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Original Research Article

Prevalence and antimicrobial resistance patterns of bacterial pathogens causing Urinary tract infection in a tertiary healthcare setting, Maldives

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Abstract

Objectives: To determine the prevalence and antimicrobial resistance patterns of bacterial uropathogens from culture positive sample data from a tertiary healthcare setting.
Methods: A retrospective analysis of culture isolates obtained from urine samples received at Department of Laboratory Medicine, Indira Gandhi Memorial Hospital, Male', Maldives was performed between January 2017 and December 2017.
Results: A total of 3901 urine specimens received were analyzed and 24.1% were from males and 75.9% were from females. *Escherichia coli* was the most common gram-negative isolate (37.9 %) followed by *Klebsiella* spp (25.79%). Tested third generation cephalosporin resistances were: *E. coli* (male 49%, female 30%), *Klebsiella* spp (male 55%, female 28%). Carbapenem resistance percentages were as follows: *E.coli* tested against imipenem (males:33%, females: 26%) and meropenem (males:44% females55%). *Klebsiella* spp imipenem (males 23% females 27%), and meropenem (males 35%, females 68%).
Conclusion: The high level of resistance especially to carbapenems amongst common isolates is reason to modify therapy until susceptibility testing has been carried out. Regional surveillance programs are required to gain a broader understating for surveillance and modify national guidelines.
Keywords: Uropathogens, Antimicrobial resistance, Urinary tract infection.

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1. Introduction

Urinary tract infection (UTI) is one of the most commonly seen infections in clinical practice. It also accounts for one of the most common nosocomial infection in many healthcare settings [1]. Urinary tract infection occurs due to the presence of pathogenic microorganisms along the urinary tract and can involve the urethra, prostate, bladder and/or kidneys[2]. Amongst healthcare-associated infections, UTI prevalence accounts up to 24% in developing countries[3],[4]. A high proportion of healthcare-associated UTIs are associated with indwelling catheters[5]. In light of the additional hospital stay and healthcare costs from nosocomially acquired UTIs it is increasingly important for accurate and timely diagnosis of urinary tract infections.

Risk factors associated with UTI in community settings are age, previous history of UTI as well as diabetes mellitus. In men there is an increased incidence of UTIs with age [6]. In women there is a decrease in UTIs at middle ages followed with increased rates after the age of 65[7]. The reason for the high incidence of UTI in women maybe due to anatomical predisposition and other host factors [8]. The susceptibility to UTI in women is attributed to the variation in the number and type of bacteria on vaginal mucosa[9].

Although urinary tract infections are mostly caused by bacteria, it can also be caused by fungal and viral infections[10]. The causative organism for 90% of urinary tract infections are seen to be gram-negative bacteria while gram positive bacteria has been implicated in 10% of the cases [11]. *Escherichia coli* is seen as the leading cause of pathogen in uncomplicated UTIs, followed by *Proteus* spp., *Staphylococcus saprophyticus*, *Klebsiella* spp and other Enterobacteriaceae [12]. In healthcare-associated UTIs, a diverse spectrum of uropathogens are implicated, with a majority of gram-negative bacteria[13].

Antibiotic therapy has been utilized successfully in the treatment of uncomplicated community acquired UTIs. These antimicrobials include β-lactams, trimethoprim-sulfamethoxazole (TMP-SMX), nitrofurantoin, ciprofloxacin, levofloxacin or related chemical derivatives as well as certain penicillins such as amoxicillin[14]. Widespread and indiscriminate use of antimicrobials have shown increasing trends of pathogens resistant to commonly prescribed antimicrobials agent[15]. The prevalence and pattern of antimicrobial susceptibility of uropathogens are important both for appropriate drug selection as well as empirical therapy[16]. For this reason, local pathogen spectrum and antimicrobial susceptibility information is important in establishing empirical treatment, especially in the healthcare setting[4]. There are few official publications to show information regarding the etiology and resistance pattern of UTIs in Maldives. As such this study was conducted to ascertain the prevalence of bacterial uropathogens and their susceptibility to commonly used antimicrobials among patient samples at a tertiary care hospital in the capital city, Male', Maldives.

2. Materials and Methods

2.1 Study area and Sample Collection

This retrospective analysis included 3901 positive culture isolates from Urine culture registers from January 2017 to December 2017. These samples included both the inpatient and outpatient samples from tertiary care hospital, Indira Gandhi Memorial Hospital, Male', Maldives. Patients were advised to collect clean-catch midstream or catheter-catch urine into sterile containers. This information was given prior to sample collection.

2.2 Sample processing and antimicrobial susceptibility testing

Urine culture samples were inoculated aseptically by using a calibrated loop onto Cystine-Lactose-Electrolyte Deficient (CLED) agar (Hi Media Laboratories, Mumbai, India). The plates were incubated at 37°C for 24 h and for 48h if negative. Specimens were considered positive for UTI if an organism was cultured at a concentration of $\geq 10^5$cfu/mL or when cultured at a concentration of $\geq 10^4$cfu/mL and >5 pus cells per high power field observed on microscopic examination of urine sample[17]. Mueller-Hinton agar was used for antimicrobial susceptibility testing (AST) following Kirby-Bauer disc diffusion method[18] against a panel of antibiotics (Oxoid, UK); Amoxicliin (10 U), Piperacillin (100µg), Ampicillin/Sulbactam (10/10µg), Augmentin (30µg), Piperacillin/tazobactam (100/10µg), Cephalexin (30 µg), Cefuroxime (30µg), Cefotaxime (30µg), Ceftazidime (30µg), Ceftriaxone (10 µg), Cefixime (5µg), Cefepime (30µg), Vancomycin (30 µg), Imipenem (10 µg), Meropenem (10 µg), Gentamicin (30 µg), Tobramycin (10 µg), Amikacin (30 µg), Ciprofloxacin (5 µg), Norfloxacin (30 µg), Co-trimoxazole (25µg), Nitrofurantoin (30 µg).

2.3 Ethics statement:

Ethical clearance was obtained from The Maldives National University as well as National Health Research Committee, Ministry of Health, Male', Maldives. Patient data was kept anonymous throughout the study and kept confidential.

2.4 Data analysis:

The data were analysed using Chi-square (χ^2) test, confidence interval (CI), odds ratio (OR) analysis, and students t-test for paired samples. Relative risk and odds ratio were performed to compare the risk factors in male and female patients. The Chi-square test was conducted to find out the significant difference between the isolated uropathogens, infected male and female patients related to different age groups. A P value of <0.05 was considered as statistically significant for all tests and a 95% level of confidence interval. All statistical tests were performed by Statistical Package for Social Sciences (SPSS) software, Inc.

3. Results

From the 3901 urine culture positive samples obtained in 2017, there were 941 (24.1%) samples from males and 2960 (75.9%) from females. This indicates the prevalence of UTI to be higher in females in comparison to males. The *P* value and odds ratio showed a significant variation between male and female patients (Table I).

Table I: **Distribution of growth patterns**

Sex	Significant growth (> 10^5cfu/mL)		Total (%)	Odds ratio			Relative risk			x^2	p value
	Gram Negative ($n = 3063$)	Gram Positive ($n = 838$)		Value	Lower	Upper	Value	Lower	Upper		
Male	791	150	941[24.1]	1.597	1.315	1.939	1.095	1.058	1.133	22.576	0.000

The highest susceptible age group of patients to UTI was the age category 19-44 years (41.0%) followed by 65-80 years (17.0%), 45-64 years (17%) and 1 month-2 years (10.0%). Comparatively neonates have the lowest percentage of isolates at 1.0%. The highest prevalence of UTI in females was found in the age group 19-44 years (95.2%); however, in males the highest susceptible age group was 1 month to 2 years (73.3%). The Chi square test showed statistically significant variations ($P < 0.05$) at 95% level of confidence interval for the gram positive and gram-negative isolates for male and female patients variables among all age groups. For the gram positive and negative male patients variable the Chi-square test values were $\chi 2 = 48.838$; $p = 0.000$ and the values for gram positive and gram-negative female patients were $\chi 2 = 135.537$; $p = 0.000$ (Table II).

Table II: Prevalence of UTI in different age groups and genders

Age Category	Total	Male (n=941)				Female (n=2960)			
		Gram Negative (n=791)	Gram Positive (n=150)	χ^2	p value	Negative (n=2272)	Positive (n=688)	χ^2	p value
Under 30 days	41 (1%)	24 (59%)	4 (10%)			12 (29%)	1 (2%)		
1 month to 2 years	371 (10%)	243 (65%)	29 (8%)			87 (23%)	12 (3%)		
3 to 6 years	245 (6%)	108 (44%)	14 (6%)			104 (42%)	19 (8%)		
7 to 12 years	119 (3%)	9 (8%)	7 (6%)			75 (63%)	28 (24%)		
13 to 18 years	112 (3%)	4 (4%)	5 (4%)	48.838	**0.000**	63 (56%)	40 (36%)	135.537	**0.000**
19 to 44 years	1589 (41%)	59 (4%)	18 (1%)			1063 (67%)	449 (28%)		
45 to 64 years	664 (17%)	81 (12%)	33 (5%)			452 (68%)	98 (15%)		
65 to 84 years	677 (17%)	224 (33%)	30 (4%)			393 (58%)	30 (4%)		
over 84 years	83 (2%)	39 (47%)	10 (12%)			23 (28%)	11 (13%)		

The total of 3901 uropathogens comprised of 3063 ([78.5%) gram negative and 838 (21.5%) gram positive that were isolated from the culture positive samples. *Escherichia coli* was found to be the most dominant bacteria among all isolated cases (37.96%). The second most prevalent isolate was *Klebsiella* spp (25.79%) followed by coagulase negative *Staphylococcus* (10.56%), *Enterococcus* spp (5.06%), *Proteus mirabilis* (4.29%), *Streptococcus* spp (4.14%), *Pseudomonas aeruginosa* (3.96%) and *Acinetobacter* spp (3.96%). There was no statistically significant variation (P>0.05) found among the isolates (Table III).

Table III. Distribution frequency of isolated uropathogens

Bacterial Pathogens	Frequency (%)	χ^2	p value
Gram Negative Isolates	3063 (78.5)		
Klebsiella spp	1008 (25.8)		
Acinetobacter spp	155 (4.0)		
Pseudomonas aeruginosa	155 (4.0)		
Pseudomonas spp	53 (1.4)		
Escherichia coli	1471 (37.7)		
Proteus spp	52 (1.3)	120	0.242
Proteus mirabilis	168 (4.3)		
Salmonella spp	1 (0.0)		
Gram Positive Isolates	838 (21.5)		
Streptococcus spp	162 (4.2)		
Staph CoNs	413 (10.6)		
Staphylococcus aureus	65 (1.7)		
Enterococcus	19 ([5.1)		

Staph CoNs=coagulase-negative *Staphylococcus*

Out of the 3063 gram negative bacteria, 791 (25.82%) were isolated from males and 2272 (74.17%) were from female patients Among the 838 gram positive bacteria, only 150 (17.90%) were isolated from males and 688 (82.1%) were isolated from females. The highest number of gram negative and gram positive uropathogens were found in the female patients of the age group 19-44 years.

Table IV: Frequency distribution of uropathogens between different age groups

Organism	Total	Under 30 days	1 month to 2 years	3 to 6 years	7 to 12 years	13 to 18 years	19 to 44 years	45 to 64 years	65 to 84 years	over 84 years
Klebsiella spp	1008 (25.8)	23 (2.3)	96 (9.5)	42 (4.2)	2 ([2.8)	27 (2.7)	380 (37.7)	182 (18.1)	208 (20.6)	22 (2.2)
Acinetobacter spp	155 (4.0)	2 (1.3)	2 (1.3)	1 (0.6)	0 (0.0)	2 (1.3)	87 (56.1)	34 (21.9)	24 (15.5)	3 (1.9)
P.aeruginosa	155 (4.0)	0 (0.0)	14 (9.0)	7 (4.5)	4 (2.6)	3 (1.9)	28 (18.1)	32 (20.6)	56 (36.1)	1 ([7.1)
Pseudomonas spp	53 (1.4)	0 (0.0)	2 (3.8)	0 (0.0)	2 (3.7)	0 (0.0)	14 (26.4)	14 (26.4)	17 (32.1)	4 (7.5)
Escherichia coli	1471 (37.7)	11 (0.8)	135 (9.2)	90 (6.1)	44 (3.0)	33 (2.2)	589 (40.0)	257 (17.5)	292 (19.9)	20 (1.4)
Proteus spp	52 (1.3)	0 (0.0)	19 (36.5)	17 (32.7)	2 (3.8)	0 (0.0)	3 (5.8)	2 (3.8)	7 (13.5)	2 (3.8)
Proteus mirabilis	168 (4.3)	0 (0.0)	62 (36.9)	55 (32.7)	4 (2.4)	2 (1.2)	20 (11.9)	12 (7.1)	13 (7.7)	0 (0.0)
Streptococcus spp	162 (4.2)	0 (0.0)	1 (0.6)	3 (1.9)	2 (1.2)	9 (5.6)	96 (59.3)	43 (26.5)	8 (4.9)	0 (0.0)
Staph CoNs	413 (10.6)	0 (0.0)	20 (4.8)	20 (4.8)	23 (5.6)	30 (7.3)	263 (63.7)	45 (10.9)	8 (1.9)	4 (1.0)
Staphylococcus aureus	65 (1.7)	2 (3.1)	4 (6.2)	0 (0.0)	3 (4.6)	4 (6.2)	39 (60.0)	7 (10.8)	5 (7.7)	1 (1.5)
Enterococcus spp	198 (5.1)	3 (1.5)	16 (8.1)	10 (5.1)	7 (3.5)	2 (1.0)	69 (34.8)	36 (18.2)	39 (19.7)	16 (8.1)

The highest prevalence rate for the occurrence of different uropathogens and the age group with the highest number of isolates were as follows: *Escherichia coli* age group 19-44 years (40.0%), *Klebsiella* spp age group 19-44 years (37.7%), coagulase-negative *Staphylococcus* (CoNS) 19-44 years (63.7%), *Enterococcus* spp 19-44 years (34.8%), *Proteus mirabilis* 1 month-2 years (36.9%), *Proteus* spp 1 month-2 years (36.5%), *Streptococcus* spp 19-44 years (59.3%), *Pseudomonas aeruginosa* 65-84 years (36.1%), *Pseudomonas* spp 65-84 years (32.1%), *Acinetobacter* spp 19-44 years (56.1%) and *Staphylococcus aureus* in the age category 19-44 years (60.0%)[Table IV].

Antibiotic resistance percentages showed variability among the tested uropathogens. *E.coli* showed highest level of resistance to Amoxicillin/Sulbactam (86% and 91%) among samples tested from males and females. The cephalosporins showed high resistance among both males and females tested with Cephalexin (60%, 39%), Cefuroxime (55%, 32%), Cefotaxime (49%, 30%), Ceftriaxone (50%, 30%), Cefixime (57%, 36%), Cefepime (87%,83%); however, carbapenem Imipenem showed decreased percentages of resistant strains in both males and females tested (33%,26%). *Klebsiella* spp showed a high percentage of resistance to Ampicillin/sulbactam in both males and females tested (89%, 100%). It showed high percentage of resistance with piperacillin/tazobactam (73%, 88%) as well as with cephalosporins Cephalexin (715, 46%), Cefuroxime (615, 35%), Cefotaxime (55%, 28%) and Cefepime (81%, 100%). The lowest percentage of resistant strains was seen with the aminoglycoside Amikacin (14%, 7%). *P. aerugonisa* showed 100% resistance to tested antibiotics Amoxicillin, Ampicillin/Sulbactam, Augmentin, Cephalexin, Cefixime and Nitrofurantoin. It exhibited the lowest percentage of resistance to Gentamicin in both males and females tested (24%, 10%). *Proteus* spp showed a high percentage of resistance to Amoxicillin in both males and females tested (45%, 67%), as well as Augmentin (42%, 47%), Cephalexin (46%, 56%), Nitrofurantoin (42%, 47%) (Table V). In contrast to this, *Proteus mirabilis* showed a relatively low percentage of resistance, with the highest percentage of resistance to the antibiotic nitrofurantoin (82%, 71%). Among the gram positive uropathogens *Enterococcus* spp showed highest levels of resistance with the antibiotics Cephalexin (90%,83%), Gentamicin (84%, 91%), Ciprofloxacin (67%, 48%), Norfloxacin (62%, 52%), Co-trimoxazole (86%,78%) among males and females tested (Table VI).

Table V: Resistant percentages of gram negative uropathogens for antimicrobials

	Klebsiella spp		*Acinetobacter* spp		*Pseudomonas aeruginosa*		*Pseudomonas* spp		*Escherichia coli*		*Proteus* spp		*Proteus mirabilis*	
	% Resistance		% Resistance		% Resistance		% Resistance		% Resistance		% Resistance		% Resistance	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Amoxicillin	237 (91)	770 (82)	17 (71)	138 (52)	4 (100)	4 (100)	2 (100)	1 (0)	288 (76)	1181 (62)	33 (45)	18 (67)	117 (14)	50 (26)
Piperacillin	-	1 (0)	1 (100)	-	69 (23)	66 (8)	17 (59)	30 (10)	-	1 (0)	-	-	-	-
Ampicillin/ Sulbactam	28 (89)	34 (100)	2 (100)	19 (95)	8 (100)	3 (100)	7 (100)	1 (100)	14 (86)	22 (91)	-	1 (100)	-	-
Augmentin	203 (38)	653 (25)	14 (50)	115 (35)	7 (100)	3 (100)	2 (100)	2 (0)	247 (25)	985 (14)	26 (42)	19 (47)	86 (7)	41 (5)
piperacillin/ tazobactam	30 (73)	43 (88)	4 (100)	20 (95)	9 (89)	4 (50)	8 (88)	1 (0)	16 (50)	25 (56)	-	1 (0)	-	-
Cephalexin	206 (71)	660 (46)	14 (93)	118 (92)	5 (100)	4 (100)	3 (67)	-	250 (60)	1002 (39)	28 (46)	18 (56)	89 (13)	41 (15)
Cefuroxime	238 (61)	766 (35)	17 (65)	137 (54)	11 (100)	14 (86)	3 (100)	3 (67)	288 (55)	1177 (32)	33 (18)	19 (37)	116 (6)	50 (4)
Cefotaxime	204 (55)	655 (28)	14 (43)	118 (40)	10 (40)	15 (13)	3 (33)	4 (0)	249 (49)	995 (30)	28 (4)	19 (26)	89 (4)	41 (5)
Ceftazidime	237 (37)	766 (17)	17 (41)	137 (33)	79 (22)	74 (7)	18 (44)	34 (3)	288 (22)	1181 (11)	33 (0)	19 (21)	117 (6)	51 (4)
Ceftrioxone	221 (54)	691 (30)	14 (43)	123 (44)	13 (62)	14 (14)	3 (33)	5 (0)	263 (50)	1068 (30)	31 (3)	19 (16)	98 (3)	44 (7)
Cefoperazone	-	-	-	1 (100)	-	-	-	-	-	1 (0)	-	-	-	-
Cefixime	236 (61)	766 (39)	17 (76)	137 (84)	12 (100)	9 (100)	4 (100)	2 (50)	287 (57)	1175 (36)	32 (13)	18 (28)	117 (9)	50 (6)
Cefepime	31 (81)	41 (100)	4 (100)	20 (100)	8 (100)	5 (80)	7 (100)	1 (100)	15 (87)	23 (83)	-	1 (0)	-	-
Imipenem	31 (23)	44 (27)	4 (100)	21 (81)	9 (78)	4 (50)	8 (75)	1 (0)	15 (33)	23 (26)	-	1 (0)	-	-
Meropenem	23 (35)	28 (68)	4 (100)	14 (93)	2 (50)	3 (67)	3 (67)	-	9 (44)	13 (54)	-	-	-	-
Gentamicin	137 (28)	438 (16)	5 (60)	69 (49)	41 (24)	41 (10)	12 (58)	22 (14)	179 (20)	671 (15)	21 (0)	15 (27)	49 (0)	27 (0)
Tobramycin	-	-	1 (100)	-	69 (36)	67 (10)	17 (71)	29 (17)	-	-	-	-	-	-
Amikacin	237 (14)	767 (7)	16 (31)	137 (19)	79 (27)	76 (8)	19 (58)	34 (12)	286 (7)	1182 (3)	33 (0)	19 (5)	117 (3)	51 (2)
Ciprofloxacin	203 (43)	649 (24)	14 (43)	116 (41)	67 (33)	64 (13)	16 (63)	31 (13)	246 (41)	989 (37)	24 (4)	19 (37)	86 (7)	41 (2)
Norfloxacin	237 (42)	768 (26)	17 (47)	138 (39)	70 (34)	69 (12)	19 (63)	28 (7)	286 (43)	1182 (37)	33 (3)	19 (37)	117 (5)	51 (2)
Co-trimoxazole	202 (34)	623 (24)	14 (21)	118 (21)	5 (100)	4 (50)	3 (33)	-	244 (36)	980 (29)	27 (7)	17 (41)	88 (15)	39 (23)
Nitrofurantoin	237 (43)	763 (31)	17 (100)	138 (91)	5 (100)	4 (100)	2 (100)	1 (0)	288 (14)	2077 (4)	33 (42)	19 (47)	117 (82)	49 (71)

Table VI: Resistant percentages of gram positive uropathogens for antimicrobials.

	Streptococcus spp		Staph CoNs		*Staphylococcus aureus*		*Enterococcus*	
	% Resistance		% Resistance		% Resistance		% Resistance	
	Male	Female	Male	Female	Male	Female	Male	Female
Amoxicillin	14 (14)	146 (3)	44 (61)	367 (19)	9[56]	34 (41)	71 (14)	122 (11)
Augmentin	13 (8)	121 (1)	38 (3)	306 (0)	6[17]	30 (0)	60 (10)	91 (8)
piperacillin/ tazobactam	5 (0)	67 (0)	1 (0)	3 (0)	2[100]	-	70 (10)	117 (9)
Cephalexin	12 (0)	122 (4)	39 (38)	316 (8)	6[50]	29 (7)	63 (90)	93 (83)
Cefuroxime	-	1 (100)	-	4 (0)	1[100]	2 (50)	2 (100)	-
Cefotaxime	8 (0)	106 (1)	37 (38)	292 (9)	6[33]	32 (3)	52 (58)	81 (40)
Ceftazidime	-	1 (0)	1 (100)	2 (0)	7[29]	16 (0)	-	-
Ceftrioxone	2 (0)	5 (0)	-	16 (19)	1[0]	8 (0)	3 (67)	4 (50)
Vancomycin	-	-	-	-	-	-	9 (67)	11 (27)
Imipenem	-	-	-	-	2[50]	-	-	1 (0)
Meropenem	4 (0)	43 (2)	-	3 (0)	2[50]	-	50 (36)	82 (17)
Gentamicin	5 (100)	61 (92)	29 (41)	197 (12)	9[33]	24 (17)	43 (84)	66 (91)
Tobramycin	-	-	-	-	6[67]	13 (23)	-	-
Amikacin	-	13 (69)	5 (0)	45 (0)	10[30]	18 (11)	4 (100)	11 (91)
Ciprofloxacin	13 (15)	116 (28)	39 (33)	312 (12)	12[50]	44 (25)	61 (67)	98 (48)
Norfloxacin	15 (20)	142 (28)	44 (27)	363 (13)	16[44]	47 (23)	73 (62)	109 (52)
Co-trimoxazole	12 (50)	111 (33)	34 (24)	284 (2)	6[17]	27 (4)	51 (86)	78 (78)
Nitrofurantoin	14 (0)	140 (15)	41 (2)	353 (9)	10[10]	33 (3)	72 (18)	116 (21)

4. Discussion

This study provides data which can help determine the prevalence of UTIs, and also the susceptibility profiles of common uropathogens isolated. Among the 3901 culture positive samples, 941 (24.1%) were males and 2960 (75.9%) were females. The high prevalence of UTI in females shown in this study correlates with other findings which revealed that the frequency of UTI in females is higher in comparison to males[19], [20].The higher incidence of urinary tract infections in females is due to the short urethra and its close proximity to the anus [21], [22].

From the adult population, the highest incidence of UTI occurred in the young adults (19-44 years, 41%), followed by the elderly (65-84 years, 17%), adults (45-65 years, 17%). In comparison to this the oldest age category of over 84 years showed a lower incidence of UTI at 2%. This correlates with studies which indicate that the incidence is higher in among the age group 20 to 50 years[23] also increase in UTI is seen after the age of 65. Among children the highest incidence of UTI occurred in infants (1 month-2 years, 10%), in comparison to young children (3-6 years, 6%) and children (7-12 years, 3%). This is similar to studies which indicate that there is a preponderance of UTI in males within the first year of life[24] especially among the uncircumcised[25].

In this study, gram negative bacteria constituted 78.5% of the total isolates while gram positive bacteria constituted 21.5%. *Escherichia coli* was the most common organism isolated with 37.96% of the cases, followed by *Klebsiella* spp [25.79%], coagulase negative *Staphylococcus* (10.56%), *Enterococcus* spp (5.06%), *Proteus mirabilis* (4.29%), *Streptococcus* spp (4.14%), *Pseudomonas aeruginosa* (3.96%) and *Acinetobacter* spp (3.96%). These results correlate with reports from other studies which showed a high incidence of gram-negative bacteria, with the most common organism isolated being *Escherichia coli* [26].These findings does not correlate with reports in which *Proteus* spp[27], *Enterococcus*[28]or *Staphylococcus saprophyticus*[29] was reported as the second most common uropathogen. However it correlates with studies done in India[30], [31],Iran[32] Nepal[33] and Sri Lanka [34] which showed *Escherichia coli* and *Klebsiella* spp among the commonest uropathogens implicated in UTI.

The carbapenems used in the study, meropenem (MRP) and imipenem (IMP) showed resistance percentages amongst the most common isolates. The resistance percentages were as follows: *E.coli* tested against imipenem (males: 33%, females: 26%) and meropenem (males: 44% females55%).*Klebsiella* spp imipenem (males 23% females 27%), and meropenem (males 35%, females 68%). These results are significant in light of the fact that carbapenems are one of the most effective β-lactam antibiotics against ESBL producers. The resistance mechanisms can be due to decreased permeability, production of carbapenem hydrolyzing enzymes called carbapenemases and over-expression of efflux systems [35].

The tested fluoroquinolone in this study Ciprofloxacin showed high resistance among uropathogen *Enterococcus* spp (males 67%, females48%), *E.coli* (males 41%, females 37%), *Klebsiella* spp (males 43%, females 24%). In contrast to this combination antibiotic co-trimoxazole showed relative low resistance percentages with *E.coli* (males 36%, females 29%) and *Klebsiella* spp (males 34%, females 24%). However, *Enterococcus* spp showed a high percentage of resistance with this antibiotic (males 86%, females 78%).

The third generation cephalosporins tested, Cefotaxime percentage resistances were: *E.coli* (male 49%, female 30%), *Kebsiella* spp (male 55%, female 28%), *Enterococcus* spp (male 58%, females 40%). With Ceftriaxone the resistance percentages were: *E.coli* (male 50%, females 30%), *Klebsiella* spp (male 54%, females 30%), *Enterococcus* spp (males 67%, females 50%). The high rates of resistance gives an indication that many of the strains could be possible ESBL producers [36]. Another possible explanation could be that third generation cephalosporins have been used as empirical therapy for a prolonged period of time indiscriminately. Among the leading factors which can lead to emergence of multi drug resistance strains is the inappropriate use of broad-spectrum antibiotics, insufficient hygiene, immunosuppression and prolonged hospital stay [37]. In light of the high level of resistance to carbapenems seen in Enterobacteriaceae, it could be either due to the production of carbapenemases or the combined effect of β-lactams with no intrinsic carbapenemase activity and decreased outer membrane permeability[38]. This study provides valuable data as starting point to monitor the status of antimicrobial resistance as there is a paucity of reports of UTI in Male' city. As such this is the first study conducted to determine the prevalence of UTI, the effect of gender and age as well as resistance profile for the common uropathogens.

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Author's contributions

AM collected, analyzed and interpreted the patient data and wrote the manuscript, MSA was a contributor in writing a part of the manuscript. All authors read and approved the final manuscript.

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References

[1] Gales A. C. and Jones R. N., 'Antimicrobial activity and spectrum of the new glycylcycline, GAR-936 tested against 1,203 recent clinical bacterial isolates', *Diagn. Microbiol. Infect. Dis.*, 2000; 36 (1): 19–36.

[2] Stamm WE, Norrby SR. Urinary tract infections: disease panorama and challenges. *The Journal of infectious diseases.* 2001 Mar 1;183 (Supplement_1): S1-4.

[3] Allegranzi B, Nejad SB, 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. The Lancet. 2011; 377(9761):228-41.

[4] Tandogdu Z, Wagenlehner FM. Global epidemiology of urinary tract infections. *Current opinion in infectious diseases*. 2016; 29(1):73-9.

[5] Warren JW. Catheter-associated urinary tract infections. *International journal of antimicrobial agents*. 200;17(4):299-303.

[6] Griebling TL. Urologic diseases in America project: trends in resource use for urinary tract infections in women. The Journal of urology. 2005; 173(4): 1281-7.

[7] Schaeffer AJ, Rajan N, Cao Q, Anderson BE, Pruden DL, Sensibar J, Duncan JL. Host pathogenesis in urinary tract infections. International journal of antimicrobial agents. 2001 Apr 1;17(4):245-51.

[8] Stamey TA. Recurrent urinary tract infections in female patients: an overview of management and treatment. Reviews of infectious diseases. 1987 Mar 1;9(Supplement_2):S195-208.

[9] Amdekar S, Singh V, Singh DD. Probiotic therapy: immunomodulating approach toward urinary tract infection. Current microbiology. 2011 Nov;63(5):484-90.

[10] Gupta K, Hooton TM, Stamm WE. Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. Annals of internal medicine. 2001 Jul 3;135(1):41-50.

[11] Kahlmeter G. The ECO• SENS Project: a prospective, multinational, multicentre epidemiological survey of the prevalence and antimicrobial susceptibility of urinary tract pathogens—interim report. Journal of Antimicrobial chemotherapy. 2000 Aug 1;46(suppl_1):15-22.

[12] Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, Lynfield R, Maloney M, McAllister-Hollod L, Nadle J, Ray SM. Multistate point-prevalence survey of health care–associated infections. New England Journal of Medicine. 2014 Mar 27;370(13):1198-208.

[13] Stamm WE, Hooton TM. Management of urinary tract infections in adults. New England journal of medicine. 1993 Oct 28;329(18):1328-34.

[14] Moellering Jr RC, Graybill JR, McGowan Jr JE, Corey L. Antimicrobial resistance prevention initiative—an update: proceedings of an expert panel on resistance. The American Journal of Medicine. 2007 Jul 1;120(7):S4-25.

[15] Kumar Y, Sood S, Sharma A, Mani KR. Antibiogram and characterization of resistance markers among Escherichia coli Isolates from urinary tract infections. The Journal of Infection in Developing Countries. 2013 Jul 15;7(07):513-9.

[16] Collee JG, Mackie TJ, McCartney JE. Mackie & McCartney practical medical microbiology. Harcourt Health Sciences; 1996.

[17] Bauer AW. Antibiotic susceptibility testing by a standardized single disc method. Am J clin pathol. 1966;45:149-58.

[18] Dash M, Padhi S, Mohanty I, Panda P, Parida B. Antimicrobial resistance in pathogens causing urinary tract infections in a rural community of Odisha, India. Journal of family & community medicine. 2013 Jan;20(1):20.

[19] Oladeinde BH, Omoregie R, Olley M, Anunibe JA. Urinary tract infection in a rural community of Nigeria. North American journal of medical sciences. 2011 Feb;3(2):75.

[20] Dibua UM, Onyemerela IS, Nweze EI. Perfil da frequência, análise urinária e suscetibilidade de patógenos causando infecções do trato urinário no estado de Enugu, Sudeste da Nigéria. Revista do Instituto de Medicina Tropical de São Paulo. 2014 Feb;56(1):55-9.

[21] Kwok WY, de Kwaadsteniet MC, Harmsen M, van Suijlekom-Smit LW, Schellevis FG, van der Wouden JC. Incidence rates and management of urinary tract infections among children in Dutch general practice: results from a nation-wide registration study. BMC pediatrics. 2006 Dec;6(1):1-7.

[22] Shaifali I, Gupta U, Mahmood SE, Ahmed J. Antibiotic susceptibility patterns of urinary pathogens in female outpatients. North American journal of medical sciences. 2012 Apr;4(4):163.

[23] Schlager T. A., 'Urinary Tract Infections in Infants and Children', *Microbiol. Spectr.*, 2016; 4 (5): 2016.

[24] Arshad M. and Seed P. C., 'Urinary tract infections in the infant', *Clinics in Perinatology*, 2015; 42 (1). W.B. Saunders, 17–28.

[25] Dimitrov TS, Udo EE, Emara M, Awni F, Passadilla R. Etiology and antibiotic susceptibility patterns of community-acquired urinary tract infections in a Kuwait hospital. *Medical principles and Practice.* 2004;13(6):334-9.

[26] Goldstein FW. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections in France. European journal of clinical microbiology and infectious diseases. 2000 Mar;19(2):112-7.

[27] Barišić Z, Babić-Erceg A, Borzić E, Zoranić V, Kaliterna V, Carev M. Urinary tract infections in South Croatia: aetiology and antimicrobial resistance. International journal of antimicrobial agents. 2003 Oct 1;22:61-4.

[28] Haque R, Akter ML, Salam MA. Prevalence and susceptibility of uropathogens: a recent report from a teaching hospital in Bangladesh. BMC research notes. 2015 Dec;8(1):1-5.

[29] Chandrasekhar D, Dollychan A, Roy BM, Cholamughath S, Parambil JC. Prevalence and antibiotic utilization pattern of uropathogens causing community-acquired urinary tract infection in Kerala, India. Journal of basic and clinical physiology and pharmacology. 2018 Nov 1;29(6):671-7.

[30] Kalal BS, Nagaraj S. Urinary tract infections: a retrospective, descriptive study of causative organisms and antimicrobial pattern of samples received for culture, from a tertiary care setting. Germs. 2016 Dec;6(4):132.

[31] Farajnia S, Alikhani MY, Ghotaslou R, Naghili B, Nakhlband A. Causative agents and antimicrobial susceptibilities of urinary tract infections in the northwest of Iran. International Journal of Infectious Diseases. 2009 Mar 1;13(2):140-4.

[32] Gautam S. and Sapkota R. , 'Comparative Study of Isolates Associated With Urinary Tract Infection among Diabetic and Non-Diabetic Patients Attending Tertiary Care Hospital, Chitwan, Nepal', *Int. J. Innov. Sci. Res. Technol.*, 2020; 5 (2): 2020.

[33] Fernando MM, Luke WA, Miththinda JK, Wickramasinghe RD, Sebastiampillai BS, Gunathilake MP, Silva FH, Premaratna R. Extended spectrum beta lactamase producing organisms causing urinary tract infections in Sri Lanka and their antibiotic susceptibility pattern–a hospital based cross sectional study. BMC infectious diseases. 2017 Dec;17(1):1-6.

[34] Fuste E, López-Jiménez L, Segura C, Gainza E, Vinuesa T, Vinas M. Carbapenem-resistance mechanisms of multidrug-resistant Pseudomonas aeruginosa. Journal of medical microbiology. 2013 Sep 1;62(9):1317-25.

[35] Rao SP, Rama PS, Gurushanthappa V, Manipura R, Srinivasan K. Extended-spectrum beta-lactamases producing Escherichia coli and Klebsiella pneumoniaei: a multi-centric study across Karnataka. Journal of laboratory physicians. 2014 Jan;6(01):007-13.

[36] Mukherjee M, Basu S, Mukherjee SK, MajuMder M. Multidrug-resistance and extended spectrum beta-lactamase production in uropathogenic E. coli which were isolated from hospitalized patients in Kolkata, India. Journal of clinical and diagnostic research: JCDR. 2013 Mar;7(3):449.

[37] Nordmann P, Poirel L, Dortet L. Rapid detection of carbapenemase-producing Enterobacteriaceae. Emerging infectious diseases. 2012; 18(9):1503.