Uropathogenic Bacterial Detection and Surveillance of Antimicrobial Resistance Pattern in Urine Specimens Referred to Al anbar Province

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ABSTRACT
For clinicians treating patients, antimicrobial resistance is becoming a significant concern. This brief study was therefore conducted to find out how common it is for bacterial isolates that are resistant to multiple drugs (MDR), XDR, and PDR, as well as extensively drug-resistant (XDR), in Anbar hospital. The microbiology department cultivated the clinical samples and identified the bacterial strains. The detection of MDR, XDR, and PDR microorganisms was accomplished by analyzing the antibiotic susceptibility profile of various bacterial isolates. 257 children and adult patients from both sexes were included in this study. The total number of urine samples that gave positive bacterial culture results were 114 (44.4%) and the number of samples that gave negative results was 143(55.6%) . The antibiotic susceptibility profile of 114 bacterial strains was studied. 90(78.9) of gram-negative bacteria strains were MDR, (8.9%) (72.2%) XDR, and (18.9%) PDR was isolated. 24 (21.1%) Gram positive bacterial egative bacteria strains were MDR, (33.3%) (54.2%) XDR, and (12.5%) PDR was isolated. To effectively combat the threat of antibiotic resistance, all clinical microbiology laboratories need to closely monitor MDR, XDR, and PDR.

1. Introduction

The conditions that associate between clinical symptoms and detection of pathogenic microorganisms in the urine, urethra, bladder, kidneys, and even in prostate, is described as urinary tract infection (UTI)[1]. Urinary tract infection is an inflammatory response of the urothelium to bacterial invasion that is usually associated with bacteriuria and pyuria[2]. UTI is considered as the most common and costly health-related problem worldwide. The severity of UTI differs by age and gender, as women and elderly are more vulnerable than men and younger individuals[3].The resistance pattern of uropathogens is increasing very rapidly because of the unsorted, insufficient, and incoherent usage of antibiotics. Bacterial urinary tract infection is among the most common community and hospital acquired infections. Therefore, to know the status of the community and hospital-acquired urinary tract infection, antimicrobial susceptibility patterns, and associated factors among urinary tract infection profiles are essential to physicians and health workers to implement appropriate intervention[4]. The major causative organisms for UTI are bacteria organisms. They account for more than 90% of cases. Both Gram-negative and Gram-positive bacteria can cause infection and account for 81–87% and 17–22%, respectively. Urinary tract infection starts with contamination of the periurethral by uropathies residing in the bowel flora colonization[5]. Urethra infection can ascends to the bladder and migrates to the kidney or prostate. The result of host-pathogen complex interactions ultimately determines whether uropathogens are successful in colonization or eliminated. The most common are first rank of *E. coli* and *Klebsiella pneumoniae* [6]. In community- acquired UTI, *Eschirechia coli, Klebsiella pneumoniae* and *Staphylococcus saprophyticus* accounts for 85% and 8% to 20% of outpatients, respectively, across the various regions of the world, and the remaining 5% to 10% of cases are *Staphylococcus aureus* and Gram-negative rods such as *Proteus mirabilis, pseudomonas aeruginosa, Acinetobacter baumannii* and other Enterobacterial family[7]. There are different types of antibiotics routinely prescribed for UTI treatment, but they share similar mechanisms of action like: inhibition of cell wall synthesis, inhibition of protein synthesis, interference with nucleic acid synthesis, interference with signaling pathways involved in biosynthetic processes, and disruption of cell membrane integrity[8].

Many antibiotics and their super generations are used to prevent the UTIs. Unfortunately, several studies indicate that many uropathogens have become resistant to a wide range of antibiotics due to

abuse, overuse, and uncompleted dosages [9]. The resistance to antibiotics could be natural (intrinsic) or due to genetic alterations such as Penicillin G, may holdback from entering the cell of Gram negative bacteria due to the natural composition of the cell wall. Other bacteria may efflux antibiotics before they reach their targets, through enzymes known as translocases. Others microorganisms may naturally lack the target for certain antibiotics, e.g. mycoplasma doesn't produce peptidoglycan which is the main target for penicillin[10]. Other bacteria may cancel the cytotoxic effects of drugs by activating alternative pathways, e.g. aminoglycoside antibiotics are acetylated or phosphorylated by the action of family of enzymes knows as transferases [11].

Antimicrobial resistance (AMR) is described as molecular evolution, as different types of mutations may trigger certain mechanisms allowing microorganisms to thrive within unfavorable conditions. For understanding AMR, scientists proposed a concept known as resistome, which mainly studies the total genetic elements that functions to reverse the toxic effects of antibiotics [12]. Antimicrobial resistance may be caused by random mutations in chromosomal DNA, or via transferring and acquiring new genetic materials between bacteria (by plasmids or transposons) from the same or different genera[13]. The antimicrobial resistance emergence of bacterial uropathogenic has challenged the current therapies to treat and control the spread of infections, and treatment has not improved and does not prevent reinfections [14] . Especially, UTIs caused by resistant bacteria are an important global medical cause of severe infections with increasing rates of morbidity and mortality, and they can also result in prolonged hospital stays and poverty for pediatric patients [15]. Multi drug resistant bacterial uropathogens, that increase the need for the routine application of antimicrobial susceptibility testing to detect the antibiotic of choice as well as the screening of the emerging MDR strains[16] . MDR, extensively drug-resistant (XDR), and pan drug-resistant (PDR) bacteria have been clearly defined according the Center for Disease Control and Prevention (CDC) and CLSI, as MDR, an agent must have gained non susceptibility to at least one antimicrobial agent from three or more categories. Being resistant to at least one agent in all but two or fewer antimicrobial categories is XDR (i.e., bacterial isolates remain susceptible to only one or two antimicrobial categories). Non-susceptibility to any agent in any antimicrobial category is PDR[17]. In Iraq, up to our knowledge, there are limited studies available on the prevalence, antibiotic susceptibility profiles, and associated factors of UTIs in patients and this subject has never been addressed in the study area.

Aim study:

This study aimed to determine distribution of phenotypes of bacteria that causes urinary tract infections in al-anbar province, and the rate of multi drug resistance, extensively drug-resistant, and pan drug-resistant phenotypes in patients with urinary tract infection.

2.Material and methods

2. 1. Patients and controls:

During the period from 1st November 2023 to 25th February 2024, children and adult patients from both genders who were suffering from Urinary tract infections who were attended Ramadi General Teaching Hospitals and private clinics were included in the study. Patients were examined by senior urologists and all inclusion criteria recommended for their cases of UTIs were applied. Midstream urine specimens were taken from each patient following WHO guidelines. Each specimen was examined macroscopically and microscopically. Urine cultures were done within 60 minutes following[18]. Bacterial isolates were identified according to their microscopic appearance, culture characteristics, and biochemical reactions as described by ([19]). Diagnosis was confirmed by Vitek-2 compact system techniques.Mid-stream urine samples were taken from 60 persons who never complain of any urinary infections or complications and their urine samples do not contain any pus cells as controls. Cultures and all investigations that were done for patients were also done for control individuals.

2.2.-Materials:

2.2.1-Culture media:

The following culture media were used :

Table.1:

Series	Medium	Company/origin
1-	MacConkey Agar	**HiMedia, India**
2-	Blood agar base	**HiMedia, India**
3-	Manitol salt agar	**HiMedia, India**
4-	**Muller Hinton agar**	**HiMedia, India**

2.1. 2.Types of antimicrobial Discs and Concentrations

The Antibiotic discs used in present study are described in the following table:

Table 2: Antibiotics Discs

Antibiotics	Symbols	Concentrations µg.
Amikacin	AK	**30**
Amoxycillin- clavulanic acid	AUG	**30**
Cefixime	CFM	**30**
Cefotaxime	CTX	**30**
Ceftriaxone	CTR	**30**
Ciprofloxacin	CIP	**5**
Doxycycline	Dox	**25**
Gentamicin	GN	**10**
Levofloxacin	Lev	**5**
Meropenim	Mem	**30**
Ofloxacin	OFX	**30**
Nitrofurantion	F	**30**
Trimethoprim- sulfamethoxazole	**SXT**	**25**

2.2. Methods:

2.2.1. Preparation of the Culture Media:

All culture media that were used in the present study were prepared following the Manufacturer's instructions .

2.3. Urine specimens:

A-Urine specimens for culture:

The clean catch midstream urine specimens were collected carefully from all patients and controls, especially in females following WHO guidelines (2003). The patients were instructed to clean the periurethral area well with mild detergent (soap) to avoid contamination [18]. The first drops of urine were allowed to pass, then 15 ml of urine were collected in a sterile screw-cap container [18]. A positive diagnosis of urinary tract bacterial infection was based on a colony count 10^5 CFU of single type of organism [18, 19].

B-Microscopic examination of urine specimen:

After collection of urine, about 10 ml of urine sample were transferred to clean centrifuge tube and centrifuged at 4000 rpm for 5 minutes. One drop of sediment was dropped on a clean slide and examined under microscopic using lens (40 x) to detect the microscopic findings like RBCs**,** Pus cells (WBC), Crystals, Casts, Fungi, Bacteria and Epithelial . PH of urine, albumin, bile pigments, urobilinogen, sugar and specific gravity were estimated using specific strips for urine [21] .

2.4. Isolation and identification of Bacteria:

2.4. 1.Urine Culture:

Quantitative urine culture was performed. Obtained urine samples were cultured directly onto the prepared media (MacConkey and Blood agar plates) by direct streaking method using a calibrated bacteriological loop measuring 0.001 ml of urine, the inoculated plates were incubated aerobically at 37°C for overnight then examined for growth, if no growth was detected, plates were re-incubated for another 24 hours before discarding as negative cultures [18].

2.4.2. Identification of microorganisms:

A single colony was taken from each primary positive culture and its identification depended on the morphology properties (Colony size, shape, color and nature of pigments, translucency, edge, elevation, and texture). Gram staining of the bacterial smear, specific biochemical tests were done to reach the final identification, colonial morphology on culture media was studied after 24 hours incubation at 37°C according to [19].

2.5. Biochemical tests:

2.5.1. Oxidase Test:

A piece of filter paper was saturated with oxidase reagent (Tetramethyl Paraphenylene Diamine Dihydrochloride) then a colony of organism was spread onto the filter paper. When the color of the colony turned from rose to purple, oxidase test was considerd positive [19].

2.5.2.Catalase test:

Sufficient amount was picked up from cultured colonies with a clean sterile loop and transferred on a surface of clean and dry glass slide, then drops of 3% hydrogen peroxide solution were added, the production of gas bubbles almost immediately indicates a positive result [19].

2.5.3. Novobiocin sensitivity test:

Novobiocin disks were used to distinguish *Staphylococcus saprophyticus* which is resistant from *Staphylococcus epidermidis* which is (sensitive). The test bacterium was inoculated on brain-heart infusion broth overnight, then the inoculum was streaked on Muller Hinton agar and incubated at 37 ^{o}C overnight [18.]

2.6.Isolation and identification by VITEK2 compact System

This test was used to classify various groups of species as follows: (Gram Negative) fermenting and non-fermenting bacilli (Gram Positive) cocci and non-spore forming bacilli, yeasts and yeast-like species [22;23].

2.7. Antimicrobial Susceptibility Test

Thirteen types of antibiotics were used in present study in table 4 . The antimicrobial susceptibility test was carried out depending on the method of diffusion of the disc as Kirby Bauer *et al.* described (1966)[24] as follow:

1-Three – Five Pure Fresh culture isolated Colonies have been suspended in 5 ml of physiological solution with mixed appropriates and turbidity resulting in an, optical density equal to 0.5 McFarland levels (equivalent to 1.5 X10^{8} cell / ml).

2-A sterile Cotton swab was dipped into the suspension and then rotated several times firmly above the broth point on the inside wall of the tube to avoid excess inoculum from the cotton swab.

3-The surfaces of the Mueller Hinton agar plate were streaked with cotton dipping swab. The petri dishes were; allowed to dry at room temperature around 10-20 min before using the antibiotic disks.

4-The antibiotic discs were distributed onto the inoculated agar plate surface.

Discs were gently squeezed by sterilized forceps to touch the agar surface.

5-Following the dispensation of antibiotic disks plates were inverted and placed at temperature 37 C0 for 18-24 hr in an incubator.

6-A transparent ruler was used to measure the diameter growth inhibition zones on the plates around the disks. The results compared which were provided with the CLSI protocol (2023)[25].

Agar disk diffusion procedure included inoculating agar plates with a standardized test microorganism inoculum. Filter paper disks (about 6 mm in diameter) which contain the test compound at the desired concentration are then placed on the surface of the agar. Under ideal conditions the Petri dishes are incubated. Generally, the antimicrobial agent spreads into the agar inhibiting germination and growth of the test microorganism and then measuring the diameters of inhibition growth zones by CLSI[25] standard.

Statistical analysis

The collected data were coded, entered, presented, and analyzed by computer using the available data base software program statistical package of IBM SPSS-29 (IBM Statistical Packages for Social Sciences- version 29, Chicago, IL, USA). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (χ^2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

Result and Discussion

Urinary tract infections are common, and they are caused by a variety of bacteria that ascend into the urinary tract from the periurethral region .Urinary tract infections (UTIs) in children are very common. They are often associated with a high risk of sepsis and death. In recent years, antibiotic-resistant

uropathogens *E coli, Klebsiella pneumoniae Enterococcus faecium, Staphylococcus saprophyticus, Staphylococcus aureus, , Acinetobacter baumannii, Pseudomonas aeruginosa,* and *proteus mirabilis* are increasingly encountered in UTIs. These bacteria, usually multidrug-resistance (MDR), extensive drug-resistance (XDR), pandrug-resistance (PDR), , represent a global threat for the management of adult and children UTIs [26].

3.1. Number and gender of patients and control groups:

Two hundred fifty seven (257) children and adult patients from both sexes were included in this study. The total number of urine samples that gave positive bacterial culture results was 114(44.4%) and the number of samples that gave negative results was 143(55.6%) . Twenty one 21 (18.4%) patients that gave positive results, were males and 93 (81.6%) were females. Sixty (60) adult individuals were presented as control groups, all Urine specimens from both sexes showed non significant bacteriuria (Negative bacteriuria) (Table 4.1). The age of patients and controls is ranged from 17- 60 years old.

Table 3.1:- Number and gender of patients and control groups.

Groups	**Male No. %**	**Female No.%**	**Total No.%**	**P value**
Positive culture Growth	21(18.4)	93(81.6)	114(44.4)	**0.518**
Growth Negative culture	31(21.7)	112(78.3)	143(55.6)	
Total	52 (20.2)	205 (79.8)	257(100)	
***Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.005 level.**				

The present study showed that female patients were affected more than males, due to the anatomic feature of urethra since it is shorter in females and can be exposed to ascending infection more than males. These results are in agreement with many investigators [28, 29].

3.2. Distribution of patients according to the age groups and gender in positive culture patients:

One hundred fourteen (114) patients of positive Urine culture were included four groups ranged from 1-60 years old. Females showed the highest ratio in all age groups, particularly groups (17-27) and (28-38) years old (Table 3.2). Regarding to Majority of patients were females (76.7%) .Young and adult females were exposed to UTI more than males because of higher sexual activity which predispose infection due to hormones, contraceptives and contamination which may increase exposure to UTI [29] .A diaphragm used with spermicide or without spermicide, changes the vaginal enviroment, the same occurs in menopause, disappearance of the previously predominant *Lactobacilli* from the vaginal microflora and a rise in pH [30]These results are in agreement with the findings of [29, 30, 31].

Table 3.2.Distribution of patients according to the age groups and genders in positive culture groups.

Age groups	**Males No. (%)**	**Females No.(%)**	**Total No.(%)**	**P value**
<20	8(29.6)	19(70.4)	27(23.6)	**0.003**
20-29	8(22.2)	28 (77.8)	36(31.5)	
30-39	9(31.0)	20(69.0)	29(25.1)	
40-49	6(40.0)	9(60.0)	15(13.1)	
50-59	4(57.1)	3(42.9)	7(6.5)	
Total	35(30.7)	79(69.3)	114(100%)	
***Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.**				

3.3.Bacterial types in Urine positive culture patients:

Escherichia coli took the first rank of isolation (38.6%) from urine specimens of UTI patients followed by *Klebsiella pneumonia* (26.3%) while *Staphylococcus saprophyticus* became next (12.3%) . Other

types of bacteria showed lower rates of isolations, the percentage for each was *Staphylococcus aureus* (8.8%), *Proteus mirabils* (5.3%), *Pseudomonas aeruginosa* (4.4%), *Acinetobacter baumannii(2.6%) Enterococcus faecalis* (1.7%) respectively, (P<0.01) as Table3.3. and figure1. Regarding types of bacteria isolated from urine , the present study showed that *Escherichia coli* is the predominant causative bacteria, due to easy contamination with fecal contents like *E. coli* which account above 1×10^5 cell / gram of stool [32]. Uropathogenic *E. coli* serotypes are a specific subset of extra intestinal pathogenic *E. coli*; that is, not all strains of *E. coli* are capable of causing UTI .Also Some strains of *E coli* show attraction to uroepithelium uropathogenesis factors as Virulence factors synthesized by pathogens include fimbriae, toxins, flagella, iron acquisition systems, and proteins that function in microbial invasion and Uropathogenic *E coli* strains possess an impressive repertoire of adhesions that enable them to aggregate and adhere to host cellular surfaces [33]. Almost similar results were reported by [29, 34]. *Klebsiella pneumonia* is the second important pathogen because these bacteria are among the intestinal flora. The chance of infection of the urinary system increases because it posses a protective capsule which makes it more resistant to body immune defenses specially phagocytosis [35]. Similar results were reported by [36]. The third and fourth bacterial pathogens isolated in the present study were *Staphylococci, saprophyticus* and *aureus* .*Staphylococcus saprophyticus* was reported to be an important cause to UTI in sexual active young women because active sexual intercourse of women who used Exogenous Hormones leads to decrease immune system [28]. These results are in agreement with findings of [37, 38] .*Staphylococcus aureus* is well known that *Staphylococcus aureus* containing micro capsule which acts as anti phagocytic action and predispose the adhesion to the host tissue, in addition to many other virulent factors [32]. *Pseudomonas aeruginosa, proteus mirabilis and enterococcus faecalis* were found to be the causative agents of few cases, which is supported by the results reported by[39]. This might be attributed to the nature of this organism as nosocomial pathogen [40].

Table 3.3: Bacterial types in Urine positive culture specimens from patients.

No.	Types of organisms	No.(%)
1	***Escherichia coli***	**44 (38.6)**
2	***Klebsiella pneumonia***	**30 (26.3)**
3	***Staphylococcus saprophyticus***	**14 (12.3)**
4	**Staphylococcus aureus**	**10 (8.8)**
5	***Proteus mirabilis***	**6 (5.3)**
6	***Pseudomonas aeruginosa***	**5(4.4)**
7	***Acinetobacter baumannii***	**3(2.6)**
8	***Enterococcus faecalis***	**2 (1.7)**
	Totals	**114 (100)**

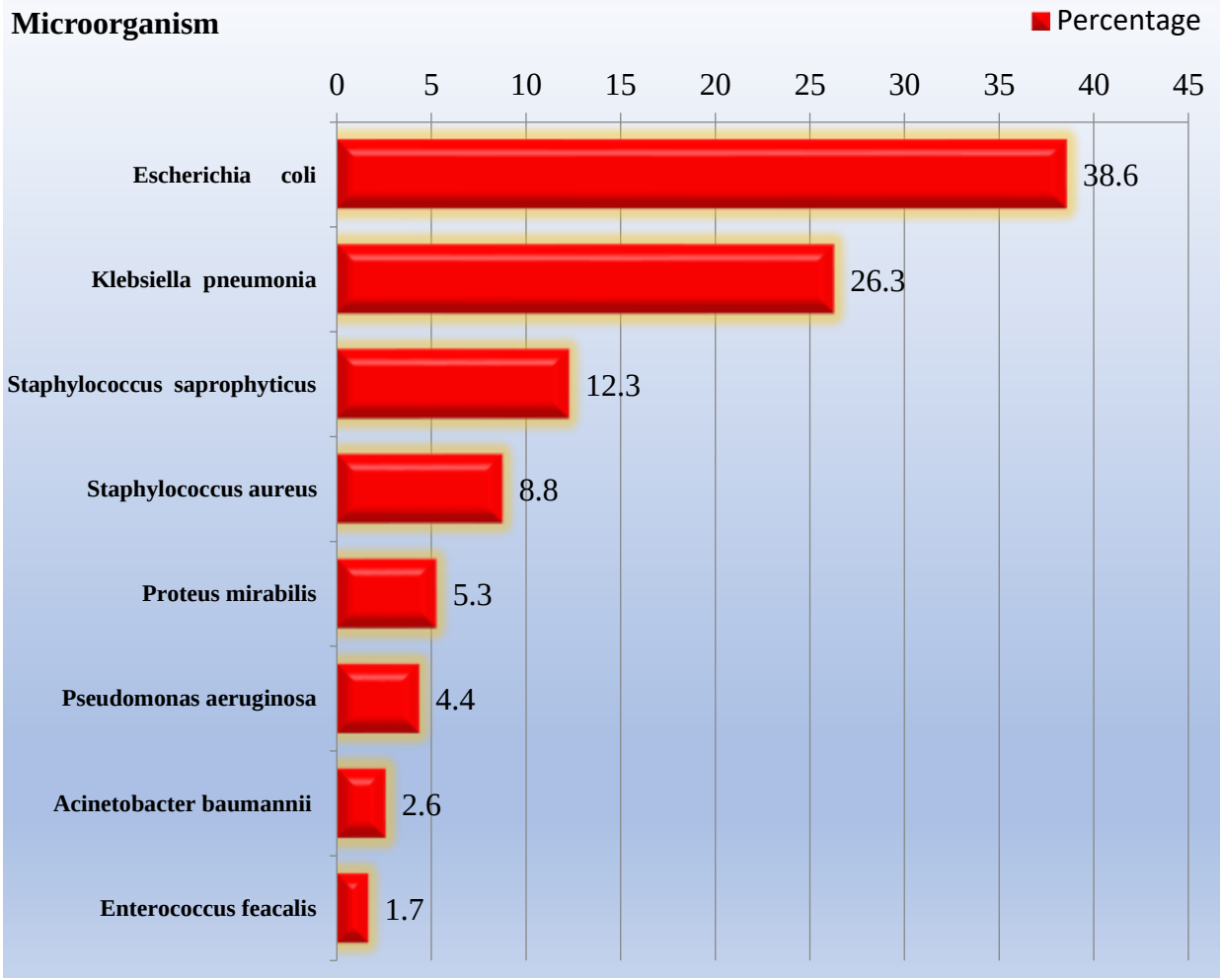

Fig.1: The percentage distribution of bacterial types in Urine positive culture patients

3.4.Distribution of the antibiotic sensitivity according to gram negative bacterial isolates

Urinary tract infection (UTI) is one of the most important causes of morbidity inthe general population, and is the second most common cause of hospital visits. The common etiologic agents of UTI include enterobacteriaceae like such organisms, specifically, *E coli*, *Klebsiella pneumoniae* as well as Gram positive organisms like *Staphylococcus sp.* and *Enterococci sp.*, *beside*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*. Urinary tract infections (UTI) are caused by pathogenic invasion of the urinary tract which leads to an inflammatory responseof the uroepithelium. Proliferation of bacteria in the urinary tract is the cause of urinary tract infection[41]. UTIs are a significant cause of morbidity in infant boys, older men, and females [42] .With the increasing trends of multidrug resistance (MDR) and pandrug resistance (PDR)in UTI isolates, novel and clinically more relevant resistance categories were proposed to be used in UTIs [43]. The etiological distribution and antibiotic susceptibility surveillance are of great importance for empirical antimicrobialtherapy. In the present study, the results showed prevalence of gram-negative bacteria 67/98 (68.4%) with *E coli* isolates 40/90 (48.9%) are resistant to Amikacin (27.3%), Gentamycin (50%), Levofloxacin, (56.8%), Ciprofloxacin , (61.4%), Ofloxacin (52.6%), Norfloxacin (40.9%), Nitrofurantoin (31.8%), Ceftriaxone and Trimethoprim-Sulfamethoxazole (90.9%), Cefotaxime and cefixime (93.2%), Meropenem(45.5%) and doxycycline (79.5%). According to *Klebsiella pneumoniae* 30/90 (33.3%) are resistant to Amikacin(30%), Gentamycin (40%), Levofloxacin, (53.3%), Ciprofloxacin, (58.7%), Ofloxacin and Norfloxacin (66.7%) Nitrofurantoin (46.7%), , Ceftriaxone (80%) , Cefotaxime (82.1%), Cefixime (86.7%) .Trimethoprim-Sulfameth-oxazole are resistant with (70%), Meropenem (63.3%) and doxy cyclin(40%).*Proteus mirabilis* 6/90 (6.7%) resistant to Amikacin Ciprofloxacin, Levofloxacin, Norfloxacin, Trimethoprim-Sulfamethoxazole and Meropenem are (33.3%). While

Gentamycin, Ofloxacin and Nitrofurantoin are (16.7%), Ceftriaxone and doxy cyclin are (50%), Cefotaxime and Cefixime (66.7%) . *Pseudomonas aeruginosa* 5/90 (5.6%) are resistant to Amikacin, Norfloxacin and Doxycycline are (80 %). The Gentamycin (100%), while Levofloxacin Ofloxacin and Trimethoprim-Sulfamethoxazole (60%). Ciprofloxacin, Cefotaxime, Cefixime and Nitrofurantoin (40%).

Acinetobacter baumanii 3/90 (3.3%) are resistant to Amikacin (90.9%), Gentamycin Nitrofurantoin, Ceftriaxone, Cefotaxime, cefixime and Trimethoprim-Sulfamethoxazole are (100%). Levofloxacin, (56.8%), Ciprofloxacin, Ofloxacin, Norfloxacin, Meropenem and doxy cyclin (33.3%). *Enterococcus faecalis* are resistant to Amikacin, Gentamycin, Ciprofloxacin, Norfloxacin Ceftriaxone, Cefotaxime, cefixime (50%). While Nitrofurantoin, Trimethoprim-Sulfamethoxazole Levofloxacin Ofloxacin, Meropenem and doxycyclin are (100%).All results are showed in table 4. In the present study, showed resistance to commonly used antibiotics in table 4. This high resistance of antibiotics is attributable partly to self-medication, which is very common in the community and partly due to treatment of patients by the physicians without proper diagnosis in the laboratory[44].These finding are similar with [41,45].

Table 4.Distribution of the antibiotic sensitivity according to gram negative bacterial isolates

Total Gram negative bacteria = 90 (78.9%)						
Antibiotics	*E coli* Total no.& S /R 44/90 (48.9%)	*K. pneumoniae* Total no.& S /R 30/90 (33.3%)	*Proteus mirabilis* Total no.& S /R 6/90 (6.7%)	*P. aeruginosa* Total no.& S /R 5/90 (5.6%)	*A. baumanni* Total no.& S /R 3/90 (3.3%)	*E. Faecalis* Total no.& S /R 2/90 (2.2%)
Ak	S=32 (72.7%) R=12 (27.3%)	S=18 (60 %) R=12(30 %)	S= 4(66.7%) R= 2 (33.3%)	S=1(20%) R=4 (80%)	S=0 (9.1%) R=3(90.9%)	S= 1(50 %) R=1 (50 %)
Gen	S=22 (50%) R=22(50%)	S=18(60%) R=12(40%)	S= 5(83.3 %) R= 1 (16.7%)	S=0 (0%) R=5(100%)	S=1 (0%) R=2 (100%)	S= 1(50%) R= 1 (50 %)
Lev	S=19 (43.2%) R=25 (56.8%)	S=14(46.7%) R=16 (53. 3%)	S= 4(66.7 %) R= 2(33.3 %)	S=2 (40%) R=3 (60%)	S=2(66.7%) R=1(33.3%)	S= 2(100 %) R= 0 (00%)
Cip	S=17 (38.6%) R=27 (61.4%)	S=13(43.3%) R=17 (56.7%)	S= 4(66.7 %) R= 2(33.3 %)	S=3(60%) R=2(40%)	S=2(66.7%) R=1(33.3%)	S= 1(50%) R=1 (50 %)
Ofx	S=26 (47.4%) R=18 (52.6%)	S=10(33.3%) R=20(66.7%)	S=5 (83.3%) R= 1 (16.7%)	S=2 (40%) R=3 (60%)	S=2 (66.7%) R=1(33.3%)	S= 2(100 %) R= 0 (0%)
Nor	S=23(59.1%) R=21 (40.9%)	S=10(33.3%) R=20(66.7%)	S= 4(66.7 %) R= 2(33.3 %)	S=1 (20%) R=4 (80%)	S=2(66.7%) R=1(33.3%)	S= 1(50%) R=1(50 %)
F	S=30 (68.2%) R=14 (31.8%)	S=16 (53. 3%) R=14(46.7%)	S= 5(83.3 %) R= 1 (16.7%)	S=3 (60%) R=2 (40%)	S= 0 (0) R=3 (100%)	S= 0(0) R= 2(100 %)
CRO	S=4 (90.9%) R=40 (9.1%)	S=6(20%) R=24 (80%)	S= 3(50%) R= 3 (50%)	S=1 (20%) R=4 (40%)	S= 0 (0%) R=3 (100%)	S=1 (50 %) R= 1 (50%)

CTX	S=3 (6.8%) R=41 (93.2%)	S=5 (17.9%) R=25(82.1%)	S=2 (33.3 %) R= 4(67.7 %)	S=1 (20%) R=4 (40%)	S= 0 (0%) R=3 (100%)	S= 1(50%) R=1(50 %)
CFM	S S=3 (6.8%) R=41 (93.2%)	S=4 (13.3%) R=26(86.7%)	S=2 (33.3 %) R= 4(67.7 %)	S=1 (20%) R=4 (40%)	S=0 (0%) R=3 (100%)	S= 1(50%) R=1 (50 %)
SXT	S=4(9.1%) R=40 (90.9%)	S=9 (30%) R=21(70%)	S= 4(66.7 %) R= 2(33.3 %)	S=2(40%) R=3(60%)	S= 0(0%) R=3(100%)	S= 2(100 %) R= 0 (0%)
Mem	S=24(54.5%) R=20 (45.5%)	S=11 (36.7%) R=19 (63.3%)	S= 4(66.7 %) R= 2(33.3 %)	S=3 (60%) R=2 (40%)	S=2(66.7%) R=1(33.3%)	S= 2(100 %) R= 0 (0)
Dox	S=9(20.5%) R=35 (79.5%)	S=18 (60%) R=12 (40%)	S= 3(50%) R= 3 (50 %)	S=1 (20 %) R= 4 (80 %)	S=2(66.7%) R=1(33.3%)	S= 2(100 %) R= 0 (0 %)
P value	**0.0001***	**0.0001***	**0.721**	**0.731**	**-**	**-**
***Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.**						

3.5.Distribution of the antibiotic sensitivity according to gram positive bacterial isolates

The present study to antibiotic resistant to *Staphylococcus saprophyticus* and *Staphylococcus aureus* 24/90 (21.1%) were showed *Staphylococcus saprophyticus* 14/24 (58.3%) are resistant to Amikacin and Trimethoprim-Sulfamethoxazole are (64.3%). Gentamycin and Norfloxacin are (42.9%) . Levofloxacin and Ofloxacin are (28.6%), Ciprofloxacin (35.7%), Cefoxitin (78.6%.), chloramphenicol (50%), Nitrofurantoin(57.1)and Doxycycline (21.4%) . The *Staphylococcus aureus* 10/24 (41.6%) are resistant to Cefoxitin (100%), Amikacin and Ciprofloxacin are (80%). The next Gentamycin and Ofloxacin and are (60%) followed Levofloxacin Trimethoprim-Sulfamethoxazole and chloramphenicol are (70%) .while Norfloxacin and Doxycycline (50%) and Nitrofurantoin are (40%). The result showed in table 4.

UTIs are quite common in community settings. However, many patients refuse to seek medical attention because of the social stigma associated with UTIs. In urban areas, The high cost of medical consultation in doctors' clinics and long queues during medical consultations, discouraging many patients who opt for self-medication, largely responsible for the selection of resistant strains. Also, the lack of education and the uncontrolled sale of counterfeit or substandard antibiotics are two additional factors favouring the emergence and dissemination of bacterial resistance in urban UTIs [46]. These finding are agreement with [47,48,49].

Table 3.4. Distribution of the antibiotic sensitivity according to gram positive bacterial isolates

Total Gram positive bacteria = 24 (21.1%)				
Antibiotics	*S. saprophyticus* 14/24 (58.3%)		*S.aureus* 10/24(41.6%)	
	S	R	S	R
Amikacin	5 (35.7%)	9 (64.3%)	2 (20%)	8(80%)
Gentamycin	8 (57.1%)	6 (42.9%)	4 (40%)	6(60%)
Levofloxacin	10 (71.4%)	4 (28.6%)	3 (30%)	7(70%)
Ciprofloxacin	9 (64.3%)	5(35.7%)	2 (20%)	8(80%)
Ofloxacin	10 (71.4%)	4 (28.6%)	4 (40%)	6(60%)
Norfloxacin	8 (57.1%)	6 (42.9%)	5(50%)	5 (50%)
Cefoxitin	3 (21.4%)	11 (78.6%)	0 (0)	10 (100%)
Chloramphenicol	7(50%)	7(50%)	3(30%)	7 (70%)

Trimethoprim-Sulfamethoxazole	5(35.7%)	9(64.3%)	3(30%)	7(70%)
Nitrofurantion	6(42.9%)	8 (57.1%)	6(60%)	4(40%)
Doxycycline	11 (78.6%)	3(21.4%)	5(50%)	5(50%)
P value	***0.015**		**0.236**	
***Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.**				

3.5 .Distribution of MDR, XDR and PDR according to bacterial isolates

Distribution of gram negative and gram positive bacteria of isolation were 114/257 (44.4%) from total positive culture samples .The present study showed non-susceptibility rates for commonly used antibiotics per pathogen are given in Table 5 includes *E coli* (38.6%) with XDR (68.2%), PDR(25%) and MDR (26.3%) phenotypes, followed *K. pneumoniae* (26.3%) was highly non- susceptible (26.3%) almost antimicrobial agents tested, and was exclusively classified as XDR(90%), (97%), MDR(35.7%) and PDR (14.3%) phenotypes. None of the other pathogens were non- susceptible of *Staphylococcus saprophyticus* (12.3%) to antimicrobial agents tested with (50.0 %) XDR , (35.7%) MDR and (14.3%)PDR phenotypes, the next frequent pathogen in *Staphylococcus aureus*(8.8%) classed as XDR, MDR and PDR were (60%) (30%) and (10% receptively . The lower non susceptibility to antimicrobial agents tested was *Proteus mirabilis*(5.3%) was non- susceptible to antimicrobial agents tested, included (50, 33.3, 16.7) % for MDR, XDR followed *Pseudomonas aeruginosa* with (75, 25, 0)%to XDR, PDR and MDR receptively phenotypes .Next pathogen, *Acinetobacter baumanni* (2.6%) no susceptibility to antimicrobial agents tested were (67.3, 33.3, 0) % receptively, and *Enterococcus feacalis* (1.7%) with (50%) XDR, MDR and non PDR phenotypes receptively showed in table 3.5.

Table 3.5. Distribution of MDR, XDR and PDR according to bacterial isolates

Bacterial types	**Total no.(%)**	**MDR no. (%)**	**XDR no. (%)**	**PDR no.(%)**
E coli	44/90 (38.6%)	3 (6.8%)	30 (68.2%)	11(25%)
Klebsiella .pneumoniae	30/90 (26.3%)	1(3.3%)	27(90%)	2 (6.7%)
Proteus mirabilis	6/90 (5.3%)	3(50%)	2(33.3%)	1(16.7%)
Pseudomonas aeruginosa	5/90 (4.4%)	0 (0)	4(75%)	1(25%)
Acinetobacter baumanni	3/90 (2.6%)	0 (0)	1(33.3%)	2(66.7%)
Enterococcus feacalis	2/90 (1.7%)	1(50%)	1(50%)	0 (0)
Staphylococcus saprophyticus	14/24 (58.3%)	5(35.7%)	7(50%)	2(14.3%)
Staphylococcus aureus	10/24 (41.7%)	3(30%)	6(60%)	1(10%)
P value	**-**	**0.002***	**0.039***	**0.146**
***Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.**				

The increased incidence of drug resistant strains observed in present study may be because the most patients get different antibiotics from general practitioners or due to over-the- counter sell of antibiotics often in improper dose. The limitation of this study is that this is a single center study for only three-month period in hospital in Ramadi teaching hospital. To reflect the trend of infections caused by MDR, XDR and PDR strains of bacteria in the region, a multicenterstudy involving all types of healthcare setups for a minimumperiod of one year would be needed[50].

The limited of data regarding to antibiotic resistance in health care setup not only in Anbar province in Iraq country but also worldwide. Unless and until multidrug resistant organisms are detected and their incidence is known, the strategies for their control cannotbe adopted properly in healthcare setup. Hence, detection, prevention of transmission of multi antibiotic resistance by following infectioncontrol practices, antimicrobial surveillance, and management need of the hour. Misuse and overuse of

antibiotics, over-the-counter selling of antibiotics without prescription to common people, must be stopped by strict implementations of rules and regulations. The results are agreement with[51,52,53] .

Conclusion

This study describes for the first time the resistance phenotypes MDR, XDR and PDR index in Anbar province west of Iraq. The prevalence of UTIs was high with a strong involvement of the uropathogens *E. coli, K. pneumoniae, proteus mirabilis, Pseudomona aeruginosa, Acinetobacter baumanni, Enterococcus spp. , S. aureus* and *coagulase negative staphylococci.* Neonates, infants and adult both of male and female gender were predominantly affected by UTIs. The study also showed that the majority of (20-40) years old are the most UTIs and non-susceptible to standard antibiotic therapy. However, the presence high percentage of MDR, XDR, and PDR phenotypes in the population should alert health authorities to the need to set up a national surveillance system for antimicrobial resistance in anbar province and Iraq country. 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.

Reference

[1] 1.Sammon JD, Sharma P, Rahbar H, Roghmann F, Ghani KR, Sukumar S, et al. Predictors of admission in patients presenting to the emergency department with urinary tract infection. World J Urol 2013;32:813–9.

[2] 2.Nabeel Ahmed Rajab, Shihab A. Lafi and Neama Hamad Hassan(2014): A Study of some Immune Factors in Patients with Bacterial Urinary Tract Infections Caused by Aerobic Bacteria. J. of University of Anbar for pure science : Vol.8:NO.3: 2014

[3] 3.Taylor J, Hafner Marco, Yerushalmi Erez, Smith Richard, Bellasio Jacopo, Var- davas Raffaele, et al. Estimating the economic costs of antimicrobial resistance: model and results. The Wellcome Trust; 2014. p. 49.

[4] 4.Berhanu Adugna, Bekele Sharew, and Mohabaw Jemal (2012): Bacterial Profile, Antimicrobial Susceptibility Pattern, and Associated Factors of Community- and Hospital-Acquired Urinary Tract Infection at Dessie Referral Hospital, Dessie, Northeast Ethiopia. International Journal of Microbiology. Volume 2021, Article ID 5553356, 14 pages https://doi.org/10.1155/2021/5553356

[5] 5.B. Foxman, "Urinary tract infection syndromes, " Infectious Disease Clinics of North America, vol. 28, no. 1, pp. 1–13, 2014.

[6] 6.M. Dommergues, F. Da¨ıkha-Dahmane, F. Muller, M. C. Aubry, S. Lortat-Jacob, and C. Nihoul-Fe´ke´te´, "Kidney and urinary tract disorders, " Fetal Medicine E-Book: Basic Science and Clinical Practice, vol. 459, 2008.

[7] 7 .T. M. Hooton, S. F. Bradley, D. D. Cardenas et al., "Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 international clinical practice guidelines from the infectious diseases society of America, " Clinical Infectious Diseases, vol. 50, no. 5, pp. 625–663, 2010.

[8] 8.Gualerzi CO, Brandi L, Fabbretti A, Pon CL. Antibiotics: targets, mechanisms andresistance. Wiley; 2013, 26 and 173.

[9] 9.Alam J, Asma R, Chowdury SS, Rahimgir M. Sensitivity pattern of cefotaxime against common uropathogens in vitro in Dhaka, Bangladesh. Drugs Ther Perspect. 2019;35(3):145-9. doi: 10.1007/s40267-019-00603-1.

[10] 10.Hogg S. Essential microbiology. Wiley; 2005. p. 358–64.

[11] Munita JM, Arias CA. Mechanisms of Antibiotic Resistance. Microbiol Spectr 2016:481–511.

[12] 12.Morar M, Wright GD. The genomic enzymology of antibiotic resistance. Annu Rev Genet 2010;44:25–51.

[13] 13.Madigan MT, Madigan MT, Brock TD. Brock biology of microorganisms. San Francisco, CA: Pearson/Benjamin Cummings; 2009. p. 802–6.

[14] 14.Fenta A, Dagnew M, Eshetie S, Belachew T. Bacterial profile, antibiotic susceptibility pattern and asso- ciated risk factors of urinary tract infection among clinically suspected children attending at Felege- Hiwot comprehensive and specialized hospital, Northwest Ethiopia. A prospective study. BMC Infec- tious Diseases. 2020; 20(1):1–10.

[15] 15.WHO. Anti microbial risistance 2020.

[16] 16.McLellan LK, Hunstad DA. Urinary tract infection: pathogenesis and outlook. Trends in molecular medi- cine. 2016; 22(11):946–57. https://doi.org/10.1016/j.molmed.2016.09.003 PMID: 27692880

[17] 17.Shume T, Tesfa T, Mekonnen S, Asmerom H, Tebeje F, Weldegebreal F. Aerobic Bacterial Profile and Their Antibiotic Susceptibility Patterns of Sterile Body Fluids Among Patients at Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia. Infection and Drug Resistance. 2022; 15:581. https://doi. org/10.2147/IDR.S351961 PMID: 35228808

[18] 18.Vandepitte .J and J. Verhaegen, K. Engbaek, P. Rohner, P. Piot, C. C. Heuck (2003). Basic laboratory procedures in clinical bacteriology2nd ed. World Health Organization Geneva2003. ISBN 92 4 154545 3.

[19] 19.Forbes B. A., Sahm D.F., & Weissfeld A.S. (2007) : 'Bailey and Scott's 'Diagnostic Microbiology . 12th ed. Mosby Company. Missouri ., PP;842-844.

[20] Henry J.B.; Davey F.R.; Herman C.J.; McPherson R.A.; PincusM.R.; Threatte G.A. and Woods G.L.(2001): Clinical Diagnosis and Management by Laboratory Methods.20thed, W.B.

[21] 21.Ramnik sood MD .Urine analysis.(2009):Medical laboratory Technology.

[22] Methods and Interpretation. 6Th ed.Jaypee brothers Medical publishers(p)Ltd NewDelhiA.pp:99-160

[23] 22.BioMérieux VITEK® 2 Systems Product Information. bioMérieux, Inc. USA.(2014).

[24] Pincus D.H. (2006) .Microbial identification using the bioMerieux VITEK ® 2 system. Encyclopedia of Rapid Microbiological Methods.pp;1-32.

[25] 24.Bauer, A.W.; Kirby, W.M.M.; Sherris, j.s. and Turk, M. (1966). Antibiotic susceptibility testing by a standardized single disk method . American Journal of Clinical Pathology, 45:493-496.

[26] 25.CLSI:Clinical and Laboratory Standards Institute Performance.(2023). Standards for Antimicrobial Susceptibility Testing 29th ed. CLSI supplement M100-S26. Wayne, PA: Clinical and Laboratory Standards Institute .

[27] 26.Yann Mouanga Ndzime, Richard Onanga, Neil Michel Longo Pendy, Michelle Bignoumba and Cyrille Bisseye (2023):Epidemiology of community origin of major multidrug resistant ESKAPE uropathogens in a paediatric population in South East Gabon. Antimicrobial Resistance & Infection Control (2023) 12:47 https://doi.org/10.1186/s13756 023 01250 y

[28] 27.Joseph DiPiro, R.T., Gary Yee, Gary Matzke, Barbara Wells, L. (2011) :Michael Posey Pharmacotherapy: A Pathophys-iologic Approach. McGraw-Hill Medical.

[29] Asaduzzaman M, Hasan Z, Khatun M, Alam J, Hossain N, Das B, et al. Resistance pattern of levofloxacin against uropathogens causing urinary tract infection in selected areas of Dhaka city. Bangladesh. J Biol Agric Healthc. 2018;8(4):74–81.

[30] 29.Runa Asma Md. Jahangir Alam, Md Rahimgir, Mohammad Asaduzzaman, AKM Mynul Islam, Nasir Uddin, Md. Saiful Islam Khan, Nur-Wa-Bushra Jahan, Syeda Subrina Siddika, Suvamoy Datta(2019) Prevalence of Multidrug-Resistant, Extensively Drug-Resistant and Pandrug-Resistant Uropathogens Isolated From Urinary Tract Infection Cases in Dhaka, Bangladesh. Avicenna Journal of Clinical Microbiology and Infection. doi:10.34172/ajcmi.2019.09

[31] Asaduzzaman M, Shamim A, Mian S, Alam J, Juliana FM, Hossain N, et al. Resistance pattern of cefixime against uropathogens causing urinary tract infection in selected areas of Dhaka city, Bangladesh. Int J Eng Sci. 2018;7(1):33-9.

[32] 31.AL-begat Saad Taha MutlkHmidan. (2007):Study of most common aerobic bacte-ria causing lower urinary tract (UTI)in Ramadi general hospital .MSC Thesis, Cllege of medicine, AL-Anbar university.

[33] 32.Jawetz E.; Melink, J.L.and Adelberg, E.A. (2010):Review of Medical Microbiology.25rd Ed. Lange Medical Book.Appleton and Lange California.

[34] Pizarro-Cerda´ and Pascale Cossart.(2006): Bacterial Adhesion and Entry into Host Cells. Cell:124, 715–727, February 24, 2006, Elsevier Inc.

[35] Nimri Laila.(2010):Community-Acquired Urinary Tract Infections in aRural Area in Jordan: Predominant Uropathogens, And their antimicrobial Resistance . WebmedCentral Microbiology ;1(9): WMC00660.

[36] 35.Al-Banea H. Z., (2006):Factors Affecting on Haemolysin Production from Pathogenic Bacteria Isolated from Diabetes Patients Urine and Its Resistance to Some Antibiotics.M.Sc.Thesis, College of Science, Al-Mustansiyra University.

[37] 36.M. Dommergues, F. Da¨ıkha-Dahmane, F. Muller, M. C. Aubry, S. Lortat-Jacob, and C. Nihoul-Fe´ke´te´, "Kidney and urinary tract disorders, " Fetal Medicine E-Book: Basic Science and Clinical Practice, vol. 459, 2008.

[38] Berhanu Adugna, Bekele Sharew, and Mohabaw Jemal (2021).Bacterial Profile, Antimicrobial Susceptibility Pattern, and Associated Factors of Community- and Hospital-Acquired Urinary Tract Infection at Dessie Referral Hospital, Dessie, Northeast Ethiopi

[39] Al-Greti Salim Hussien Hassan.(2012):Evaluation of urinary secretary immunog-lobulin (sIg) level in diabetic patients at Karbala city.Kerbala Journal of Pharmaceutical Sciences Number 3 .(Iraqi academic scientific Journal).

[40] 39.Jonas Salm, Florian Salm, Patricia Arendarski, Tobias Siegfried Kramer (2020):High antimicrobial resistance in urinary tract infections in male outpatients in routine laboratory data, Germany, 2015 to 2020. Euro Surveill. 2022;27(30):pii=2101012. https://doi.org/10.2807/1560-7917.ES.2022.27.30.2101012.

[41] 40.Gaston JR, Johnson AO, Bair KL, White AN, Armbruster CE. Polymicrobial interactions in the urinary tract: is the enemy of my enemy my friend? Infect Immun. 2021;89(4):IAI.00652-20. https://doi.org/10.1128/IAI.00652-20 PMID: 33431702

[42] 41.Vijaya V Swetha, U.Sreenivasa Rao, P. Hema Prakash and S. Subbarayudu(2014): Aerobic bacteriological profile of urinary tract infections in a tertiary care hospital. Int.J.Curr.Microbiol.App.Sci (2014) 3(3): 120-125

[43] 42.Flores-Mireles, A. L., Walker, J. N., Caparon, M., and Hultgren, S. J. (2015). Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat. Rev. Microbiol. 13, 269–284. doi: 10.1038/nrmicro3432

[44] Shaki, D., Hodik, G., Elamour, S., Nassar, R., Kristal, E., Leibovitz, R., et al. (2020). Urinary tract infections in children < 2 years of age hospitalized in a tertiary medical center in Southern Israel: epidemiologic, imaging, and microbiologic characteristics of first episode in life. Eur. J. Clin. Microbiol. Infect. Dis. 39, 955–963. doi: 10.1007/s10096-019-03810-w

[45] Khalil Ahmed and Imran. 2008. Prevalence and Antibiogram of Uncomplicated Lower Urinary Tract Infections in Human Population of Gilgit, Northern Areas of Pakistan. Pakistan J. Zool. 40(4): 295-301.

[46] 45.Lei Huang, Chenwei Huang, Yan Yan, Liying Sun and Haixia Li .(2022):Urinary Tract Infection Etiological Profiles and Antibiotic Resistance Patterns Varied Among Different Age Categories: A Retrospective Study From a Tertiary General Hospital During a 12-Year Period

[47] 46.Shaikh, N., Hoberman, A., Keren, R., Ivanova, A., Gotman, N., Chesney, et al. Predictors of antimicrobial resistance among pathogens causing urinary tract infection in children. J Pediatrics. 2016;171, 116–121.

[48] 47.Garrido D, Garrido S, Gutiérrez M, Calvopiña L, Harrison AS, Fuseau et al. Clinical characterization and antimicrobial resistance of Escherichia coli in pediatric patients with urinary tract infection at a third level hospital of Quito, Ecuador. Boletin Medico Del Hospital Infantil de Mexico. 2017;74(4), 265–71.

[49] 48.Dikoumba A-C, Onanga R, Nguema PPM, Mangouka LG, Iroungou BA, Kassa FK, et al. Phenotipic prevalence of antibiotic resistance in gabon. Open J Med Microbiol. 2021;11(2):100–18.

[50] 49.Yann Mouanga-Ndzime, Richard Onanga, Neil-Michel Longo-Pendy, Michelle Bignoumba and Cyrille Bisseye (2023):Epidemiology of community origin of major multidrug-resistant ESKAPE uropathogens in a paediatric population in South-East Gabon. Antimicrobial Resistance & Infection Control. 12:47 https://doi.org /10.1186 /s13756-023-01250-y

[51] 50.Runa Md. Jahangir Alam ID , Md Rahimgir, Mohammad Asaduzzaman, AKM Mynul Islam, Nasir Uddin, Md.

Saiful Islam Khan, Nur-Wa-Bushra Jahan, Syeda Subrina Siddika, Suvamoy Datta (2019). Prevalence of Multidrug-Resistant, Extensively Drug-Resistant and Pandrug-Resistant Uropathogens Isolated From Urinary Tract Infection Cases in Dhaka, Bangladesh. Avicenna Journal of Clinical Microbiology and Infection doi: 10.34172 /ajcmi.2019.09

[52] 51.Shaki, D., Hodik, G., Elamour, S., Nassar, R., Kristal, E., Leibovitz, R., et al. (2020). Urinary tract infections in children < 2 years of age hospitalized in a tertiary medical center in Southern Israel: epidemiologic, imaging, and microbiologic characteristics of first episode in life. Eur. J. Clin. Microbiol. Infect. Dis. 39, 955–963. doi: 10.1007/s10096-019-03810-w.

[53] 52.Klein, R. D., and Hultgren, S. J. (2020). Urinary tract infections: microbial pathogenesis, host-pathogen interactions and new treatment strategies. Nat. Rev. Microbiol. 18, 211–226. doi: 10.1038/s41579-020-0324-0

[54] 53.Lei Huang, Chenwei Huang, Yan Yan, Liying Sun and Haixia Li .(2022):Urinary Tract Infection Etiological Profiles and Antibiotic Resistance Patterns Varied Among Different Age Categories: A Retrospective Study From a Tertiary General Hospital During a 12-Year Period