 146 (48.99%) was most common followed by *Klebsiella* 38 (12.75%) and least common was *Acinetobacter* 7 (2.34%) and *proteus* species (2.34%).

Table II Organism Wise Distribution

Type of organisms	Positive	case (%)
Escherichia coli	146	(48.99%)
Klebsiella	38	(12.75%)
Enterococcus	35	(12.75%)
Citrobacter species	21	(7.04%)
Staphylococcus species	19	(6.37%)
Pseudomonas species	16	(5.36%)
Acinetobacter	7	(2.34%)
Proteus species	7	(2.34%)
Enterobacter	9	(3.02%)
Total	**298**	

Figure II: Organism Wise Distribution

Table III shows the sensitivity pattern of gram negative organisms isolated from urine for the antibiotic drugs. E coli showed maximum sensitivity with Polymixin-B (97.26%) followed by Meropenum (93.83%) and least sensitive with Co-trimoxazole (27.39%).

Klebsiella showed maximum sensitivity with Imipenem (81.57%) followed by Levofloxacin (78.94%) and least sensitivity with Cotrimoxazole (23.68%).Citrobacter showed maximum sensitivity with Meropenem (85.71%) %) followed by Imipenem (80.95%) and least sensitivity with Cefuroxime (23.80%) Acinetobacter showed 100% sensitivity with Polymixin-B. Other antibiotics also showed sensitivity with pathogens.

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Table III: Antibiotic Sensitivity Pattern Of Gram Negative Isolates

Antibiotic	E.coli n=146	Klebsiella n=38	Citrobacter n=21	Pseudomonas spp. n=16	Proteus spp. n=7	Acinetobacter n=7	Enterobacter n=9
Amikacin	76 (52.05%)	15 (39.47%)	13 (61.90%)	15 (93.75%)	3 (42.85%)	2 (28.57%)	7 (77.77%)
Gentamycin	80 (54.79%)	18 (47.36%)	7 (33.33%)	4 (25.00%)	4 (57.14%)	4 (57.14%)	6 (66.66%)
Co-trimoxazole	40 (27.39%)	9 (23.68%)	0	7 (43.75%)	2 (28.57%)	2 (28.57%)	6 (66.66%)
Ciprofloxacin	62 (42.46%)	15 (39.47%)	7 (33.33%)	4 (25.00%)	0	0	7 (77.77%)
Amoxicillin	76 (52.05%)	13 (34.21%)	2 (9.52%)	0	2 (28.57%)	-	1 (11.11%)
Livofloxacin	121 (82.87%)	30 (78.94%)	15 (71.42%)	2 (12.5%)	0	2 (28.57%)	9 (100%)
Cefuroxime	116 (79.45%)	25 (65.78%)	5 (23.80%)	0	0	-	2 (22.22%)
Cefepime	72 (49.31%)	-	7 (33.33%)	4 (25.00%)	-		2 (22.22%)
Ceftazidime	51 (34.93%)	18 (47.36%)	-	4 (25.00%)	0	3 (42.85%)	6 (66.66%)
Ampicillin	76 (52.05%)	11 (28.94%)	-	0	0	2 (28.57%)	-
Aztreonam	51 (34.93%)	11 (28.94%)	6 (28.57%)	5 (31.25%)	3 (42.85%)		4 (44.44%)
Imipenem	129 (88.35%)	31 (81.57%)	17 (80.95%)	14 (87.5%)	0	5 (71.42%)	9 (100%)
Meropenem	137 (93.83%)	28 (73.68%)	18 (85.71%)	12 (75.00%)	0	5 (71.42%)	8 (88.88%)
Piperacillin +tazobactum	51 (34.93%)	-	7 (33.33%)	12 (75.00%)	0	3 (42.85%)	3 (33.33%)
Nitrofurantoin	128 (87.67%)	11 (28.94%)	10 (47.61)	-	-	-	3 (33.33%)
Colistin	-	-	-	7 (43.7%5)	-	6 (85.71%)	-
Polymixin B	142 (97.26%)	19 (50.00%)	16(76.19%)	15 (93.75%)	-	7 (100%)	5 (55.55%)
Doxycyclin	-	-	-	-	-	4 (57.14%)	-
Ofloxacin	62 (42.46%)	27 (71.05%)	7 (33.33%)	8 (50.00%)	0	0	7 (77.77%)

Table IV shows the sensitivity pattern of gram positive organisms isolated from urine for antibiotic drugs. *Enterococcus* showed maximum sensitivity with Vancomycin (91.42%) followed by Linezolid (82.85%) with Ampicillin/Sulbactum (77.14%) followed by Erythromycin (71.42%) and least sensitivity was with Cotrimoxazole (28.57%) followed by ofloxacin (42.85%). Staphylococcus showed maximum sensitivity with vancomycin (94.73%) followed by Linezolid and Levofloxacin (84.21%) with Ampicillin/Sulbactum (57.89%) Erythromycin (52.63%), Cefotaxime (42.10%) and least sensitivity was with Amoxycillin/Clavulanic acid (21.05%) followed by Ofloxacin (42.00%). *Staphylococcus aureus* showed less than 50 % sensitivity with most of the drugs.

Table IV: Antibiotic Sensitivity Pattern In Gram Positive Organisms

Antibiotic	Enterococcus n=35	Staph aureus n=19
Amoxy/Clavulanic acid	11 (31.42%)	6 (31.57%)
Amoxycillin	15 (42.85%)	4 (21.05%)
Cefotaxime	18 (51.42%)	8 (42.10%)
Co-trimoxazole	10 (28.57%)	7 (36.84%)
Ampicillin/Sulbactum	27 (77.14%)	11 (57.89%)
Cephalixin	12 (34.28%)	9 (47.36%)
Ciprofloxacin	17 (48.57%)	8 (42.10%)
Norfloxacin	16 (45.71%)	7 (36.84%)
Levofloxacin	22 (62.85%)	16 (84.21%)
Vancomycin	32 (91.42%)	18 (94.73%)
Norfloxacin	11(31.42%)	6 (31.57%)
Erythromycin	25 (71.42%)	10 (52.63%)
Amikacin	15 (42.85%)	15 (78.94%)
Clindamycin	21 (60%)	9 (47.36%)
Ofloxacin	15 (42.85%)	8 (42.10%)
Linezolid	29 (82.85%)	16 (84.21%)

DISCUSSION

UTI is a common problem despite age and sex worldwide. This study provides valuable data to compare and monitor the status of antimicrobial resistance among uropathogens to improve efficient empirical treatment. Increasing antimicro- bial resistance has been documented globally. [13]

UTIs still stays the second most common infections, each within the hospitalized patients and within the out patients. In our study 750 clinically diagnosed patients 298 (39.73%) patients were found to be infected with pathogenic organisms rest 453 (60.61%) are sterile. Thus prevalence of UTI in the population was 39.73% in comparison to higher than the prevalence rate of 31.35% significant bacteriuria recorded by Savitha T et al.[14] As it is less than prevalence rate of 66.78% recorded by Mahesh EL et al. [15] In our study, the females are more prevalent to UTI than males. From the total 298 isolates obtained, 224 (75.16%) were from female patients while 74 (24.83%) were from males. This proves that UTI is more frequent in females as compared to males. While comparing the study of Akram M. et al.[16] incidence rate in female (70.50%) and male (29.5%) and Kolawole et al. [17] prevalence rate in female (66.67%) and male (33.33%). It is also comparable with the study done by Oladiende BH et al.[18], Ahmad SM et al. [19], and Barate DL et al.[20] The reason being the females are more susceptible for developing urinary tract infection may be because of short length of urethra, characteristic anatomical course and physiological changes. Urethral proximity to anus is also an important factor for acquiring infection. Other reason being the stasis of urine during pregnancy, dilatation of urethra and trauma to urethra during sexual intercourse. *E.coli* (81.5%) is a most common or bacteria isolated in these patients, *Klebsiella* (1.5%) *P. aeruginosa* (%), and *S. aureus* (10.5%). This type of pattern was similar with study of Chedi BAZ et al[21] Savitha T et al. [14] The important barricade that interferes with the effective treatment is the development of antimicrobial resistance within uropathogens. This study has thrown light over the anti-microbial sensitivity pattern among the gram negative bacteria isolated and it is shown in Table III. Enterobacteriaceae family showed heavy resistance to amoxicillin, Cotrimoxazole and some Cephalosporins. *E. coli & Klebseilla* showed maximum sensitivity with first line drugs like cefuroxime 79.45% and 65.78% respectively and is in accordance with the study done by Rizvi M et al[22], Akram M et al[16], and Barate DLet al[20].

Urinary tract infection by *Enterococcus* was also quite common in our study showing 35 (11.74%) of case next to the gram negative bacilli especially in the patients who received antibiotic treatment or who were treated by instrumentation in the urinary tract. It was reported by the previous studies that prevalence of *Enterococci* as a cause of nosocomial infection is increased during the last three decades. Maximum sensitivity was shown with Vancomycin (91.42%) followed by Linezolid (82.85%) and least sensitive with Levofloxacin (62.85%). and is in accordance with the study done by Patel SK et al[23], Rizvi M et al[20], Kolawole et al[17] and Arul Prakasam KC et al.[24] Gram positive bacteria played lesser role in UTI. However *Staphylococcus aureus* was isolated and accounted for 6.37% of acute infection in young females. Maximum sensitivity was shown with Vancomycin (94.73%) followed by Linezolid (84.21%) and least sensitive with clindamycin (47.36%). Similar finding is with the study done by Hazarika J[25], Mokta KK et al.[26] and Naik H et al.[27] So the Vancomycin, Tobramycin and linezolid can be used as drug of choice in against UTI caused by Gram positive cocci. Thus emergence of drug resistance among uropathogens is a worldwide concern and is possessing a global threat. Wide spread usage of cotrimoxazole and penicillin has led to the emergence of resistant strains. Another latest drugs like fluoroquinolones and cephalosporins are also being affected day by day.

CONCLUSION

It is concluded that Gram-negative bacilli (Enterobacteracea) were responsible for urinary tract infections and most of the strains were multi-drugs resistant. The most common isolated bacteria from urinary tract infections was E. coli and the most effective antimicrobial agents were imipenem, meropenem ,polymyxin B, gentamycin cefuroxime amikacin, and ciprofleoxacin against Gram-negative bacilli and also the most effective antibiotics against Gram-positive cocci were vancomycin, linezolid, Ampicillin/ Sulbactum, levofloxacin and ciprofleoxacin.

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