Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(12D): 4524-4530 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i12.064

Original Research Article

Evaluate the Sensitivity Pattern and Prevalence of Community-Acquired Multidrug-Resistant Urinary Tract Infections in Hospitalized Patients in Tertiary Care Hospital

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ABSTRACT

Background: A pressing issue that is causing significant concern within medical communities in developing nations is the emergence of multi-drug resistant organisms, presenting formidable challenges in treating infections. Of particular concern are the situation surrounding urinary tract infections (UTIs) in Bangladesh, where physicians are encountering difficulties in treating hospitalized patients due to the ineffectiveness of conventional antibiotic usage, failure of empirical treatments, and the emergence of multi-drug resistant Escherichia coli strains. ***Objectives:*** The main goal of the study was to evaluate the sensitivity pattern and Prevalence of community-acquired multidrug-resistant urinary tract infections in hospitalized patients in a tertiary care hospital. ***Methods:*** It was a cross-sectional study from August 2011 to February 2012, in the Department of Medicine & Department of Gynecology of UAMCH and 100 cases were considered in this study. Detailed information was obtained in each case according to protocol complete history was taken either from the patient or accompanying attendants. A thorough clinical examination was done. Relevant investigation reports were collected. All the information was recorded in the fixed protocol. Collected data was classified, edited, coded, and entered into the computer for statistical analysis by using SPSS version 19.0. ***Results:*** Out of the 100 samples collected for urinary tract infections (UTIs), 45 were identified as multidrug-resistant (MDR) Escherichia coli, while the remaining 55 were non-MDR strains. Among the patients, 79% were female, and the remaining 21% were male, with an average age of 44.85±17.81. Based on the antibiogram test results of the MDR UTI samples, the highest resistance was observed in all 100 samples against beta-lactam and cephalosporin antibiotics. The majority of the age group was 28% 31- 40 years, and 23% were 60 years. 21% were 21-30 years. 12% were 41-50 years age group. This was followed by 44 samples (97.88%) resistant to quinolones, and 12 samples (26.66%) resistant to aztreonam and nitrofurantoin. Mecillinam showed a resistance rate of 20% (9 samples). The most common resistance pattern observed among the MDR UTI patients was against beta-lactam, cephalosporin, and quinolones, accounting for 97.77% of the cases. The highest resistance among the MDR strains was observed against amoxicillin, amoxiclav, cephradine, cefuroxime, cefixime, ceftriaxone, ceftazidime, and nalidixic acid, all showing 100% resistance. ***Conclusion:*** The MDR agents displayed significant resistance against various antibiotics, including amoxicillin, amoxiclav, cephradine, cefuroxime, cefixime, ceftriaxone, ceftazidime, and nalidixic acid, with a resistance rate of 100% for all of them. However, all MDR E. coli strains were found to be sensitive to both imipenem and meropenem. These findings highlight the concerning prevalence of antimicrobial resistance among E. coli strains causing UTIs in patients admitted to a tertiary-care hospital. It underscores the need for regular monitoring of antimicrobial drug resistance and the development of improved guidelines for empirical antibiotic therapy.

Key words: Urinary Tract Infection, Sensitivity Pattern, Escherichia Coli, Multidrug-Resistant.

INTRODUCTION

The most prevalent organisms causing both complicated and uncomplicated UTIs are uropathogenic Escherichia coli, followed by Klebsiella pneumonia, Enterococcus facials, Proteus mirabilis, and group B Streptococcus (GBS) [1]. Mmulti-drug-resistant (MDR) E. coli and K. pneumoniae are increasingly recognized as causative agents of both community-acquired and hospital-acquired UTIs [2, 3]. Although UTIs can affect individuals of any age and sex, female children, women in their reproductive age, and older women are particularly vulnerable to this infections [4]. In

Bangladesh, UTI represents a significant public health concern, resulting in considerable morbidity [5] and healthcare costs [6] due to frequent treatment failures and recurrent infections. Nowadays, a big concern among medical and clinical practitioners is the emerging MDR organisms and their associated complications in developing countries [7]. These conditions make the treatment more challenging and many even threaten the respective patients' lives considering the majority of UTI cases are caused by E coli and the increasing use of antibiotics followed by growing resistance in bacteria and emerging MDR strains it seems necessary to conduct regional research into resistance pattern of the bacteria. The present study seeks to investigate and identify the MDR patterns of uropathogenic E. coli in a tertiary care hospital UAMCH. The results can help adopt more effective strategies for UTI treatment in the region and consequently reduce the increasing number of MDR organisms. The ureters consist of a pair of slender, muscular tubes with thick walls, serving as conduits for transporting urine from the kidneys to the urinary bladder.

Positioned beneath the peritoneum, they closely adhere to the posterior abdominal wall in the upper section and the lateral pelvic wall in the lower section. Each ureter spans approximately 25 cm in length, with the upper half located within the abdomen and the lower half within the pelvis. While the ureter maintains an average diameter of around 3 mm, it experiences slight constriction at three specific points: the pelvic-ureteric junction, the brim of the lesser pelvis, and its passage through the bladder wall. The ureter is composed of (I) the innermost mucous membrane lined by transitional epithelium, (II) middle layer of a well-developed smooth muscle layer and (III) Outer tunica adventitia. The hilum leads into a central recess named the renal sinus. Which is lined by the continuation of the capsule of the kidney and is almost filled in by the pelvis of the kidney and renal vessels? Numerous nipples-like elevations termed the renal papillae indent the wall of the sinus. The renal pelvis extends outside the hilum to become continuous with the ureter. A study conducted in 2012 among 443 suspected UTI patients at a regional medical college hospital in Bangladesh revealed that 43% of patients exhibited significant bacterial growth of uropathogens in their urine samples [8]. Furthermore, a recent study indicated that over 75% of E. coli strains causing UTIs are resistant to third-generation cephalosporins [9].

Existing reports on UTIs in Bangladesh are limited in scope, relying on small sample sizes, targeting specific populations or age groups, analyzing retrospective data from hospital registries, or characterizing convenience samples of bacterial isolates obtained from urine samples of UTI patients [10, 11]. Within the sinus, the pelvis is divided into two to three large branches which are termed major calyces, and each of these again divided into several small branches named minor calyces. There are usually seven to thirteen calyces. Each minor calyx ends in an expansion, which is indented by one to three renal papillae. The urinary bladder is made of smooth muscle, the detrusor muscle and is lined by a loose mucous membrane surfaced both sexes. The ureters pierce the muscle and mucosal walls very obliquely, more than any sphincteric muscular action the valve-like flap of mucosa thus produced is the important factor in preventing reflux of urine when intravesical pressure rises. The ureteric orifices closed by this pressure, except to open rhythmically in response to ureteric peristalsis. Micturition is the process by which the urinary bladder empties when it becomes filled. This involves two main steps. First, the bladder fills progressively until the tension in its walls rises above a threshold level, this elicits the second step, which is a nervous reflex called the micturition reflex that empties the bladder or if this fails at least causes a conscious desire to urinate. Micturition reflex is an autonomic spinal cord reflex it can also be inhibited or facilitated by centers in the cerebral cortex or brain stem. Voluntary urination is usually initiated in the following way. First, a person voluntarily contracts his or her abdominal muscles, which increase the pressure in the bladder and allows extra urine to enter the bladder neck and posterior urethra under pressure, thus stretching their walls This stimulates the stretch receptors, which excites the micturition reflex and simultaneously inhibits the external urethral sphincter Ordinary all the urine was emptied, with rarely more than 5 to 10 ml left in the bladder [12].

AIM AND OBJECTIVES

General:

To describe the prevalence of community-acquired MDR UTI in hospitalized patients and their sensitivity pattern.

Specific:

1. To describe the prevalence of MDR E. coli in community-acquired UTI in patients admitted to a tertiary care hospital**.**

2. To describe the associations between patients' demographic parameters and multi-drug resistance.

MATERIALS AND METHODS

This study was conducted at the Department of Medicine and Department of Gynaecology of UAMCH between August 2011 and February 2012. It was a prospective, cross-sectional study that included a total of 100 patients. These patients were recruited from the emergency and outpatient departments of the Department of Medicine and Department of Gynaecology during the specified study period. The study focused on patients admitted to UAMCH with urinary tract infections (UTIs) who met the clinical criteria and had positive urine routine examination (R/E) and culture results.

Sampling Method

All patients attending UAMCH who met the inclusion and exclusion criteria were considered for

inclusion in the study. Patients with E. coli UTIs were selected for participation.

Inclusion Criteria

The study included community-acquired, culture-positive hospitalized UTI patients with E. coli. The criteria for community-acquired UTI were met if at least one of the following conditions was fulfilled:
a) Positive urine culture for E. coli with 100,000 microorganisms/cm3 involving two species. b) Urine culture with 100,000 colonies/mL of E. coli as a single uropathogenic. Patients over 18 years of age with both complicated and uncomplicated UTIs were included. The study also encompassed cases of relapse, re-infection, and resistance. Exclusion Criteria: Patients who developed an infection within 48 hours of hospitalization, those under 18 years of age, cases with culture-negative results or growth of organisms other than E. coli or multiple organisms, and those who did not provide informed consent were excluded from the study. The collected questionnaires underwent careful checks to identify errors in the data. Data processing involved registration, scheduling, editing, and computerization, preparation of dummy tables, data analysis, and data matching.

Sample Size

The sample size for this study was determined considering the available time and resources. The following statistical formula was employed: n = z'pq/d^2, where: n = desired sample size Z = standard normal deviate, set at 1.96 for a 5% level of significance (corresponding to a 95% confidence level) p = estimated prevalence of the characteristic in the target population q = 1 - p d = desired level of precision, set at 5%
Assuming a prevalence of 15% (p = 0.15) among attending patients with UTIs, using a Z statistic of 1.96 for a 95% confidence level and a precision level of 5%, a sample size of 100 patients was determined. The sample included both male and female patients from the departments of medicine and gynaecology at UAMCH.

Data Collection and Procedure

When a patient with suspected urinary tract infection was admitted as the primary or secondary disease along with a concomitant primary illness, the indoor medical officer and study physician were notified. The study physician conducted a thorough examination of the patient. If the patient met the inclusion and exclusion criteria, they were enrolled in the study and assigned a unique ID. The objectives of the study, risks and benefits, freedom to participate, and confidentiality were explained to the patient, and informed consent was obtained. The study physician completed the prestructured case record form (CRF) for each patient.

Ethical Implications

The study protocol was ethically reviewed and approved by The Ethical Review Committee of UAMC. Institutional clearance was obtained from the principal and hospital director of UAMCH. Written informed consent was obtained from the patients or their relatives, and detailed information about the study was provided in the local language through a printed handout. All aspects, including confidentiality and the right to not participate, were duly considered.

RESULT

This cross-sectional study, conducted at UAMCH from August 2011 to February 2012, aimed to explore and identify multidrug-resistant (MDR) patterns of uropathogenic E. coli in Bangladesh. The findings from this study can provide valuable insights to develop more effective strategies for UTI treatment in the region. By understanding the MDR organisms better, it may be possible to mitigate the rising prevalence of multidrug resistance.

Table 1: Demographical data of the study population (N=100)

Age group	Frequency	Percent (%)
up to 20 years	06	06.0
21-30 years	21	21.0
31-40 years	28	28.0
41-50 years	12	12.0
51-60 years	10	10.0
> 60 years	23	23.0
Mean (SD)	44.85±17.81	
Gender		
Female	79	79.00
Male	21	21.00

The majority of the age group was 28% 31- 40 years, and 23% were 60 years. 21% were 21-30 years. 12% were 41-50 years age group. The majorities 79% were female and 21% were male.

Table-2: Clinical presentation of UTI (N=100)

Clinical presentation	Frequency	Percentage
Asymptomatic	34	34
Abdominal pain	67	67

Urinary burning	92	92
Frequency	94	94
Urgency	80	80
Hesitancy	52	52
Strangury	52	52
> 1 symptoms	94	94

The table shows the clinical presentation of UTL among 100 patients 34% were Asymptomatic. 94% had more than one symptom, like abdominal pain, urinary burning, and frequency. Urgency, Hesitancy, Strangury.

Figure 1 shows the History of extramarital exposure was 11% in UTI.

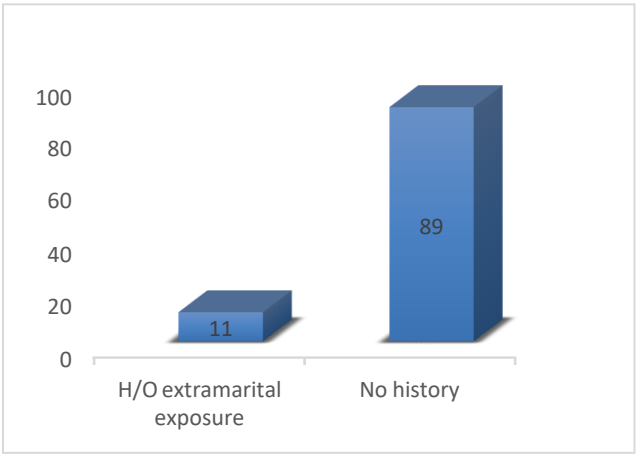

Figure -1: History of extramarital exposure

Table-3: Association of sex with MDR UTI patients

Sex	UTI		Total	P value
	MDR	No MDR		
Male	04(19%)	17(81.0%)	21(100)	0.001
Female	41(51.9%)	38(48.1%)	79(100)	
Total	45	55	100	

Table shows association of sex with MDR in UTI patients, Out of 45 MDR 04(19%) were male and 41(51.9%) were female ($P<0.05$) which is statistically significant.

Figure 2 shows the complicating factors like DM, CKD, HTN Stroke, and HD. All were identically distributed among UTI patients. It also gives an overall picture that more than one complication patient has a higher rate of UTI.

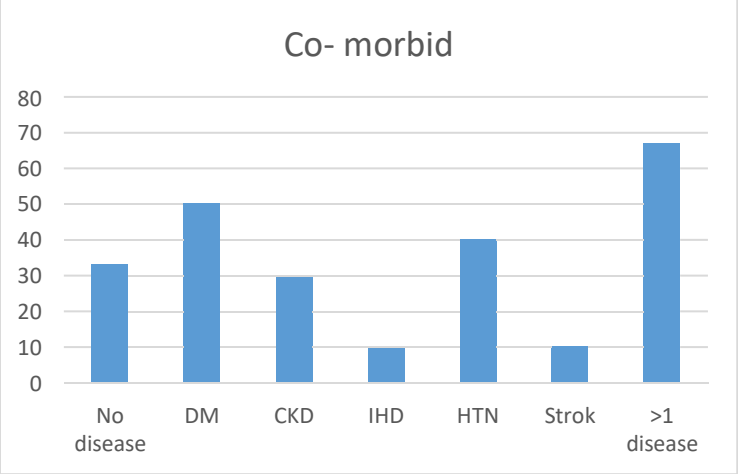

Figure -2: Co-morbidity of the study population (n=100)

Table-4: Individual antibiotic sensitivity pattern of E. coli in UTI and MDR UTI patients

Name of Antibiotic	Antibiotic sensitivity pattern In UTI N=100	Antibiotic sensitivity pattern MDR UTI (N=45)
Amoxycillin	00(00%)	00(00%)

Amoxyclave	25(25%)	00(00%)
Cephradine	02(02%)	00(00%)
Cefuroxime	37(37%)	00(00%)
Cefixime	35(35%)	00(00%)
Ceftriaxone	35(35%)	00(00%)
Ceftazidme	37(37%)	00(00%)
Nalidixic acid	15(15%)	00(00%)
Ciprofloxacin Levofloxacin	39(39%) 37(37%)	01(2.22%) 03(6.67%)
Cotrimoxazole	52(52%)	14(31 11%)
Aztreonam	43(43%)	11(24.44)
Nitrofurantoin	86(86%)	33(73.33%)
Mecillinam	90(90%)	36(80.0%)
Amikacin	86(86%)	38 (84 44%)
Netilmycin	94(94%)	43(95.55%)
Imipenem	100(100%)	45(100%)
Meropenem	100(100%)	45(100%)

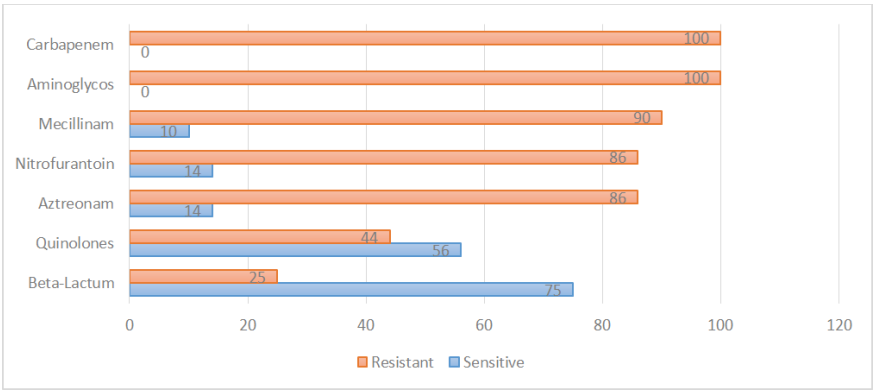

Figure -3: Sensitivity pattern of different groups of antibiotics of E. coli in UTI

Table-5: Groups of antibiotic-resistant MDR UTI by E. coli.

Name of Antibiotic	Frequency	Percent
6 groups of antibiotic	08	17.77%
Bet Cph Qui+Azt+Mec+Nit	02	4.4
Bet +Cph+Qui+Azt+Nit+Cot	06	13.3
5 groups of antibiotic	07	15.55%
Bet +Cph+Qui+Azt+Nit	04	8.9
Bet+Cph+Qui+Mec+Cot	03	6.7
4 groups of antibiotic	20	44.44%
Bet +Cph+Qui+Mec	02	4.4
Bet +Cph+Qun+Cot	18	40.0
3 groups of antibiotic	10	22.22%
Bet+Cph+Mec	01	2.2
Bet +Cph Qun	09	20.0
Total	45	100

Bet Beta-Lactum, Cph Caphalosphonn, Qui Quninolones, Azte Aztreonam, Mec Mecillinam, Nite Nitrofurantoin and Cot-Cotrimoxazole.

Table-6: Comparison of the Resistance to the Antibiotics Used in Treatment of Infections Caused by E. coli in Different Countries

Name of Antibiotic	Drug-resistant Bangladesh in UAMCH in the present study	Drug-resistant Iran in 2010 (%)	Drug-resistant Iran in 2003 (%)	Drug-resistant in different countries %

Amoxycillin	100			
Amoxyclave	75			
Cephradine	98			
Cefuroxime	63	18.7		
Cefixime	65	19.7		
Ceftriaxone	65			
Ceftazidme	63	11.1	14.1	India (3.4), Europe (1.6), Spain (0.4). Hungary (0.3)
Co-trinioxazole	48	81.1	48.1	India (48.3), USA (404) Australia (36)
Aztreonam	57			Canada (0.4)
Nitrofurantoin	14	3.1		USA (11) Australia (5.8)
Mecillinam	10			Europe (1-4). Australia (2.5), India (0.0), USA (0.0)
Nalidixic acid	85	26.6	16.8	India (55.2), USA (29.3)
Ciprofloxacin	61	8.8	6.9	Lebanon (0.0)
Levofloxacin	63			
Amikacin	14	3.3	6.8	Canada (0.4)
Netilmycin	06			
Imipenem	00	0	1.8	USA (11) Australia (5.8)
Meropenum	00			

DISCUSSION

From a microbiologic perspective, urinary tract infection exists when pathogenic microorganisms are detected in the urine, urethra, bladder, kidney, or prostate. In most instances, the growth of 10 organisms per milliliter from a properly collected midstream "clean-catch" urine sample indicates infection. However significant bacteriuria is lacking in some cases of true urinary tract infection. Especially in symptomatic patients, a smaller number of bacteria (102 to 104/MI) may signify infection In urine specimens obtained by suprapubic aspiration or "in-and-out" catheterization and in samples from a patient with an indwelling catheter colony counts of 10 to 10"/ mi generally indicate infection Conversely colony counts of >10/MI of mid-stream urine are occasionally due to specimen contamination, which is especially likely when multiple bacterial species are found [13]. Urinary tract infection is one of the commonest bacterial infections. Around 1 percent of boys and 3 percent of girls will develop urinary tract infections during childhood, and 50 percent of women have a history of at least one episode of urinary tract infection with recurrent infection in a significant minority. Urinary tract infection is rare in men until after the age of 60 when the rising prevalence of prostatic bladder outflow obstruction leads to an increased risk of infection. Asymptomatic bacteriuria is found in about 10 percent of elderly men and in 20 percent of elderly women. Urinary tract infection is responsible for over 25 percent of all community-acquired bacteraemias more than any other source of infection, and accounts for over 40 percent of hospital-acquired infections, often as a result of bladder catheterization [13, 14].

Recent North American studies [15, 16, 17, 18] and studies performed in other countries [19, 20] have not addressed the issues of regional variation in antimicrobial resistance, emerging resistance trends such as multi-drug resistance, and patient demographic associations with antimicrobial resistance in any detail. With regard to patient age, the peak age of incidence of MDR UTI is in the 4th decade. Levels of resistance to Beta-Lactum Cephalosporin, Ciprofloxacin. Nitrofurantoin, appeared relatively consistent irrespective of patient age. Previous studies describing associations between patient age and antimicrobial resistance with which to compare the current data are unavailable. Antibiotic therapy is the first and foremost for UTI, in which the invasive agents are controlled. Therefore, a correlation between the overuse of antimicrobials and the increasing emergence of resistant bacteria seems natural [21, 22]. Worldwide reports of antibiotic-resistant E. coli isolates indicate the unwise and excessive consumption of antimicrobial drugs which in turn has brought about failure in treatment, and consequently concerns about the related issues in all nations including the developed and developing ones. As an example. TMP-SXT was conventionally used for uncomplicated cystitis in most regions, however, due to the resistance to it floroquinolon and cephalosporin took its place and unfortunately, after sometime resistance to these two drugs was also recognized and reported [23, 24]. There are also reports from some countries on E coli strains resistant to beta-lactam, co-trimoxazole and ampicillin [25, 26].

The gradual 4041 increasing resistance of the strains to floroquinolon is another growing concern among clinical practitioners. Since most UTI patients in particularly developing nations, cannot afford the medical visits and lab tests. They recurs empirical therapies which are not effective enough. Studies also show that even in US and developed countries many antibiotics are prescribed and consumed unwisely

[27,28] which results in the emerging resistance [24]. The growing antimicrobial resistance may be due to irrational use of antibiotics and the transfer of resistance genes by transport means including antibiotic-resistant plasmids, bacteriophages, transposons and integrons. Since a plasmid or transposon can carry several resistance indexes, simultaneous resistance to multiple antimicrobial agents may be developed and the result would be MDR organisms. In the present study most frequent pattern of resistant found to Beta-Lactam, Caphalosphorin and Quninolones (97.77%) among the 45 MDR UTI patients. For example, resistance to co-trimaxazole is usually accompanied by resistance to Ampicillin, cephalothin and Tetracycline to alleviate this suffering situation in developing nations clinicians should prescribe antibiotics wisely and sufficiently and there should be periodic supervisions on the drug consumption by the respective organizations [21]. But in our study, MDR percentage is 45% Different rates for MDR from Iran have been reported in 2003 t was 10.9% [29] in Kashan central Iran and 65% in recent years [30, 22]. According to the same table, the level of resistance to co-trimoxazole, tetracycline, ceftazidime, and chloramphenicol in Iran is highest, compared to other nations [22, 31, 30], which might be due to several factors including improper policy in antibiotic prescription against bacterial infections.

In sum, the present finding, suggests that a great percentage of E. coli acts as the main risk for developing MDR UTI. Further research on the characterization of resistant bacteria, their epidemiology and the spread of such bacteria by transport means, and their relationship with prescription and consumption of antibiotics are warranted. Finally, insufficient attention and care about resistance mechanisms, spread and prevalence rates of them may cause presently effective antibiotics to become ineffective in the treatment of bacterial infections and consequently bring about serious challenges in medical practices. Urinary tract infection defines a condition in which the urinary tract is infected with a pathogen causing inflammation it results from the encounter of an uropathogenic and the host. The microorganisms may have particular uropathogenic properties explaining infection in an otherwise normal urinary tract. Usually, non-uropathogenic strains can induce acute infection in cases of urologic abnormalities or when the host's defense mechanisms are impaired, for example in children and elderly people, during pregnancy, in diabetic patients and in immunocompromised patients including patients after renal transplantation. Acute infections of the urinary tract can be subdivided into two general. Anatomic categories: (a) lower tract infection which includes urethritis, prostatitis and cystitis, and (b) upper tract infection which includes acute pyelonephritis, intrarenal and perinephrne abscesses Infections at these vanous sites may occur together or independently and may either be asymptomatic or symptomatic Infection of the urethra and bladder are often considered superficial or mucosal infections, while prostatitis, pyelonephritis and renal suppuration signify tissue invasion. Urinary tract infection is a frequently encountered problem in patients with diabetes. Asymptomatic bacteriuna occurs with a higher frequency One study demonstrated 26% prevalence in diabetic women, compared to 6% in controls [32]. Staphylococcus saprophyticus accounts for 10-15% acute symptomatic UTIs in young females. Enterococci occasionally cause acute uncomplicated cystitis in women [13]. Organisms causing urinary tract infection in domiciliary practice are E coli and other coliforms more than 68% Proteus 12% Klebsiella aerogenes 4% Enterococcus faecalis6% staphylococcus saprophyticus or Epidermidis 10% [33].

Candiduna may signify contamination of the urine specimen, benign saprophytic colonization of the catheter and lower urinary tract infection, or may be indicative of true invasive infection of the upper and /or lower urinary tract [34] Ability to adhere to epithelial cells determines the degree of virulence of the organism. For E. coli these factors include flagellae for motility, aerobactin for iron acquisition in the iron poor environment of the urinary tract, hoemolysis for pore forming and above all, the presence of adhesins on the bacterial fimbriae and on the cell surface. There are two types of E col those with type 1 fimbriae with adhesin known as FimH associated with cystitis and those with type p fimbriae with adhesin known as papG commonly responsible for pyelonephritis. Bacterial adhesins are necessary for attachment of bacteria to the mucous membranes of the perineum and urothelium [33]. Increasing evidence suggests that host genetic factors influence susceptibility to urinary tract infection. A maternal history of urinary tract infection is more often found among women who have experienced recurrent urinary tract infection than among controls. The number and type of receptors on uroepithelium cells to which bacteria may attach are at least in part genetically determined. Many of these structures are components of blood group antigens and are present on both erythrocytes and uroepithelial cells. For example, p-fimbriae mediate attachment of E. coli to p-positive erythrocytes and are found on nearly all strains causing acute uncomplicated pyelonephritis. Conversely, p blood group-negative individuals who lack of this receptor, have a decreased likelihood of pyelonephritis [24].

CONCLUSION

The findings revealed a high prevalence of multidrug-resistant (MDR) UTIs, accounting for 45% of the cases. The peak age of incidence for MDR UTIs was observed in the fourth decade of life, and factors such as sex, diabetes mellitus (DM), and catheterization were identified as significant risk factors for developing MDR UTIs. Among the MDR isolates, a high level of resistance was observed against various antibiotics. Amoxicillin, amoxiclav, cephradine, cefuroxime, cefixime, ceftriaxone, ceftazidime, and nalidixic acid demonstrated complete resistance, with all of them exhibiting 100% resistance.

Recommendation: As antimicrobial resistance patterns are continually evolving properly designed and conducted regional surveillance studies will continue to be essential to ensure the provision of safe and effective empiric therapy. Clearly, the current prevalence of multidrug resistance among urinary tract isolates of E col in this study suggests that monitoring this organism is important and should be a consideration as the guidelines for the empiric treatment of MDR UTIs evolve.

Conflict of interest: None

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