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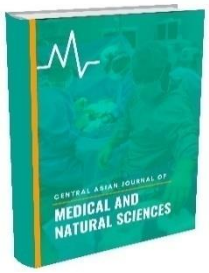

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Etiological Spectrum and Antimicrobial Resistance among Bacterial Pathogen Association with Urinary Tract Infection in Wasit Governorate/ Iraq

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Abstract: Objectives: This study aimed to determine the prevalence of uropathogens that cause urinary tract infections (UTIs) in Wasit Governorate, Iraq, and evaluate their patterns of antimicrobial resistance.

Methods: The study involved the examination of 840 urine samples taken from patients visiting the Al-Karama and Al-Zahraa Teaching Hospitals in Wassit province. The samples were collected from February 2022 to March 2023. Using a VITEK 2 compact system, we identified and tested the microorganisms responsible for the infections.

Results: Of the 840 urine samples of symptomatic patients with UTI, 669 (79.6%) were found to show significant growth of UTI, among whom the females were 470 (70.2%) episodes.

E. coli was the most frequently isolated uropathogen in both sex groups (42.2%, n=284), followed by S. aureus (21.2%, n=131), E. faecalis (12.5%, n=284), other staphylococci (5.8%, n=39), Proteus (4.7%, n=32), Group B Streptococcus (3.8%, n=26), Enterobacter (2.8%, n=19), and Pseudomonas (0.7%, n=5).

Based on Gram-negative isolates (n=389), resistance rates decreased in the following order: Ampicillin 68%< Piperacillin/tazobactam 49% < Cefoxitin 47% < Ceftriaxone 32% <Trimethoprim/Sulfamethoxazole and Ceftazidime 28% <Cefepime 27% <Ciprofloxacin 25%<Nitrofurantoin 23% Levofloxacin 22%<Gentamicin 21%<Amikacin 19% <Imepenem 2% on the other hand,

In the group of Gram-positive isolates (n=280) in decreasing order were Oxacillin 33% <Tetracycline 38% <Levofloxacin 24% <Clindamycin 21%<

Nitrofurantoin and Trimethoprim/sulfamet hoxazole 19%< Rifampicin 13%< Tobramycin 11%< Gentamicin 10% <Teicoplanin and Vancomycin 8%.

Conclusion: In Wassit Governorate, Iraq, the primary cause of UTIs was E. coli, with S. aureus being the second most common. Among Gram-negative uropathogens, high resistance rates were found for ampicillin, second and third-generation cephalosporins, trimethoprim/sulfamethoxazole, and quinolones. However, aminoglycosides exhibited comparatively lower resistance rates. Imipenem (for Gram-negative bacteria) and vancomycin and teicoplanin (for Gram-positive bacteria) maintained strong activity, making them suitable choices for antimicrobial treatment of complicated UTIs when other options are unavailable.

Keywords: urinary tract infection, etiology, antimicrobial resistance, VITEK system, Iraq.

Introduction

The most common infection in clinical settings is urinary tract infection (UTI). Around the world, empirical therapy is frequently employed for both complex and simple UTIs, since postponing treatment can lead to higher rates of illness and death [1,2,3].

The prevalence of infection is higher in females owing to specific anatomical differences. Factors that increase the risk of infection include frequent sexual intercourse, infancy, old age, urinary tract abnormalities, low socio-economic status, pregnancy, diabetes, and spinal cord injuries. [4].

UTIs are often caused by bacteria. Gram-negative bacteria like Escherichia coli, Proteus species, Pseudomonas aeruginosa, Acinetobacter species, Klebsiella species, Enterobacter species, and Citrobacter species are the most common. Staphylococcus saprophyticus, Enterococcus species, and coagulase-negative Staphylococcus are also responsible for UTIs. [5,6].

Broad-spectrum antibiotics are used to treat UTIs, and treatment starts empirically without culture and sensitivity. Depending on the local uropathogen resistance rate, first-line agents can be good for empirical UTI treatment. In this context, some guidelines recommend that antibiotics shouldn't be used as first-line empirical treatments for urinary tract infections if resistance is over 10% in the most likely infected strains within a community. [1].

Antibiotic resistance rates vary across geographical areas due to the presence of distinct strains in different regions worldwide and differences in antibiotic usage [7]. Pathogens' resistance patterns to antibiotics are constantly evolving [8,9]. Antibiotic resistance is a critical medical issue and a priority for the World Health Organization (WHO) as there is a growing global trend of antibiotic resistance, which makes it more difficult to eradicate from the urinary tract, resulting in extended illnesses and increased mortality rates [10,11]. Antimicrobial resistance also imposes a financial burden due to additional laboratory tests and the need for more expensive drugs to treat resistant strains [12].

The best way to guide empirical antimicrobial choices is to monitor uropathogen resistance and reevaluate recommended empirical antimicrobial regimens [1,13]. For tracking community-acquired uropathogens, Iraq doesn't have an antimicrobial resistance surveillance system. Because of this,

regional protocols for effectively managing community-acquired UTIs within the country aren't in place.

The primary purpose of this study was to identify the prevalence of UTI-causing pathogens and their susceptibility patterns, creating a reference database. Given the current situation, there is a concerning lack of local research on this specific topic.

Antimicrobial resistance patterns are changing at an alarming rate, with the frequent emergence of new multi-drug resistant (MDR) bacteria, leading to increased morbidity and mortality. This study aims to emphasize the importance of using appropriate antibiotics for treating UTIs. Moreover, our findings will help authorities develop antibiotic prescription policies and design antibiotic formulary guidelines in line with the Iraq Action Plan of Antimicrobial Resistance (2018-2022). Raising awareness and annually reporting these results will contribute to preventing the spread of emerging strains within the community.

METHODS

Sample collection

A total of 840 Mid-stream urine samples were collected from people admitted to Al-Karama and Al-Zahraa Teaching Hospitals of Wassit governorate from Febraury 2022 – March 2023. Samples were collected from symptomatic patients of both genders. Samples were transported to the laboratory within 30 minutes to one hour and then characterized using different conventional bacteriological and biochemical methods.

Individuals who sought medical attention at outpatient clinics for UTI diagnosis were consecutively enrolled if their urine samples showed significant bacteriuria, while those with non-significant bacteriuria were excluded.

A single organism with quantitative counts ≥102 CFU/mL isolated from a clean-catch voided urine specimen in symptomatic patients defined significant bacteriuria [14]. A checklist was used to prospectively record age, sex, past medical history, and antibiotic exposure within the past 3 months. To perform the routine culture, a standard loop was used to inoculate ten µl of each mid-stream urine sample onto culture media such as blood agar and MacConkey agar. Bacterial growth was observed by examining the cultures after they were incubated overnight at 35°C.

The VITEK 2 Compact System was utilized to identify and test the antimicrobial susceptibility of bacteria isolated from urine samples. Bacterial colonies with notable growth on culture plates were used to prepare a standardized saline inoculum, as suggested for VITEK identification. Specific ID cards for Gram-negative and Gram-positive bacteria were used in the VITEK system to identify the bacteria.

Antimicrobial susceptibility testing (AST) and determination of minimum inhibitory concentrations were conducted using specialized AST cards. The interpretation of AST results was performed following the guidelines of the Clinical and Laboratory Standards Institute, in accordance with the instructions provided by the manufacturer (BioMérieux, France), and utilizing the Advanced Expert System..

Ethics. The ethics committee of the College of Medicine, University of Wasit, approved the study protocol.

Results

At the Microbiology Laboratory of the College of Medicine/Wasit University, 840 urine samples were received for analysis and culture, out of which 669 (79.6%) displayed significant growth, indicating

the presence of UTIs. Out of the significant growth samples, 470 (70.2%) cases were diagnosed in females.

The average age (±SD) was 37±15 years. The frequency of gender distribution for UTI cases can be seen in Table 1.

Table 1: The distribution of UTI cases by gender among patients admitted to Al-Karama and Al-Zahraa Teaching Hospitals .

Variables	Frequency (%)
Male	470 (70.2)
female	199 (29.8)
Total	669 (100)

In the study, 59% (n=395) of the cases involved Gram-negative bacteria, while 41% (n=274) were Gram-positive. E. coli was the most common species linked to UTIs in the patient group, accounting for 71.89% (n=284) of cases (Figure 1). This was followed by Klebsiella species at 12.4% (49), Proteus at 8.1% (32), Enterobacter at 4.8% (19), P. aeruginosa at 1.2% (5), and other Gram-negative bacteria at 1.5% (6).

Conversely, Gram-positive bacteria made up 40% (n=280) of the cases, with Staphylococcus aureus as the primary pathogen in this group (48.9%, n=143). It was followed by Enterococcus faecalis at 30.6% (134), while other Staphylococcus species and Streptococcus species were identified in 10.9% (n=30) and 9.6% (n=26) of cases, respectively (Figure 2).

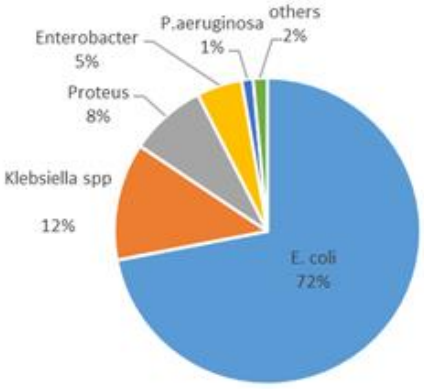

Figure 1. Species distribution of Gram-negative isolates, associated with UTIs

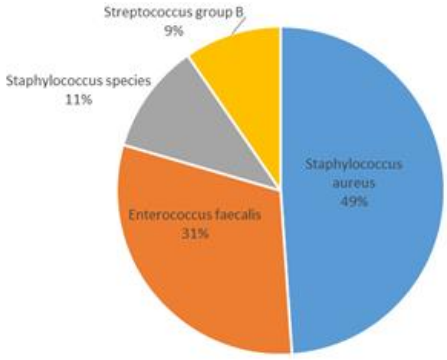

Figure 2. Distribution of Gram-positive species related to UTIs

According to Table 2, the majority of Gram-negative urinary pathogens exhibit resistance (R) to antimicrobial agents.

Overall, the rate of antibiotic resistance in Gram-negative urinary pathogens was highest for ampicillin (68%), Piperacillin/tazobactam (49%), Cefoxitin (47%)and Ceftriaxone (32%)while the lowest resistance rate was toward Imepenem (2%) and Amikacin (19%)m on the other hand , the rate of antibiotic resistance in Gram-negative urinary pathogens was highest for Tetracycline (38%) and Oxacillin (33%) and the lowest rate of resistance was against Teicoplanin (8%) and Vancomycin (8%) . moreover *E. coli* and *S.aureus* had a 88% and 82% antimicrobial resistance rate, respectively.

Table 4: Distribution of microorganisms found in UTI patient samples

Organism isolated (n=672)	Frequency (%)
E.coli	284 (42.2)
S. aureus	131(21.2)
E. faecalis	84 (12.5)
Klebsiella	49 (7.2)
Other staphylococci	39 (5.8)
Proteus	32 (4.7)
Streptococcus group B	26 (3.8)
Enterobacter	19 (2.8)
Pseudomonas	5 (.07)
Total	669 (100)

Table 2. Antimicrobial resistance in Gram-negative urinary pathogens

Tested antibiotics	Overall (n= 389)	E.coli (n=284)	Klebsiella (n= 49)	Proteus (n=32)	Enterobacter (n= 19)	Pseudomonas (n= 5)
Ampicillin	248(68)	188(66)	36 (73)	24(75)	-	-
Piperacillin/tazobactam	190(49)	129 (52)	32 (66)	9 (28)	15 (80)	5 (100)
Ceftazidime	110(28)	79 (28)	13 (27)	10 (31)	3 (15)	5(100)
Cefoxitin	172(47)	139 (49)	25(51)	9(28)	-	-
Ceftriaxone	123(32)	88 (31)	20 (41)	12 (37)	3 (15)	-
Cefepime	106(27)	77 (27)	13 (27)	9 (28)	3 (15)	4 (80)
Imepenem	6 (2)	5 (2)	1 (2)	0(0)	0(0)	0(0)
Amikacin	74 (19)	45 (16)	16 (33)	9 (28)	0(0)	4(80)
Gentamicin	83(21)	57 (20)	18 (37)	4 (13)	0(0)	4 (80)
Ciprofloxacin	97 (25)	70 (25)	17 (35)	0 (0)	6 (32)	4 (80)
Levofoxacine	87(22)	62 (22)	15 (31)	0(0)	6 (32)	4 (80)
Nitrofurantoin	82(23)	59 (21)	20 (41)	-	3 (15)	-
Trimethoprim/ Sulfamethoxazole	108(28)	70 (25)	18 (37)	13 (41)	7 (37)	-

Data presented as number (percentage of resistance) - not tested

Table3. Frequency and percentage of prevalent Gram-negative urinary pathogens resistant (R) to antimicrobial substances

Tested antibiotics	Overall (n= 280)	S. aureus (n=131)	E. faecalis (n=84)	Other staphylococci (n=39)	Streptococcus group B (n= 26)
Oxacillin	57 (33)	47 (35)	-	10 (26)	-
Gentamicin	19 (10)	15 (11)	-	3 (8)	1 (4)
Tobramycin	19 (11)	13 (10)	-	6(16)	-
Levofloxacin	69 (24)	20(15)	33 (39)	8(20)	8(30)
Clindamycin	42 (21)	20(15)	-	8(20)	14 (55)

Teicoplanin	21 (8)	8 (6)	11 (13)	2(5)	-
Vancomycin	21 (8)	8 (6)	11 (13)	2(5)	-
Nitrofurantion	48 (19)	8 (6)	36 (43)	4(10)	-
Rifampicin	23 (13)	17 (13)	-	6 (15)	-
Chloramphenicol	-	-	-	-	4(15)
Tetracycline	108(38)	27 (20)	40 (48)	27(69)	14(55)
Trimethoprim/sulfamethoxazole	38 (19)	12(9)	-	16 (61)	10(40)

Data presented as number (percentage) - not tested

Discussion

Globally, UTIs pose a significant health threat because they can lead to urosepsis, renal scarring, or progressive kidney disease. Antibiotics are used to treat UTIs, and empirical treatment with suitable antimicrobial agents plays a crucial role in disease prognosis [17]. Antimicrobial resistance exhibits geographical variation [18, 19], making it essential to periodically monitor local antibiotic sensitivity patterns for urinary pathogens through studies like this one [20]. The primary objective of this study was to examine the etiology of UTIs and to illustrate the trends in antimicrobial resistance among the predominant uropathogens, which are commonly targeted in empirical treatment.

This study reveals a higher prevalence of UTIs in females (69.8%) compared to males (29.2%), which aligns with other studies indicating that UTIs are more frequent in women than men [8,10,15]. UTIs occur when bacteria in the urine have the capacity to affect tissues in the urinary tract and nearby structures. Females are more susceptible to UTIs due to anatomical factors, such as a shorter and straighter urethra and the proximity of the urethra to the anus, which facilitate the colonization of the pre-urethral region by enteric bacteria. Additionally, UTIs can occur following sexual intercourse when bacteria may unintentionally be introduced into the urethra [16]. In this study, Gram-negative bacteria were identified in 59% (n=395) of cases, while Gram-positive bacteria were found in 41% (n=274).

The current study's results are consistent with those reported by Mahde et al. [28], demonstrating that Gram-negative bacteria had a prevalence of 52.48% while Gram-positive bacteria had a prevalence of 47.51% in UTI patients. A similar predominance of Gram-negative bacteria was also found in Duhok governorate, as reported by Hadi et al. [29]. They observed that 81.3% of UTI cases were caused by Gram-negative bacteria, while only 18.7% of cases in Basra governorate were attributed to Gram-positive bacteria.

The results obtained in this study are consistent with those reported by Alshabi et al. [26], who found a higher incidence of Gram-negative isolates compared to Gram-positive isolates, with E. coli being the most commonly identified microorganism (73.68%). However, our findings differ from those of another study [27], which reported that 90% of UTI cases were caused by Gram-negative bacteria, while only 10% were caused by Gram-positive bacteria. Additionally, different results were obtained by yet another study [25], which showed that the prevalence of staphylococci in UTIs was higher for S. epidermidis (55.5%; 10 out of 18) than for S. aureus (26.6%; 8 out of 30).

These variations may be attributed to geographical differences, antibiotic misuse leading to more virulent and invasive bacterial isolates, and varying levels of awareness across societies.

Table 4 demonstrates that the most frequently isolated pathogens were E. coli (42.2%), followed by S. aureus (28.33%), E. faecalis (12.5%), and Klebsiella (7.2%). Other bacterial pathogens included coagulase-negative staphylococcus (5.8%), Proteus (7.4%), Streptococcus group B (3.8%), Enterobacter (2.8%), and Pseudomonas (0.7%).

Comparable findings were reported by *Martin et al*. [22], who identified E. coli (41.9%) as the most common bacterial uropathogen, followed by S. aureus (31.4%). Additionally, the current study's results align with *Alhamdany* [23], who observed that the predominant isolate in UTIs was E. coli, accounting for 55% of cases.

According to the Surveillance of antimicrobial resistance in Bulgaria [21], *E. coli* is the most commonly isolated etiological agent UTIs, representing more than 50% of the urine isolates, *Klebsiella pneumoniae* and *Proteus spp*.occupy the second and third place, respectively. These results were partially agreed with the current study in regarding the predominance *E.coli* as the main causative agent of UTI. The prevalence of E. coli can be attributed to several identified virulence factors, including endotoxins found in all strains, and adhesin (pili) and capsules present in some strains. These factors are associated with UTIs and colonization [24].

The overuse and improper use of antibiotics, combined with the frequent prescription of broad-spectrum antibiotics and patients' insufficient compliance with antibiotic regimens, all contribute to bacterial genetic mutations and the subsequent emergence of antibiotic resistance [30]. Globally, antibiotic resistance is a big problem, especially since so many UTIs are treated without bacteriological testing. Gaining insight into the susceptibility patterns of the microorganisms responsible for UTIs can improve the choice of empirical treatments for these infections.

We found 66% resistance to ampicillin among E. coli isolates, considerably higher than the 30% reported in Canada [31] and 49% in the United Kingdom [32]. Furthermore, our results demonstrated a significantly higher resistance to trimethoprim/sulfamethoxazole compared to previous studies (11% in Canada and 16-18% in the United States) [31]. This difference may stem from the easier availability of these antibiotics in our country's drug market, as opposed to stricter regulations in other nations. The increased resistance to ampicillin and trimethoprim/sulfamethoxazole found in our study indicates that these antibiotics may no longer be suitable for empirical UTI treatment.

Fluoroquinolones have been proposed as potential empirical treatments for UTIs [33]. Our study disclosed resistance rates of 25% for ciprofloxacin and 22% for levofloxacin, making them moderately viable options compared to other antibiotics Although fluoroquinolones have been found to be effective in treating uncomplicated UTIs, their increased use has raised concerns about the potential development of resistance patterns in the future. In light of this, recent international clinical practice guidelines suggest using fluoroquinolones as alternative agents rather than as the primary therapy for treating uncomplicated UTIs [34]. This recommendation is in line with a recent directive by the US Food and Drug Administration, which requires fluoroquinolone package inserts to include a warning that these antimicrobial agents should not be used for routine respiratory tract infections or uncomplicated UTIs unless no other suitable alternative is available [35].

E. coli strains isolated in our study showed the highest susceptibility to imipenem (2%). The seemingly low resistance to this antibiotic might be due to its limited accessibility in our region and its expensive price.

A concerning discovery from this study revealed a high level of drug resistance among G-uropathogens to piperacillin/tazobactam (49%), Cefoxitin (47%) , Ceftriaxone (32%) , Ceftazidime (28%) and Cefepime (27%). high rate of resistance for nitrofurantoin (23%) and trimethoprim/sulfamethoxazole (28%) was also recorded in this study which is closerelated to the resut of *Gupta et al;* [36]. The observed resistance is likely a result of the extensive use of third-generation cephalosporins and fluoroquinolone antibiotics in patients with UTIs.

A favorable finding from this study is the relatively low resistance levels to gentamicin and amikacin (21% and 19% respectively). This outcome is supported by Barlam et al. [39], who stated that

aminoglycosides, such as gentamicin and amikacin, are preferred antimicrobials for parenteral andcombined therapy in severe or complicated UTIs, or infections with limited alternative treatments.

UTI bacteria and their susceptibility to antimicrobial agents keep changing over time and vary by country [37,38].

Limitations

The scope of this study was limited to a single location. Examining a wider patient population from different geographical regions and various health conditions, as well as exploring the mechanisms behind bacterial resistance development, could provide more comprehensive and valuable insights.

CONCLUSION

In Wassit governorate, Iraq, UTIs were mainly caused by E. coli, followed by S. aureus. For Gram-negative uropathogens, there were high resistance rates to ampicillin, second and third-generation cephalosporins, trimethoprim/sulfamethoxazole, and quinolones. Conversely, aminoglycosides exhibited a relatively low resistance rate.

Imipenem (in the Gram-negative group), vancomycin, and teicoplanin (in the Gram-positive group) exhibited strong activity and are suitable choices for antimicrobial treatment of complicated UTIs when other options are unavailable.

The research emphasizes the significance of regularly monitoring resistance rates of commonly used antimicrobial agents at the local level to provide guidance for empirical treatment recommendations. For optimal medical practice, it is crucial to conduct microbiological analysis of urine samples in patients suspected of having UTIs in order to determine the responsible pathogen and evaluate its susceptibility to antimicrobial treatments. Antimicrobial resistance needs to be stopped urgently. Additionally, more studies should be carried out to further evaluate the local resistance of frequently prescribed antibiotics, allowing for better empirical treatment of UTIs.

References

1. Gupta K, Hooton TM, Naber KG, et al. : International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011, 1:103- 120. 10.1093/cid/ciq257.
2. Heinz J, Röver C, Furaijat G, et al.: Strategies to reduce antibiotic use in women with uncomplicated urinary tract infection in primary care: protocol of a systematic review and metaanalysis including individual patient data. BMJ Open. 2020, 10:e035883. 10.1136/bmjopen-2019-035883.
3. Manshahia PS, Bisht M, Mittal A, Bhatia M, Handu SS: A prospective, follow up study to assess guidelines compliance in uncomplicated urinary tract infection. J Family Med Prim Care. 2020, 9:4292-4297. 10.4103/jfmpc.jfmpc_849_20.
4. Foxman, B., Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. The American journal of medicine, 2002. 113(1): p. 5-13.
5. Nguyen HT. Bacterial Infections of the Genitourinary Tract. Smith's General Urology. 16th ed New York (USA): Mcgraw-Hill Medical; 2004. p. 220.
6. Momoh A, Orhue P, Idonije O, Oaikhena A, Nwoke E, Momoh A. The antibiogram types of Escherichia coli isolated from suspected urinary tract infection samples. J Microbiol Biotech Res 2011;1:57-65.

7. Ikuta, K.S., et al., Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet, 2022. 400(10369): p. 2221-2248.
8. Mortazavi-Tabatabaei, S.A.R., et al., Pattern of antibacterial resistance in urinary tract infections: A systematic review and meta-analysis. International Journal of Preventive Medicine, 2019. 10.
9. Mamuye, Y., Antibiotic resistance patterns of common Gram-negative uropathogens in St. Paul's Hospital Millennium Medical College. Ethiopian Journal of Health Sciences, 2016. 26(2): p. 93-100.
10. Wagenlehner, F., et al., The global prevalence of infections in urology study: a long-term, worldwide surveillance study on urological infections. Pathogens, 2016. 5(1): p. 10.
11. Kyu, H.H., et al., Age–sex differences in the global burden of lower respiratory infections and risk factors, 1990–2019: results from the Global Burden of Disease Study 2019. The Lancet Infectious Diseases, 2022. 22(11): p. 1626-1647.
12. Sweileh, W.M., et al., Global research output in antimicrobial resistance among uropathogens: A bibliometric analysis (2002–2016). Journal of Global Antimicrobial Resistance, 2018. 13: p. 104-114.
13. L. Nicolle, P. A. Anderson, J. Conly et al., "Uncomplicated urinary tract infection in women. Current practice and the effect of antibiotic resistance on empiric treatment," Canadian Family Physician Medecin de famille canadien, vol. 52, no. 5, pp. 612–618, 2006.
14. D. L. Kasper, A. S. Fauci, S. L. Hauser, D. L. Longo, J. L. Jameson, and J. Loscalzo, Harrison's Principles of Internal Medicine 20 e, McGraw-Hill Education, New York, NY, USA, 2018.
15. Arul Prakasam, K.C.; Dileesh Kumar, K. G. and Vijayan, M.A .Cross sectional study on distribution of urinary tract infection and their antibiotic utilisation pattern in Kerala. Int. J. Pharm.Tech Res. 2012. Vol. 4 (3). Pp: 1309-1316.
16. Foxman, B. and Frerichs, R. R. Epidemiology of Urinary Tract Infection: 1. Diaphragm Use and Sexual Intercourse. A J P H November 1985. Vol. 75 (11).
17. Mohammad-Jafari, H., et al., Increasing antibiotic resistance among uropathogens isolated during years 2006-2009: impact on the empirical management. International braz j urol, 2012. 38: p. 25-32.
18. Rasheed, N.A. and N.R. Hussein, Staphylococcus aureus: an overview of discovery, characteristics, epidemiology, virulence factors and antimicrobial sensitivity. European Journal of Molecular & Clinical Medicine, 2021. 8(3): p. 1160-1183.
19. Rasheed, N.A. and N.R. Hussein, Characterization of different virulent factors in methicillin-resistant Staphylococcus aureus isolates recovered from Iraqis and Syrian refugees in Duhok city, Iraq. PloS one, 2020. 15(8): p. e0237714.
20. Assafi, M.S., et al., Urinary bacterial profile and antibiotic susceptibility pattern among patients with urinary tract infection in duhok city, kurdistan region, Iraq. International Journal of Pure and Applied Sciences and Technology, 2015. 30(2): p. 54.
21. Surveillance of antimicrobial resistance in Bulgaria--a synopsis from BulSTAR 2018. Available at: https:// bam-bg.net//
22. Martin, O.; Adamu, A.A.; Julius, T.; Josephat, N.M.; Eddie, W.; Charles, D.K.; Ezera, A. and Joel, B. (2019). Prevalence of Bacterial Urinary Tract Infections and Associated Factors among Patients

Attending Hospitals in Bushenyi District, Uganda. International Journal of Microbiology. Volume 2019, Article ID 4246780, 8

23. Alhamdany, M.H.A. (2018). Antibiotic Susceptibility of Bacteria Isolated from Patients with Diabetes Mellitus and Recurrent Urinary Tract Infections in Babylon Province, Iraq. Medical Journal of Babylon, 15(1): 63- 68.
24. Bien, J.; Sokolova, O. and Bozko, P. (2012). Role of Uropathogenic Escherichia coli Virulence Factors in Development of Urinary Tract Infection and Kidney Damage. Int J Nephrol. 681473.
25. Fadhel, A.N.; Abureesha, R.A. and Al-azzawi, R.H. (2013). Prevalence of S.epidermidis and S. aureus and their biofilm ability among Iraqi patients suffering from urinary tract infection Iraqi Journal of Science, 54(3): 547-552
26. Alshabi, A.M.; Alshahrani, M.S.; Alkahtani, S.A. and Akhtar, M.S. (2019). Prevalence of urinary tract infection and antibiotic resistance pattern in pregnant women, Najran region, Saudi Arabia. African Journal of Microbiology Research. 13(26): 407-413.
27. Weekes, L.M. (2015). Antibiotic resistance changing management of urinary tract infections in aged care. Med J Aust., 203(9): 352.
28. Mahde, S.A.A.; Nashwan, M.R.; Ibrahim, N.R.; Hussein, A.A.T. and Amer, A.B. (2015). Urinary Bacterial Profile and Antibiotic Susceptibility Pattern among Patients with Urinary Tract Infection in Duhok City, Kurdistan Region, Iraq. Int. J. Pure Appl. Sci. Technol., 30(2): 54-63.
29. Hadi, A.M.; Sheri, F.H. and Jaccob, A.A. (2014). Urinary Tract Infection Prevalence and Antibiotic Resistance A Retrospective Study in Basra Governorate, Iraq. AlMustansiriyah Journal of Pharmaceutical Sciences (AJPS), 14(2): 129-135.
30. Mellon M, Benbrook C, BENBROOK L. Estimates of antimicrobial Abusein livestock, vol. 9. Washington: Union of Concerned Scientists Publications; 2001.
31. McIsaac WJ, Mazzulli T, Moineddin R, Raboud J, Ross S. Uropathogen antibiotic resistance in adult women presenting to family physicians with acute uncomplicated cystitis. Can J Infect Dis Medical Microbiol. 2004;15(5):266.
32. Farrell D, Morrissey I, De Rubeis D, Robbins M, Felmingham D. A UK multicentre study of the antimicrobial susceptibility of bacterial pathogens causing urinary tract infection. J Infect. 2003;46(2):94–100.
33. Karlowsky JA, Kelly LJ, Thornsberry C, Jones ME, Sahm DF. Trends in antimicrobial resistance among urinary tract infection isolates of Escherichia coli from female outpatients in the United States. Antimicrob Agents Chemother. 2002;46(8):2540–5
34. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;52(5):e103–e20.
35. US Food and Drug Administration. Fluoroquinolone antibacterial drugs. Drug Safety Communication - FDA advises restricting use for certain uncomplicated infections. Posted May12,2016.http://www.fda.gov/Safety/ MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm5 00665.htmAccessed May 15, 201 .Accessed May 15, 2016
36. Gupta K, Stamm WE. Outcomes associated with trimethoprim/ sulphamethoxazole (TMP/SMX) therapy in TMP/SMX resistant community-acquired UTI. Int J Antimicrob Agents 2002;19:554-6.

37. Livermore DM, Pearson A. Antibiotic resistance: Location, location, location. Clin Microbiol Infect 2007;13 Suppl 2:7-16.

38. Magliano E, Grazioli V, Deflorio L, Leuci AI, Mattina R, Romano P, et al. Gender and age-dependent etiology of community-acquired urinary tract infections. ScientificWorldJournal 2012;2012:349597.

39. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016;62(10):e51-77. doi: 10.1093/cid/ ciw118.