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SAKARYA UNIVERSITY
INSTITUTE OF HEALTH SCIENCE

EVALUATION OF URINE CULTURES OF ADULT PATIENTS; DATA FROM ERBIL

M.Sc. THESIS

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Institute Department: Medical Microbiology

Thesis Supervisor: Assoc. Prof. Dr. Tayfur DEMIRAY

JUNE-2021

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"This thesis was accepted unanimously by the jury below on 18/06/ 2021."

JURY MEMBER	OPINION	SIGNATURE
Prof. Dr. Mustafa ALTINDİŞ		
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Assoc. Prof. Dr. Tayfur DEMIRAY		

DECLARATION

T.C. Sakarya University's Institute of Health Science conducted this research. On the 28th of December, 2020, it was approved by the Ethics Committee. This thesis is entirely my own work, from conception to completion; I have engaged in no unethical activity at any point, and all of the material contained in the thesis is scholarly. and all of the material and comments I've gathered adhere to the ethical guidelines established by the sources. I cite the source and include it in the reference list, as well as the thesis work and writing. I declare that no patent infringement or copyright infringement occurred during my writing.

Date:

01/06/2021

Mohammed Sadeq SALEH

Signature

APPRECIATION

I'd like to express my gratitude to my respectful supervisor, Dr. Tayfur DEMRAY, for his excellent supervision and assistance from the beginning of my master's studies until the day of my defense. My thanks go out to the Institute of Health Science for providing me with all the helps which I needed to pursue my studies at Sakarya University's Department of Medical Microbiology. In addition, I'd like to thank Dr. Mustafa ALTINDIŞ for his invaluable assistance, which was important in teaching me how to conduct experiments. Dr. Handa Toptan has also been a wonderful mentor to me. I'd want to thank Dr. Eman Alaany for her tireless efforts and unwavering support, which began with my master's request and continued until the last day of my studies. I'd want to express my gratitude research team for a memorable time spent in the lab and in social situations. My gratitude also goes out to my brother Adnan Sadeq, my wife Bayar Salah and all other members of my family, and I’d want to thank all other academic colleagues for their encouragement and support during my studies.

APPROVAL

On June 30, 2021, the Ethics Committee of Sakarya University's Faculty of Medicine accepted this study request. All isolates were acquired through normal testing, anonymously analyzed, and epidemiological data was gathered retrospectively from Erbil hospitals and clinics.

CONTENTS

LIST OF ABBREVIATIONS

AES	: Advanced Expert System
AMK	: Amikacin
CAUTI	: Catheter-Associated Urinary Tract Infection
CAUTI	: Catheter-Associated Urinary Tract Infection
CAZ	: Ceftazidime
CFU	: Colony Forming Unit
CFU	: Colony Forming Unit
CIP	: Ciprofloxacin
CLSI	: Clinical and Laboratory Standards Institute
CRE	: Carbapenem-Resistant Enterobacteriaceae
CRO	: Ceftriaxone
CVA	: Cerebrovascular Accident
CXM	: Cefuroxime
DNA	: Deoxyribonucleic Acid
ERP	: Ertapenem
ESBL	: Extended Spectrum Beta-Lactamase
ExPEC	: Extra-Intestinal Pathogenic *E. coli*
FEP	: Cefepime
FOX	: Cefoxitin
GEN	: Gentamicin
HAUTI	: Hospital-Acquired Urinary Tract Infections
IMP	: Imipenem
MDR	: Multi Drug Resistance
MDR	: Multidrug-Resistant
MEM	: Meropenem
MIC	: Minimum Inhibitory Concentration
MRSA	: Methicillin-Resistant *Staphylococcus aureus*
MSSA	: Methicillin-Susceptible *Staphylococcus aureus*
QS	: Quorum Sensing

SAM	: Ampicillin/ Sulbactam
SPSS	: Statistical Package for The Social Sciences
TGC	: Tigecycline
TMP/SMX	: Trimethoprim/Sulfamethoxazole
TZP	: Piperacillin/Tazobactam
UTI	: Urinary Tract Infections

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Yetişkin Hastaların İdrar Kültürlerinin Değerlendirilmesi; Erbil'den Veriler

Giriş

İdrar yolu enfeksiyonları (İYE) yaygın bir enfeksiyon hastalığıdır ve büyük bir ekonomik yük getiren bir halk sağlığı sorunudur. İnsanlarda İYE'nin ana nedeni gram negatif bakteriler, özellikle *Escherichia coli*'dir. Bu çalışmanın amacı Erbil kliniklerine ve hastanelerine başvuran hastaların idrar örneklerinde gram negatif üropatojenlerin prevalansını belirlemek ve antimikrobiyal duyarlılıklarını değerlendirmektir. Erbil hastanelerine son 5 yılda (2015-2020) başvuran hastaların tüm idrar kültürü sonuçları sayım yöntemine dahil edildi. Mikroorganizmalar standart kültür yöntemiyle tanımlandı ve duyarlılıkları VITEK 2 otomatik sistemi ile değerlendirildi. veriler SPSS sürüm 26.0 yazılımı kullanılarak analiz edildi. Betimsel analiz sonuçları tablo ve grafiklerle raporlandı. Değişkenler arasındaki ilişkiyi incelemek için ki-kare testi kullanıldı. 0.05 anlamlılık düzeyi kabul edildi.

3380 şüpheli İYE vakasının idrar kültürü sonuçları incelendi, (69%)1'i kadın ve %30,9'u erkektir. Gözlemlenen 3097 pozitif kültürden toplam 1961 (63.3%) izolat gram negatif bakteri ve 1136 (36.7%) gram pozitif patojendi. Bu çalışmada belirlenen en yaygın gram negatif üriner patojen *Escherichia coli* idi. Gram negatif üriner patojenlerin en yüksek dirençleri antibiyotik ampisilin, Trimetoprim/Sulfamethoxazole ve seftriakson'a karşı, en düşük dirençler ise amikasin, meropenem, ertapenem ve imipenem içindi.

Anahtar Kelimeler: İdrar Kültürü; İdrar Yolu Enfeksiyonları; Antimikrobial Direnç

ABSTRACT

Introduction

Urinary tract infections (UTIs) are a common infectious disease and a public health problem that imposes a large economic burden. The main cause of UTI in humans is gram-negative bacteria, especially *Escherichia coli*. The aim of this study was to determine the prevalence of gram-negative uropathogens in urine samples of patients referred to Erbil clinics and hospitals and to evaluate their antimicrobial susceptibility. all urine cultures result of patients referred to Erbil hospitals in the last 5 years (2015-2020) were included in the census method. Microorganisms were identified by standard culture method and their susceptibility was assessed by VITEK 2 automated system. the data were analyzed using SPSS version 26.0 software. The results of descriptive analysis were reported by tables and graphs. Chi-square test was used to examine the relationship between variables. A significance level of 0.05 was considered.

The results of urine culture of 3380 suspected UTI cases were examined, of which 69.1% were female and 30.9% were male. Out of 3097 positive cultures observed, a total of 1961 (63.3%) isolates were gram-negative bacteria and 1136 (36.7%) were gram-positive pathogens. The most common gram-negative urinary pathogen determined in this study was *Escherichia coli*. The highest resistances of gram-negative urinary pathogens were against the antibiotic ampicillin, Trimethoprim / Sulfamethoxazole and ceftriaxone, and the lowest resistances were for amikacin, meropenem, ertapenem and imipenem.

Keywords: Urine Culture; Urinary Tract Infections; Antimicrobial Resistance

1. INTRODUCTION

1.1. INTRODUCTION

Infections of urinary tract (UTIs) with a significant burden of economic are considered as common human's diseases of infectious and are a general health issue. UTIs, in the United States, are the most common urinary tract disease and are responsible for annual physician visits of more than 7 million and 15% of all antibiotics of community prescribed. Many European countries have similar incidence rates as well (Bonkat et al., 2017). UTI-related health care costs are more than $ 3 billion per year globally (Anderson, Goller, Justice, Hultgren, and Seed, 2010). According to Medina and Castillo-Pino, 2019 the average prevalence rate of UTI is 19.6% in Europe, 12.9% in the United States, and in developing countries it is 24%. A systematic review by Beyer et al., reports the prevalence of UTIs in eight different countries to be between 17% and 82% (Beyer, Currea, and Holm, 2019).

UTI is a pathogenic invasion of the urothelium associated with inflammation, including infections of upper and lower urinary tract. Infections of urinary tract are between a severe situation such as uroseptic shock to easy cases such as bladder inflammation (Mansori, Shakeri-Moghadam, and Khaledi, 2019).

Gram-negative bacteria are the most common cause of UTI. The primary pathogens which lead to pyelonephritis and inflammation of uncomplicated bladder are *Escherichia coli*, and other Enterobacteriaceae strains including *Klebsiella pneumoniae* and *Proteus mirabilis*, and gram-positive pathogens including *Staphylococcus saprophyticus* and *Enterococcus faecalis* (Flores-Mireles, Walker, Caparon, and Hultgren, 2015; Gupta et al., 2011).

With the exception of the high incidence rates peaking in young women 14 to 24 years of age, the UTI prevalence enhances by age (Medina and Castillo-Pino, 2019).

The most common way of a urinary tract infection occurs is when bacteria travel to the bladder from the urethra. Preliminary animal researches have shown that when bacteria are injected in bladder and the ureter is blocked, the unblocked kidney has more possibly of developing pyelonephritis (Vivaldi, Cotran, Zangwill, and Kass, 1959). Rarely, upper urinary tract infections could be the effect of the bacterial hematogenesis spread, for instance for prolonged bacteremia, which is usually related to an important cause of infection including endocarditis. Several investigations in animals confirm this and show that injection of intravenous in *Staphylococcus aureus* could lead to pyelonephritis. Nevertheless, the spread of pyelonephritis was found to be more difficult in identical approaches with bacteria of gram-negative, recommending unusual infection route in different pathogens.

In women infections of urinary tract are frequent. A reason for this variation between the genders is due to anatomical differences such as a urethra of shorter and the fair urethra proximity to anus. Many other elements are involved, such as intercourse practices of sexual and utilizing spermicides that alter the natural flora of the vagina (Scholes et al., 2000; Walsh and Collyns, 2017).

A single bacterium species causes the majority of infections of urinary tract within non-catheterized people. Isolating higher than a certain species within a culture of urine is not unusual in the context of anatomical catheterization and abnormalities. These individuals are more likely to get infections of urinary tract resulted from gram-negative bacteria such as *Proteus*, *Klebsiella*, *Serratia*, and *Pseudomonas* due to their increased catheter usage. *Candida*, *Enterobacter*, and *Klebsiella* infections are more prevalent in diabetes people (Chu and Lowder, 2018).

Several medications including fluoroquinolones, fosfomycin trometamol, trimethoprim-sulfamethoxazole, nitrofurantoin monohydrate, and beta-lactams are recommended in international recommendations for the treatment of pyelonephritis and tract infections of uncomplicated urinary tract infections (Bonkat et al., 2017; Gupta et al., 2011). Nevertheless, there is a worrying amount of resistance of antimicrobial in urinary pathogens because of the widespread and indiscriminate applying antibiotics. Broad-spectrum beta-lactamase-producing bacteria (BSBL) show resistance to several antibiotics regardless of carbapenem and are constantly enhancing within people (Bonkat et al., 2017; Oteo, Pérez-Vázquez, and Campos, 2010).

The clinical spectrum of urinary tract infections includes pyelonephritis, prostatitis, cystitis, and urethritis (Kolman, 2019). UTIs could be classified as community related UTIs (CAUTIs) or healthcare-related UTIs (HAUTIs), which include healthcare-associated infections. Healthcare-associated UTIs account for 40% from whole UTIs of hospital. Bacteria of Gram-negative, especially Enterobacteriaceae, considered as frequent reasons of HAUTI and CAUTI (Tandogdu and Wagenlehner, 2016).

Antibiotic resistance is on the increase among gram-negative bacteria, posing a problem for doctors since treatment choices are limited. AmpC-lactamase and broad-spectrum-lactamase-producing Enterobacteriaceae, multidrug-resistant *Pseudomonas aeruginosa*, and Enterobacteriaceae of carbapenem-resistant (CRE), are all instances of these bacteria (MDR) (Hirsch et al., 2016; Linhares, Raposo, Rodrigues, and Almeida, 2013).

Patients suspected of having a urinary tract infection should first be investigated by a physical exploration and history check to identify symptoms or signs relating to the urinary tract infection, and additional diagnostic and therapeutic strategies should be applied afterward. The classic urinary tract infections` symptoms and signs of involve tenderness of suprapubic, back pain, urgency or frequent urination, hematuria, acute dysuria, fever, or tenderness or pain in vertebral-rib angle.

Laboratory tests including bacteriuria (more than 100,000 CFU / ml) and pyuria (more than 10 WBC / HPF of cells of white blood in each pluripotent field) are used to confirm the diagnosis (Baron et al., 2013; Davis, 2019; Gupta, Grigoryan, and Trautner, 2017). Urine dipstick, which is used to diagnose leukocyte esterase and nitrite, shows signs of infection based on the study clinical and population manifestations. In several patient groups, especially the elderly, this test has a strong negative predictive amount (90-100 percent). A negative urine dipstick in nitrite and leukocyte esterase implies that additional investigation for a urinary tract infection is warranted, particularly if the chance of infection is low based to symptoms and history. However, positive results are not very conclusive (Fernandes, Jaidev, and Castelino, 2018).

Upper and lower UTIs are two types of UTIs that are defined based on the infection location. Pyelonephritis, prostatitis (lower UTIs), cystitis, and Urethritis are among them (upper UTIs). Infections of urinary tract of lower and upper may be distinguished by their clinical symptoms. Fever is frequently associated with tissue invasion and inflammation in urinary tract infections, including prostatitis or pyelonephritis, though might occurring in less amounts of UTIs. Patients with acute pyelonephritis, recurrent urinary tract infection, a disorder of urinary tract infection (cUTI), or persons at risk of infection through organisms of antibiotic-resistant should have their urine cultured (Wagenlehner et al., 2020).

Various studies have been performed on organisms involved in the urinary system and their prevalence. Odoki et al. reported that the most common urinary tract pathogen in Bushni section in Uganda was *Escherichia coli* (41.9%) and then *Klebsiella pneumoniae* and *Staphylococcus aureus* (Odoki et al., 2019). It was mentioned that *Staphylococcus* spp and *E. coli* (39.3%) were frequent urinary tract pathogens in Ethiopia (Seifu and Gebissa, 2018).

A study reported *Klebsiella pneumoniae* and *Escherichia coli* as the frequent causes of UTI in Saudi Arabia (Ahmed, Shariq, Alsalloom, Babikir, and Alhomoud, 2019). A new research of Aktaş et al. (2020) also revealed *Escherichia coli* is frequent bacterium isolated from urine samples, after that *Enterococcus*, *Klebsiella*, and *Candida* urinary pathogens, respectively (Aktaş and Denktaş, 2020). Thus, in almost all studies, the most common urinary pathogen was *Escherichia coli*. *Escherichia coli*-producing broad-spectrum β-lactamase (ESBL) species are commonly found in community-acquired UTIs, with more than a quarter of *E. coli* species isolated from urinary specimens being ESBL-positive (Hertz et al., 2016).

For many times, the fast rise of antibiotic resistance among *E. coli* strains throughout the globe has been a major concern. *E. coli* was a most prevalent uropathogen within the children urine less than the age of 18 who were treated in the United States in 2013, according to Edlin et al., and these strains were the frequent resistant to TMP-SMX and ampicillin (Edlin, Shapiro, Hersh, and Copp, 2013). In 2018, Lee et al. discovered that in the treating infections of urinary tract, resistance of *E. coli* to TMP-SMX had developed considerably (Lee, Lee, and Choe, 2018). They said that, as a result of this tendency, the global use of this medicine will be impossible in the next years. Ramirez-Castillo et al. revealed that children and women are the individuals who mostly affect with urinary tract infections, most infections are community-based, and are most resistant to TMP-SMX, ampicillin, and ampicillin-sulbactam (Ramírez- Castillo et al., 2018).

Evaluation of pathogens and their sensitivity to different antibiotics has a high effect on the experimental treatment of patients with UTI, and if the appropriate antibiotic is selected by the physician, further costs and complications will be avoided. Therefore, this study aimed to evaluate the urine cultures of outpatients referred to Erbil clinics and hospitals (five-year data 2015-2020) to determine the contamination of samples, the prevalence of various pathogens, and their susceptibility to antibiotics. In this study, the prevalence of gram-negative β-lactamase-producing bacteria (ESBL) was specifically evaluated.

The aim of this study was to determine the prevalence of gram-negative uropathogens in urine samples of patients referred to Erbil clinics and hospitals. In addition, antimicrobial susceptibility and the prevalence of Extended spectrum β-lactamase-producing uropathogens among these bacteria have also been investigated.

2. LITERATURE REVIEW

2.1. INFECTION OF URINARY TRACT (UTI)

The microorganism's existence within urine or sterile genitourinary tract tissues is referred to as an infection of urinary tract (UTI). The infection may only be in the bladder or the kidneys, and in men, it may involve the prostate. Tract infections of acute uncomplicated urinary occur in women that have normal urogenital tract, and usually present as acute cystitis (bladder infection or lower duct infection). Women rarely develop kidney infections (upper ducts or kidney parenchyma), which are referred to as uncomplicated or acute non-obstructive acute pyelonephritis. Infections of complicated urinary tract happen in people with functional or structural abnormalities of the genitourinary system, including people with external organs such as urethral catheters. Recurrence of urinary tract infection may occur as reinfection with a new microorganism or with the same microorganism, and as relapse (Nicolle LE 2019).

2.2. EPIDEMIOLOGY

Urinary tract infections in human are amongst the most frequent infections in terms of prevalence, up there in frequency with respiratory and intestinal-gastrointestinal infections. These infections are much more common in women and occur at different ages (Figure 2-1). The prevalence of UTI increases with age for which the only exception is young girls. Approximately 20% of women will have minimum a single infection of urinary tract in their lives, with 3% having many episodes each year. UTIs are more common in females comparing with men at most ages, with the exception of young boys, who have a greater rate of UTIs than their female contemporaries. This occurs since they most probably develop abnormalities of congenital in the urinary system that predispose them to infection. UTIs usually reduce the quality of life, especially in women, but permanent effects are not common, and the infection leads to death only in rare cases (Kranz J et al., 2017). Urinary tract infection is the fourth most common infection associated with health care, accounting for 12.9% of cases, two-thirds of which is associated with catheter placement (Magill SS et all., 2014).

Minimum single episode of UTI affects 50 percent to 60 percent of adult females. In the USA, uncomplicated cystitis affects around 0.5 episodes per person each year in young women`s sexually active. Tract infections of uncomplicated urinary are most common in people between the ages of 18 and 39. Young women are equally susceptible to uncomplicated recurring urinary tract infections. Following the initial case of infection of urinary tract, 27% of women have a recurrence within 6 months, and 2.7 percent had a second recurrence within the same time frame. According to estimates, 250,000 instances of pyelonephritis occur annually in the USA. The estimated frequency of pyelonephritis in women aged 18 to 49 years is 28 per 10,000, with 7% of cases requiring hospitalization. Prevalence may be influenced by cultural and genetic variables (for instance, there are 590,000 infected with pyelonephritis in South Korea). Pyelonephritis has a lower recurrence rate than a simple urinary tract infection, with 9 percent of women and 5.7 percent of men experiencing a second episode within a year. (Medina M, and Castillo-Pino E 2017).

2.3. PATHOGENESIS

Pyelonephritis (the upper / kidney urinary tract infection) and cystitis (the lower / bladder urinary tract infection) are two types of infections of urinary tract (inflammation in urinary system). The pathogenesis of UTI starts with urinary pathogens (mainly from the fecal flora) colonizing the urethral or vaginal opening, which then travels via the urethra to the bladder. Pathogens move from the ureter to the kidneys, causing pyelonephritis. Pyelonephritis could result from the infiltration of blood bacteria into the kidneys as a result of bacteremia. Some cases of pyelonephritis may be caused by bacteria in the lymphatic vessels (Walsh C, and Collyns T.2017).

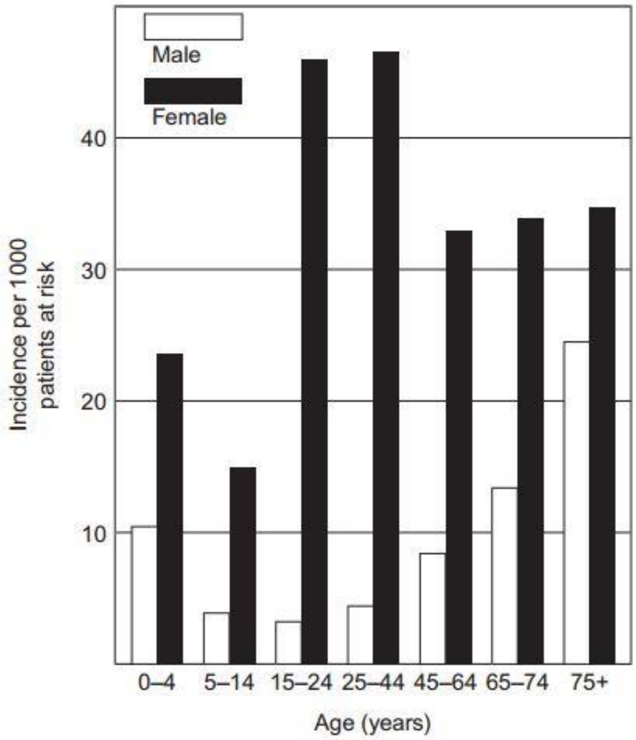

Figure 2-1: The occurrence of urinary tract infections in various ages. The black columns show the female and the white columns the male risk.

Uncomplicated acute cystitis refers to an acute infection that occurs in a non-pregnant adult woman where only the bladder is involved. Such infections have no signs or symptoms that indicate the infection has spread beyond the bladder (Hooton TM 2012). The notion acute complication infection of urinary tract (UTI) is used for referring to a tract infection of acute urinary alongside every of the below characteristics, indicating that the infection involves more than the bladder. These characteristics include fever above 37.7 °C (this temperature range is not very valid and, in each person, the basal temperature and other factors affecting the temperature should also be considered), other symptoms of systemic diseases such as chills, flank pain, costovertebral angle (CVA). and in men pelvic pain or perineal pain that are associated with prostatitis. By these definitions, pyelonephritis is a complication of a urinary tract infection, without the characteristics of patient. In infection that has organisms of drug-resistant, risk factors are not in themselves indicating a complication of urinary tract infection (Tan CW, and Chlebicki MP 2016).

It is important to recognize the uncomplicated cystitis and complicated urinary tract infections because the treatment approach is different in these two conditions. Uncomplicated cystitis is a less dangerous infection than acute complication urinary tract infection. Thus, in uncomplicated cystitis, the efficiency of an antimicrobial treatment takes precedence over the worry about undesirable ecological consequences (spreading infection or colonization with organisms of multidrug-resistant and selecting organisms of drug-resistant) that is greater priority. Furthermore, drugs intended to treat simple cystitis should not be utilized to treat severe urinary tract infections since they do not reach high enough levels in the affected tissue. Occasionally, parenteral therapy is performed in complicated urinary tract infections to ensure proper tissue surface and coverage range are achieved (Tan CW, and Chlebicki MP 2016).

2.4. CLINICAL MANIFESTATIONS

The clinical spectrum of acute urinary tract infection (UTI) includes both complicated cystitis (inflammation of the bladder) and pyelonephritis:

Cystitis symptoms and signs involve heartburn, frequent and urgent urination, hematuria, and pain of suprapubic. Patients with acute complication urinary tract infection have a fever or other systemic disease characteristics (such as rheumatism or chills), indicating that the infection could spread over bladder. Rib-vertebral discomfort sensitivity, flank pain, chills, fever, and nausea/vomiting are all typical signs and symptoms of pyelonephritis. Cystitis symptoms are common; however, they aren't always visible. Abnormal signs are also reported, including discomfort in the epigastrium or abdomen in certain individuals.

Not all patients with an acute complication of urinary tract infection experience distinct local symptoms in the urinary tract. Patients with injury of bladder and spinal cord of neurogenic, for example, may present with impaired autonomic reflexes as well as enhanced spasticity. Old or disabled patients might have more general symptoms or signs of infection (e.g, chills and fever) without obvious local symptoms in the urinary tract. Pyuria, however, is usually exist in every patient of UTI (Sussman M, 2015).

2.5. COMPLICATIONS

In addition to bacteremia, sepsis, multiple organ dysfunction, shock, and/or acute renal failure, patients that have acute complication urinary tract infection may develop acute renal failure, shock, dysfunction of multiple organs, sepsis, and bacteremia. This is more likely in individuals with urinary tract blockage, recent urinary tract catheterization, and other abnormalities of urinary tract, as well as those who are older or have diabetes. When an upper infection of urinary tract advances to a papillary necrosis, emphysematous pyelonephritis, perinephric abscess, and renal corticomedullary abscess, pyelonephritis of acute might ensue. Urinary tract blockage and diabetes mellitus are also risk factors for such consequences (particularly in necrosis of papillary and emphysematous of pyelonephritis).

Chronic pyelonephritis is a rare kind of chronic tubulointerstitial illness that is linked to recurrent infection, such as infection induced by kidney stones (potentially pyelonephritis of xanthogranulomatous) or reflux of vesicoureteral. Patients may exhibit symptoms and signs of nonspecific including nausea, exhaustion, lethargy, or stomach discomfort within weeks or months. (Gupta K et al., 2017).

2.6. EVALUATION AND DIAGNOSIS

Acute urinary tract infection should be suspected in patients who have perineal discomfort, pelvic or (in males), flank discomfort, chills, or suprapubic discomfort with fever, urgency and recurrence, or urine incontinence who seem clinically sick. Even if there are no other signs of cystitis, pyelonephritis of acute must be controlled in individuals who have just a fever and flank discomfort. Patients with feverish fever or sepsis are often suspected of having an acute UTI consequence. The evaluation includes an examination to rule out other causes of the disease and urinalysis. Physical examination should assess the sensitivity of the rib-vertebral angle, abdomen, and suprapubic area. A pelvic exam may be required in sexually active and young women, particularly when UTI signs are not convincing. A detailed examination of digital rectal is occasionally required in males with pelvic or perineal discomfort to assess a sensitive or enlarged prostate that indicates acute prostatitis (Schmiemann G et al., 2010).

For all patients suspected of having an acute complication of urinary tract infection, a urine sample is usually sent for analysis (microscopic or dipstick) and culture with antibiotic susceptibility testing. In case pyuria is detected, the results of the urine analysis will confirm the diagnosis, as pyuria is existing in most of the patients that have UTI. When it does not exist, it shows another diagnosis, especially in patients that have nonspecific signs. Casts of white cells indicate renal origin for pyuria. However, when the infection does not relate to the urinary tract or if the urinary tract is obstructed, there may sometimes be no perspiration and bacteriuria. Bacterial growth in urine culture also supports the diagnosis of urinary tract infection, and antibiotic susceptibility testing is necessary for ensuring antimicrobial therapy. When possible, warm urine staining could help limit the list of pathogens and select appropriate antibiotics (Schmiemann G et al., 2010; Rowe TA, Juthani-Mehta M 2014).

2.7. URINE CULTURE

The role of pre-treatment urine culture is to assess the bacteriuria existence and identifying and providing information of antibiotic susceptibility to the microorganism causing the UTI. Cultivation of a pure urine sample for this purpose is required in many patients that have suspected UTI, except in healthy young non-pregnant women with the usual symptoms of febrile cystitis, i.e uncomplicated UTI (Hooton TM, 2012; Gupta K, Trautner B, 2012). Among such women, the typical pattern of symptoms is sufficient for diagnosis (Bent S et al., 2002), and the causative organism is usually

Escherichia coli (Czaja CA et al., 2007). In such cases, a short course of experimental antimicrobial therapy is usually effective (McKinnell JA et all., 2011). The antibiotic choice could be examined through the pattern of local sensitivity of the history of antibiotic sensitivity of patient and *E. coli*, particularly to sulfonamides.

In asymptomatic patients, 10^5 units of colony formation (CFU) / ml is the standard threshold for bacterial growth in a urine sample that reflects bladder bacteriuria. However, in symptomatic women with pyuria, fewer bacteria in the urine (e.g., 10^2 CFU / ml) indicate bladder bacteriuria. Therefore, in such cases, a colony count of less than 10^5 and more than 10^2 CFU / ml may indicate a urinary tract infection. Fewer bacteria are associated with UTIs in men who have previously received antimicrobials and infections from organisms other than *E. coli* and *Proteus*.

Typically, the normal amount of colonies in a urine sample is less than 10^5 CFU / ml, which is primarily due to *Escherichia coli* caused by fecal contamination. Preliminary studies showed that more than 95% of patients with UTI had a bacterial count of more than 10^5 CFU / ml (Kass EH, 2002).

Subsequent studies identified a significant number of women with symptoms and purulent urinary tract infections whose colony was less than 10^5 CFU / ml (Heytens S et al., 2017, De Backer Det al., 2008). In a study of 202 premenopausal, non-pregnant women with at least two signs of acute cystitis, a pure-streamed urine sample was collected and subsequently catheterized into the urethra to collect a bladder urine sample. Of the 121 women who had *E. coli* grown in a catheterized urine sample, 49 (40%) showed a colony count of less than 10^5 CFU / ml (Hooton TM et al., 2013). The number of colonies greater than 10^2 CFU / ml in urine samples had 93% positive prognostic loss for *E. coli* bladder bacteriuria. Another study showed that 88% of women with symptoms and a colony count of more than 10^2 CFU / ml had UTI (Stamm WE et al., 1992).

2.8. ASYMPTOMATIC BACTERIURIA

A significant number of bacteria may be isolated from the urine sample in the absence of accompanying symptoms. This is more commonly reported with age, occurring in one-tenth of men and one-fifth of women over 65 (Kranz J et al., 2017). Except for young ages, where significant bacteriuria is almost 30 times higher in women than in men, this ratio decreases with age (Colgan R et al., 2006). Factors that predispose older men to bacteremia include decreased bactericidal properties of prostate secretions and enlarged prostates leading to urinary retention. In both sexes, there are many cases of spontaneous bacterial clearance followed by subsequent re-infection. Antimicrobial treatment of asymptomatic bacteriuria is rarely allowed in adults. It is more likely that the "harm" caused by it will outweigh the benefit and should therefore be avoided. These include people over the age of 65, patients with dysfunctional lower urinary tract or catheters, diabetics, and young women who are not pregnant. Evidence suggests that some bacterial species or strains play a protective role and prevent symptomatic infections by pathogenic organisms. There are only two specific groups of patients with asymptomatic bacteriuria who are routinely screened and treated, and these are the pregnant women and those undergoing an endourological procedure with the possibility of mucosal bleeding (Nicolle LE., 2014).

2.9. MICROBIOLOGY

Infections in the urinary tract may be caused by a variety of species, such as parasites, fungi, bacteria, and viruses. The most prevalent cause of acute urinary tract infections (UTIs) is *Escherichia coli*. *Enterobacteriaceae* (such as *Klebsiella* spp. and *Proteus* spp.), *Pseudomonas*, *Enterococcus*, *Staphylococcus aureus, S. aureus* methicillin-resistant MRSA), and *Staphylococcus aureus* (*S. aureus* methicillin-susceptible (MSSA) are among the other uropathogenes. The host has a role in the predominance of particular infections. *Pseudomonas,* for example, is more frequent in people receiving medical treatment or who have internal tools like catheters, whereas *S. saprophyticus* is more prevalent in young women. New utilize of antibiotics of broad-spectrum (eg, third-generation cephalosporin, trimethoprim-sulfamethoxazole, fluoroquinolone or later), obtaining health treatment, and traveling to places of the globe where multidrug-resistant organisms are widespread are all risk factors for urinary tract infections with resistant organisms (Walker E et al., 2016; Smithson A et al., 2012). Multidrug resistance refers to insensitivity to at least one agent in three or more classes of antibiotics. Increased rates of resistance to urinary pathogens have been reported worldwide. In the United States, for example, a study reported a threefold increase in the prevalence of broad-spectrum beta-lactamase-producing Enterobacteriaceae and extended-spectrum beta-lactamase (ESBL) among hospitalized urinary tract infections from 2000 to 2009 (Zilberberg MD, and Shorr AF 2013). In another study of pyelonephritis patients referred to emergency departments across the United States, approximately 6% of the 453 *E. coli* samples isolated from patients produced ESBL (Talan DA et al., 2016). In particular, a specific strain of *E. coli*, called sequence type 131 (ST131), is known worldwide as a major cause of *E. coli*-induced urinary tract infections resistant to fluoroquinolones and producing ESBL. (Lautenbach E, 2013). Carbapenem resistance has also increased among Enterobacteriaceae.

E. coli is the most prevalent cause of urinary tract infections, however not all strains of the bacteria are capable of infecting the urinary system. In the human gastrointestinal system, this bacterium is the most prevalent facultative anaerobic. Many virulence factors in uropathogenic *E. coli* strains (UPECs) boost their capacity to assault the urinary system. Some of the characteristics that make strains capable of producing urinary tract infections also enhance their capacity to cause infections outside of the gut, thus the acronym ExPEC (extraintestinal pathogenic *E. Coli*) (Kranz J et al., 2017). Fimbriae (Latin for thread) and pili (Latin for hair) are superficial nanofibers that extend from a bacterial cell and may be many micrometers long. Fimbriae serve a variety of purposes, including bacterial adhesion to host cells, bacterial accumulation, and genetic material exchange. Due to the presence of mannose-containing receptors, "Type-I" fimbriae have been found to be a crucial factor in bacterial attachment to bladder uroepithelial cells, such as uroplakin (Olson PD et al., 2015). This binding may result in the loss of host tissue cells and bacterial invasion of the bladder wall's deeper cell layers. The organism can control the production of fimbriae, allowing them to be present during the start of a urinary tract infection but not later when their presence is detrimental to the bacterium. At dosages below those necessary to suppress bacterial growth, co-trimoxazole has been demonstrated to diminish the production and function of type I fimbriae, which may explain its usefulness as a preventive drug. Fimbria P can bind to Globo-series glycosphingolipid receptors. These receptors are found in the complex of blood group P antigens and are present in 99% of all renal epithelial cells. The pathogenicity of this fimbria is determined by the finding that uncomplicated upper urinary tract infection with *E. coli* is practically not seen in other 1%. Other binding agents have also been identified in UPEC, including in Fimbria type M, G, and S (Bennett JE, 2014). *E. coli* strains that carry "Dr adhesion" factors may be associated with greater persistence and resistance in the kidney or bladder epithelial cell binding. *E. coli* bacteria include fimbrial and afimbrial structures that bind to the Dr blood group antigen, a membrane protein that blocks complement-mediated cell lysis. These adhesins link to the basement membranes and bladder epithelium to connect to the ureters. (Bahrani-Mougeot, Gunther, Donnenberg, and Mobley, 2002). After a period of apparently successful antibiotic treatment, infections caused by such organisms may result in symptomatic recurrences. UPEC may also diminish the acute immune response by limiting neutrophil transepithelial motility and lowering oxygen species generation of antibacterial reactive. According to research, certain *E. coli* strains which lead to asymptomatic bacteriuria losing their capacity to produce virulence genes. In the system of urinary the existence of such a strain may protect the host against more pathogenic strains causing symptoms. This method has been shown to be effective in the treatment of recurring urinary tract infections (Olson PD et al., 2015; Wullt B, and Svanborg C 2016).

After *E. coli, K. pneumoniae* is the most frequent UTI-related blood-borne infection (bacteremia). This species has the ability to create a wide range of fimbriae, including type 1 fimbriae. *K pneumonia,* on the other hand, produces a polysaccharide capsule with about 70 different antigens around its outer cell membrane. The presence of this capsule hinders phagocytosis and is linked to the development of UTIs in animal studies. Urease is produced by *Klebsiella* species which plays very important role in pathogenesis (Walsh C, and Collyns T 2017).

Proteus comes in a variety of species, but the most prevalent ones that cause infections in people are *Proteus mirabilis* and *Proteus vulgaris*. *P. mirabilis* may produce a simple urinary tract infection, although it generally causes an infection in the urinary system when there are structural problems or when catheterization is used. Fimbria MR / *P. mirabilis* is the most significant fimbria in controlling urinary tract infections in *P. mirabilis*. In a mouse model, these fimbriae have been linked to colonization/bladder infection, and their synthesis can be controlled similarly to type 1 fimbriae in *E. coli* (Flores-Mireles AL et al., 2015). *P. mirabilis* also produces a powerful urease enzyme, which breaks down urea into carbon dioxide and ammonia. As a result, the pH of the urine rises, causing the deposition of struvite, an ammonium magnesium phosphate compound, which leads to the development of a kidney stone. The aforementioned substances may trap live bacteria within the crystal, which may subsequently function as a source of recurring illnesses. As a result, the isolation of *P. mirabilis* from urine samples on a regular basis should raise the suspicion of kidney stones. Surprisingly, the increased alkalinity of the urine causes the loss of white blood cells in the urine, hence there is no pyuria with the infection. Urease may also be produced by *Corynebacterium urealyticum*, *Staphylococcus*, *Pseudomonas*, and *Klebsiella*. The inflammatory reaction of the host to the organism existence may also have a role in stone formation, in addition to the power and quantity of urease generated (Fox-Moon SM, and Shirtliff ME 2015).

Pseudomonas aeruginosa, like other *Pseudomonas*, may be found in a range of habitats, including plants, soil, and water. In healthy hosts, however, *P. aeruginosa* is typically not a significant element of the normal microbial flora, or "microbiome." In health-care settings, *P. aeruginosa* often causes urinary tract infections, which are often linked to urinary catheter implantation. Unless there is a serious urological condition such as blockage, recent manipulation, or neurogenic bladder, this strain seldom causes "acquired" infections in the community. Many popular antibiotics, including cephalosporins, co amoxiclav, nitrofurantoin, and trimethoprim, are naturally resistant to *P. aeruginosa*, which boosts its survivability relative to other species. This bacterium has a number of virulence factors. The established quorum sensing (QS) pathway, which allows bacterial cells to communicate and is involved in the formation and management of biofilms, is one of them. (Mittal R et al., 2009).

Staphylococcal species that cause urinary tract infections can be divided into three categories that consist of *Staphylococcus aureus*, *Staphylococcus saprophyticus*, and other coagulase-negative *staphylococci*.

S. aureus is explained as the "prince of pathogens" because of its combination of virulence elements and its success in colonizing and infecting humans. Nevertheless, it rarely led to uncomplicated urinary tract infections. In the catheter absence, the diagnosis of *S. aureus* in the urine may indicate contamination by the perineal flora. It can also be caused by the bloodstream spreading the infection from another source in the body to the kidneys. Occasionally, the source of infection may be the prostate (Yousefi M et al., 2016).

S. saprophyticus is the most common uncomplicated pathogen causing UTI in sexually active young women, after *E. coli*. However, it rarely causes infections in older men or women. This bacterium has a unique binding protein called UafA that facilitates its adhesion to uroepithelial cells. This bacterium produces urease and also contains a variety of carrier proteins that increase its survival and proliferation against changes in pH and osmotic changes. UTI caused by this organism is more common in late summer and autumn and may be associated with vaginal candidiasis (Bennett JE et al., 2014; Flores-Mireles AL et al., 2015).

The majority of infections produced by Coagulase-negative *staphylococci* occur in hospitalized patients who have a serious urological condition (Bennett JE et al., 2014). Staphylococcus epidermidis is responsible for 90% of these infections. Although this bacterium has relatively little pathogenicity in a healthy host, it has evolved to attach to foreign things and build a biofilm on them, such as urinary catheters. Autolysins, which bind directly to plastics and other substances, and bacterial products including accumulation associated protein, Bap homologous proteins, intercellular binding polysaccharides, and extracellular DNA, which aid in the formation of biofilms, are all produced by the bacteria (Walsh C and Collyns T, 2017).

Enterococcus causes less than 5% of uncomplicated urinary tract infections. However, this organism is known to be one of the causes of healthcare-related infections in the presence of urinary catheters or other urinary abnormalities or manipulations. *Enterococci* are inherently resistant to several common antibiotics. The two main strains of infection are *Enterococcus faecalis* and *Enterococcus faecium*, the latter of which are inherently resistant to penicillin such as ampicillin or piperacillin. *Enterococci* are well-suited for colonization in the human gastrointestinal tract and host-receiving antibiotics such as cephalosporins, as they can change the balance in favor of *enterococci* proliferation by inherently tolerating many classes of antibiotics. *Enterococci* can produce a variety of binders and aggregates that form and maintain biofilms. *Enterococci* have relatively little pathogenicity and may only colonize catheters rather than cause symptomatic infection. Similarly, their presence may prevent the successful invasion of pathogenic species into the urinary tract, meaning that treatment of asymptomatic bacteriuria can be associated with symptomatic infection due to the presence of a different organism (Bennett JE et al., 2014; Flores-Mireles AL et al., 2015).

Streptococcus agalactiae, like *enterococci*, is a highly susceptible bacteria found in the lower gastrointestinal tract (10% - 25%) and the female vaginal region (10%- 40 %). Female genital assaults may be exacerbated by a variety of circumstances, including increasing race, diabetes, and activity of sexual. From asymptomatic bacteremia to urosepsis, Group B *streptococci* may cause a wide spectrum of clinical symptoms. Detection of group B *streptococci* bacteriuria during pregnancy suggests significant genital tract colonization and should be avoided during delivery to avoid invasive infection in the newborn. (Bennett JE et al., 2014).

Corynebacterium is a common skin flora. This organism is no exception to this rule because its colonization is observed in the skin of more than one-third of hospitalized patients. A special feature of this bacterium is its ability to bind to uroepithelial cells and produce urease. This organism can cause chronic or recurrent urinary tract infections in patients who have a previous predisposing factor for urinary tract infections. Due to its ability to produce urease, it can cause "Encrusted cystitis" in which there is a chronic inflammation of the bladder mucosa with crystalline deposits and marginal erythema. In cases where the upper urinary tract is abnormal, there is always a possibility of encrusted pyelitis (Bennett JE et al., 2014).

Ahmed et al. published a research in 2019 that looked at the incidence of urinary pathogens in UTIs and the patterns of antibiotic resistance found in them. 273 urine samples from outpatients at Qassim University Teaching Hospital were used in this investigation. Microorganisms' antimicrobial susceptibility was identified and tested using the fully automated VITEK 2 system. Only 89 (32.6 percent) of the 273 urine samples indicated substantial growth for urinary tract infections, and medication resistance was found in 92 percent of the samples, with the majority (80 percent) being resistant to at least two medications. Antibiotic resistance was found often against ampicillin (86.3%), piperacillin (72.7%), clindamycin (66.7%), amoxicillin/clavulanic acid (66.2%), and trimethoprim/sulfamethoxazole (66.2%). (50 percent) *Escherichia coli* 24 (27 percent), *Klebsiella pneumoniae* 11 (12.4 percent), *Proteus mirabilis* 4 (4.5 percent), *Pseudomonas aeruginosa* 4 (4.5 percent), *Enterobacter cloacae* 5 (5.6 percent), *Enterococcus faecalis* 5 (5.6 percent), and *Staphylococcus saprophyticus* 3 (3.6 percent) are among the most common bacteria isolated from urine samples (Ahmed SS et al., 2019).

Kahlmeter et al. (2015) conducted a research in France, Germany, Spain, Sweden, and the United Kingdom to assess *Escherichia coli* antimicrobial resistance to the medications mecillinam, amoxicillin-Clavulanic acid, cephadroxil, Nitrofurantoin, ciprofloxacin, and trimethoprim in women with simple urinary tract infections. The findings were also compared to those of the ECO.SENS 1 and 2 investigations, which were conducted in 2000 and 2008, respectively. Disk diffusion and antimicrobial susceptibility testing methods based on the European Committee were used to determine *E. coli* susceptibility in France (166 isolates), Germany (133 isolates), Spain (169 isolates), Sweden (137 isolates), and the United Kingdom (124 isolates). Since 2000, resistance to cephadroxil has increased significantly in Germany (1 percent to 12 percent) and Spain (3 percent to 8 percent), ciprofloxacin resistance has increased significantly in Germany (2 percent to 21 percent), Spain (15 percent to 31 percent), Sweden (0 percent to 7 percent), and the United Kingdom (1 percent to 15 percent), and trimethoprim resistance has increased significantly in Germany (23 percent to 37 percent), Spain (15 percent to 31 percent), Sweden (0 percent to 7 percent), and the United Kingdom (1 percent to 15). In Spain, nitrofurantoin resistance has also decreased significantly (4 percent to 0 percent). Since 2008, there has been a considerable rise in ciprofloxacin resistance in Sweden (3 percent to 15 percent) and the United Kingdom (1 percent to 15 percent), as well as trimethoprim (13 percent to 46 percent) and nitrofurantoin resistance in the UK (0 percent to 6) (Kahlmeter G et al., 2015).

Niranjan et al. performed a research in 2014 to assess the antibiotic resistance trend in UTI-causing *Escherichia coli* strains in patients referred to a medical institution in northern India. Laboratory findings and patient information were used to gather characteristics of *E. coli* cultured in urine samples, as well as their pattern of antibiotic susceptibility. Antibiotic susceptibility was determined using the Kirby-Bauer disk diffusion test on urine samples obtained using conventional processing techniques. 119 instances (38.2%) of the 311 isolated *E. coli* samples were obtained from hospitalized patients and were included in the research. 91 (76.51 percent) of the 119 *E. coli* samples were multidrug-resistant (MDR). Resistance to co-trimoxazole (71.4%), ceftriaxone (71.4%), cefuroxime (72.2%), norfloxacin (74.2%), amoxicillin-clavulanic acid (74.4%), and ampicillin (88.4%) was found in isolated bacteria. Imipenem (82.1%), nitrofurantoin (82.1%), piperacillin-tazobactum (78.2%), and amikacin (82.6%) were all shown to be susceptible to the isolates (98.9%). Ceftriaxone was extensively used in hospitalized patients for the experimental treatment of urinary tract infections. 73 of the 93 cases with MDR *E. coli* urinary tract infections improved with therapy, whereas 12 deteriorated and were sent to higher facilities (Niranjan V, and Malini A 2014).

In 2013, Bouchillon et al. conducted a research for determining the incidence of antibiotic resistance in bacteria isolated from UTI patients' samples. The minimal concentration and inhibitory sensitivity were calculated using the Institute of Clinical and Laboratory Standards' criteria. In this research, 2135 bacterial samples from the urine of UTI patients hospitalized in 24-point US hospitals were investigated. Enterobacteriaceae accounted for 88.6% (1892 cases), with 48.9% (n = 1045) *Escherichia coli*, 2.5 percent (n = 54) *Proteus mirabilis*, 6.4 percent (n = 136) *Proteus vulgaris*, and 14.5 percent (n = 310) *Klebsiella pneumoniae*. Other Enterobacteriaceae accounted for 16.3 percent (n = 347) of the species. In all, 6.8% of *E coli* strains, 10.3 percent of *K pneumoniae*, 3.7 percent of *P mirabilis*, and 11.1 percent of *K oxytoca* produced broad-spectrum -lactamases. 67.5 percent of Enterobacteriaceae isolates came from the community, whereas 26.9% came from a hospital (7.5 percent had no demographics). During the research period, amikacin, ertapenem, and imipenem showed the greatest levels of antibacterial activity. Ampicillin-sulbactam, ciprofloxacin, and levofloxacin had the lowest antibacterial activity (Bouchillon et al. 2013).

A research has been done by Bagheri et al. in 2014 to investigate the frequency of multiple drug resistance in bacteria of gram-negative isolated from infections of urinary tract. This study was performed in Gorgan in 1990-91 on 111 gram-negative bacteria that were detected by standard microbiological methods. The antibiotic susceptibility of the samples was evaluated by the Kirby Bauer disk diffusion method. *Klebsiella* was isolated with a frequency of 40.5% of pathogens, followed by *Enterobacter* with a frequency of 26.1%, *Acinetobacter* 1.8%, *Proteus* 6.3%, *Pseudomonas* 13.5%, and other gram-negatives 18.3%. The greatest resistance of antibiotic was observed to clindamycin (99.1%) and the highest sensitivity was observed to carbapenems (94.6%). 68.5% of the findings were resistant to several antibiotics simultaneously, all *citrobacteria* were resistant to several antibiotics simultaneously in hospitalized patients (Bagheri et al. 2014).

A study was conducted by Jahromi Atashi in 2020 in Bandar Abbas for investigating the frequent causes of infections of urinary tract and their antibiotic resistance in patients admitted to Shahid Mohammadi Hospital. This retrospective study was a descriptive cross-sectional study. To collect information from these files, a two-part checklist was used, the first part of which included demographic information including age, sex, and diabetes history of the patients, and the second part which included specialized information including mass grown in urine culture and anti-resistance pattern. The data were entered into SPSS statistical software version 22 and parametric statistical tests such as Chi-square and t-test were used, and in cases where the statistical distribution was not known, non-parametric tests were used. The significance level in this study was considered p value <0.05. In the end, a total of 100 cases of patients with infections of urinary tract admitted to Shahid Mohammadi Hospital in 2020 were included in the study, of which 64 patients (64%) were female and 36 patients (36%) were male. 63 patients (63%) were admitted to inpatient wards and 37 patients (37%) were admitted to surgical wards and 43 patients (43%) had diabetes. The mean age of the patients was 1.60. The minimum age was 22 years and the highest age was 94 years. The most common agents were *E. coli*, *Klebsiella*, and *Enterococci*, respectively. The highest resistance was to ciprofloxacin, cefotaxime, and cotrimoxazole, respectively. There was no significant difference among the mean age of the patients and their diabetes mellitus in terms of bacterial factors of their urinary tract infections (P> 0.05), but the difference between sex and hospital ward was significant in terms of bacterial elements of infection of urinary tract (P <0.05). The study reports that neither bacterial factors nor antibiotic resistance was significantly different in terms of the mean age in patients (P> 0.05). Also, bacterial factors of urinary tract infections and in hospitalized patients do not differ significantly by sex (P> 0.05). Differences in antibiotic resistance of bacterial agents of urinary tract infections in terms of their sex were significant only in ciprofloxacin and ampicillin-sulbactam antibiotics (P <0.05). One of the unique results of this study was that the difference in the ward of the patients in terms of bacterial factors of their urinary tract infection was significant (P <0.05) which can be attributed to the difference in the microbial flora of each ward. Other unique results of this study include a significant difference in antibiotic resistance of bacterial agents of urinary tract infections of patients regarding their ward, which was noted only in the antibiotic cotrimoxazole (P <0.05) (Jahromi Atashi in 2020).

3. MATERIAL AND METHOD

This is a cross-sectional-analytical study with a retrospective design. Patients referred to Erbil hospitals with urine culture results in the last five years (2015- 2020). All the results of urine cultures of patients referred to Erbil hospitals in the last five years were included in the census method (Hospitals' names: Rzgary Teaching Hospital, Hawler Teaching Hospital, General Health Laboratory in Erbil, and CMC Private Hospital). A total of 3380 samples were examined.

3.1. INCLUSION AND EXCLUSION CRITERIA OF THE STUDY

Inclusion criteria: age over 18 years, positive urine culture (more than 100,000 bacteria), outpatients, mid-stream sampling. Exclusion criteria: age less than 18 years, hospitalized patients.

This cross-sectional-analytical study was performed to evaluate the results of urine culture of outpatients of Rzgary Teaching Hospital, Hawler Teaching Hospital, General Health Laboratory in Erbil, and CMC Private Hospital from 2015 to 2020. We used CLSI standards to identify uropathogens and evaluate antimicrobial susceptibility. Samples were taken from the middle stream of urine and sterilized, and the samples were transferred to the laboratory. The time between urine collection and culture was 2 hours, and in case of delay in performing the test, the samples were stored in a refrigerator at 4 ° C. Samples were cultured by standard loop method in Blood Agar and MacConkey agar (manufactured by Merck Germany) after incubation at 37 ° C for 18-24 hours. Samples with colony count equal to or greater than 10^5 CFU / ml of urine were considered as a positive culture. If it did not grow for 48 hours at 37 ° C incubation, a negative result was reported. When three or more different bacterial colonies were identified without a clear predominance of a species, the sample was considered contaminated. Microorganisms were identified, and their susceptibility was assessed by VITEK 2 continuous system.

VITEK 2 is a growth-based and technology-based automated microbiology system. Colorimetric reagent cards are automatically incubated and evaluated in this system. AES, which examines minimum inhibitory concentration (MIC) patterns and identifies phenotypes for most organisms examined, is part of the system. Rapid findings enable doctors to stop using experimental medication and instead prescribe tailored antibiotics, which improves patient outcomes and increases antibiotic monitoring. There are 64 microwells on the VITE 2 card. A substrate of antimicrobial or detectable is included in each well. Because the VITEK 2 test card is sealed, sample contamination is reduced. When compared to microtiter technologies, disposable waste is decreased by more than 80%. The results were reported based on the age groups of 18-48 years, 46-60 years and more than 60 years. Gram-negative uropathogens isolated against various antibiotic susceptibility panels including Ampicillin, Cefepime, Aztreonam, Cefixime, Ceftriaxone, Ertapenem, Amoxicillin/Clavulanate, Piperacillin/tazobactam, Amikacin, Cefotaxime, Imipenem, Meropenem, Ceftazidime, Nitrofurantoin, Levofloxacin, trimethoprim/sulfamethoxazole, Ciprofloxacin and Gentamicin were tested.

3.2. DESIGN LIMITATIONS

Since this study is retrospective, it was not possible for everyone to obtain information such as antibiotics used in the last six months, etc., which are not routinely questioned or recorded from outpatients. Since the study is multicenter, there may be differences in the devices used for microbial analysis of urine.

3.3. STATISTICAL ANALYZES

the data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0 software (IBM Corp). The results of descriptive analysis were reported by tables and graphs. Chi-square test was used to examine the relationship between variables. A significance level of 0.05 was considered.

4. RESULTS

Table 4-1: Gender distribution of the studied samples according to age groups

	18 to 45 years	46 to 60 years	>60 years	Total
Male	159 (4.7%)	397 (11.7%)	489 (14.5%)	1045 (30.9%)
Female	1330 (39.3%)	558 (16.5%)	447 (13.2%)	2335 (69.1%)
Total	1489 (44.1%)	955 (28.3%)	936 (27.7%)	3380 (100%)

As can be seen in Table 4-1, the results of urine culture analysis of 3380 suspected UTIs were evaluated in this study. 69.1% of the subjects were female and 30.9% were male. The majority of the study population (44.1%) was in the age group of 18 to 45 years. The population distribution between the ages of 46 and 60 and over 60 was almost the same. As shown in Figure 4-1, the population of women in the age group of 18 to 45 years is much larger (approximately 8 times) than population of men. In other age groups, however, this difference is small, and even in the "over 60s" age group, men number a little more than women. Chi-square test showed a significant difference between age groups in terms of gender distribution ($p = 0.000$).

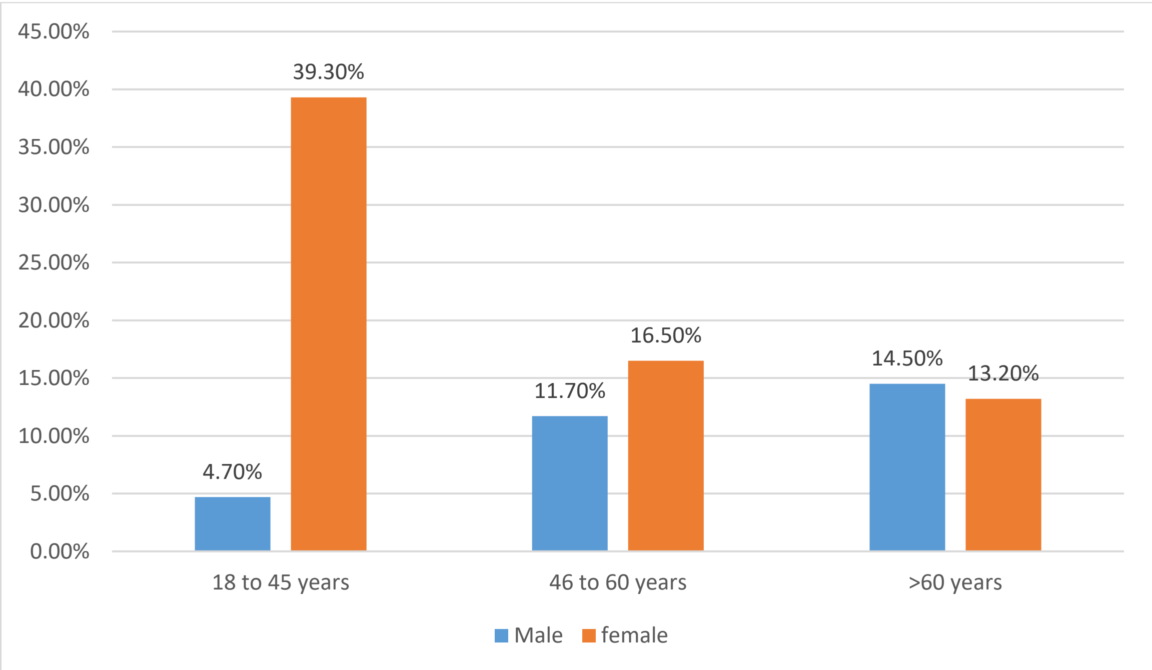

Figure 4-1: Gender distribution of the studied samples according to age groups

Table 4-2: Frequency distribution of urine samples in age groups

	18 to 45 years	46 to 60 years	>60 years	Total
No growth	79 (5.3%)	56 (5.8%)	53 (5.6%)	188 (5.6%)
Contamination	41 (2.8%)	22 (2.4%)	32 (3.4%)	95 (2.8%)
UTI	1369 (91.9%)	877 (91.8%)	851 (91%)	3097 (91.6%)
Total	1489 (100%)	955 (100%)	936 (100%)	3380 (100%)

Table 4-2 shows the results of urine cultures. 3097 samples (91.6%) were positive cultures, while “contamination” and “no growth” cases represented 2.8% and 5.6% of the total, respectively. The proportion of positive culture cases in various age groups was very similar. Overall, the culture results of 3097 samples were evaluated in the present study. Figure 4-2 also shows the cases of positive cultures by age groups, where no significant difference was observed between the age groups. The results of Chi-square test did not show a significant difference between age groups in terms of positive urine culture distribution either (p = 0.997).

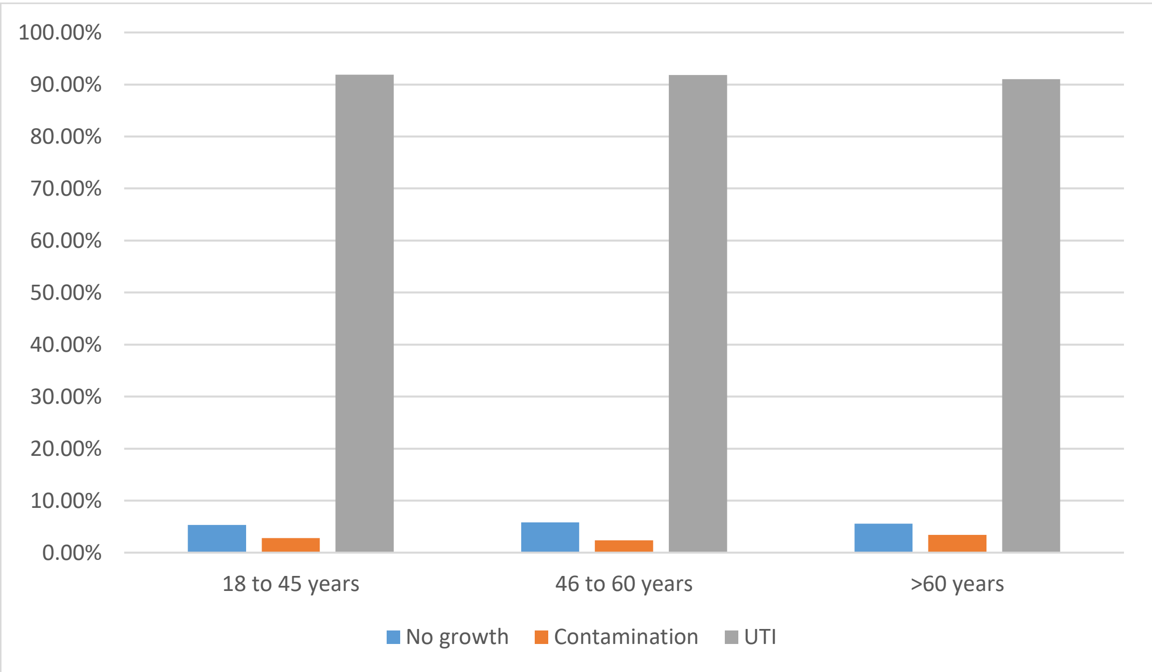

Figure 4-2: Frequency distribution of urine samples in age groups

Table 4-3: Results of gram staining of pathogens isolated from urine samples

	18 to 45 years	46 to 60 years	>60 years	Total
Gram-negative	867 (28%)	553 (17.9%)	541 (17.5%)	1961 (63.3%)
Gram-positive	502 (16.2%)	324 (10.5%)	310 (10%)	1136 (36.7%)
Total	1369 (44.2%)	877 (28.3%)	851 (27.5%)	3097 (100%)

Table 3-4 shows the results of gram staining for positive culture samples. In total, 1961 (63.3%) isolates were gram-negative bacteria and 1136 (36.7%) were gram-positive pathogens. The tests in this study are performed on gram-negative bacteria (and therefore the final sample size) will include 1961 gram-negative bacteria. Figure 4-3 also shows that in all three age groups, gram-negative bacteria were more common than gram-positive pathogens, but the results of Chi-square test showed no significant difference between the results of gram-staining and age groups (p = 0.975).

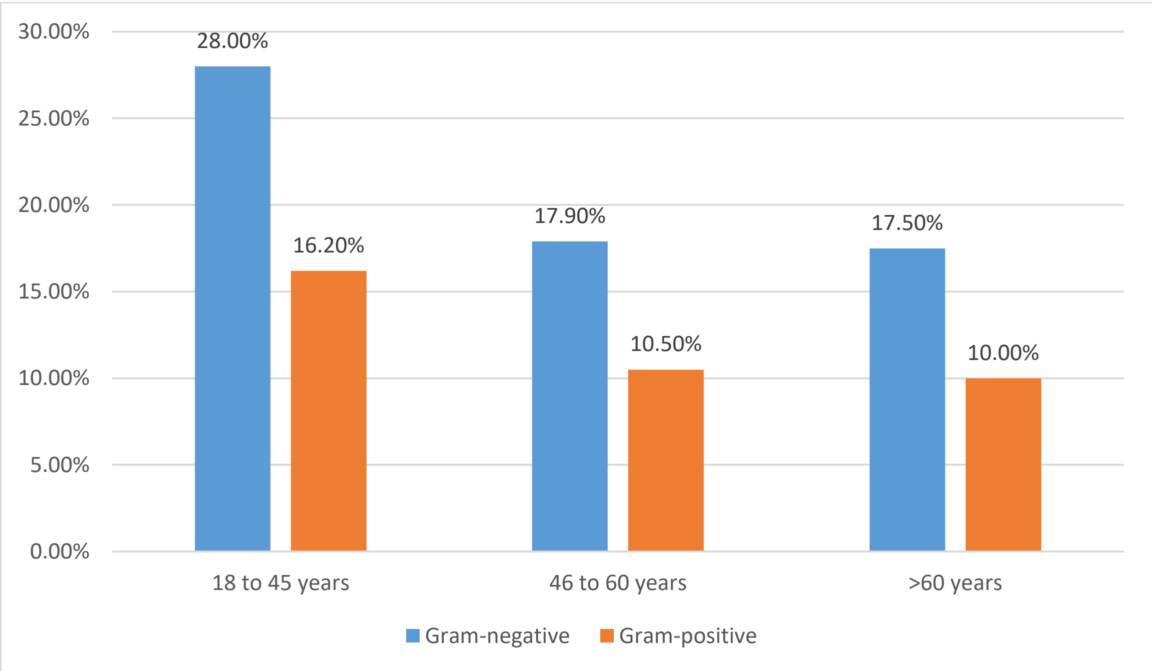

Figure 4-3: Results of gram staining of pathogens isolated from urine samples by age groups

Table 4-4: Prevalence of gram-negative bacteria in urine samples by fermentative/ none fermentative and prevalence of broad-spectrum beta-lactamase-producing strains

		Frequency	ESBL
Non-fermentative (n=93)	*P. aeruginosa*	67 (3.4%)	0 (0%)
	S. paucimobilis	4 (0.2%)	0 (0%)
	A. baumannii cplx	13 (0.7%)	0 (0%)
	A. haemolyticus	4 (0.2%)	0 (0%)
	A. lwoffii	5 (0.3%)	0 (0%)
Fermentative (n=1868)	*E. coli*	1373 (70%)	530 (38.6%)
	K. pneumoniae	334 (17%)	134 (40.1%)
	P. mirabilis	77 (3.9%)	6 (7.8%)
	E. cloacae complex	27 (1.4%)	10 (37%)
	E. aerogenes	25 (1.3%)	9 (36%)
	K. oxytoca	12 (0.6%)	5 (41.7%)
	M. morganii	9 (0.5%)	0 (0%)
	S. marcescens	5 (0.3%)	0 (0%)
	Salmonella group	3 (0.2%)	0 (0%)
	Shigella group	3 (0.2%)	2 (66.7%)
Total		1961 (100%)	696 (35.5%)

Table 4-4 shows the frequency of gram-negative urinary pathogens in the study sample. In total, 4.7% (93 cases) of the studied gram-negative bacteria were non-fermenters. The most common pathogen identified was *Escherichia coli*, which accounted for 70% of gram-negative isolates. *Klebsiella pneumoniae* (17%), *Proteus mirabilis* (3.9%) and *Pseudomonas aeruginosa* (3.4%) were the following most common pathogens, respectively. of the *Escherichia coli* isolates, 38.6% were broad-spectrum beta-lactamase-producing strains. Figure 4-4 also illustrates these findings. However, the strains with the highest ESBL production were *Shigella group* (66.7%; 2 out of 3), *Klebsiella oxytoca* (41.7%; 5 out of 12) and *Klebsiella pneumonia*. (40.1%; 134 out of 334 cases). Overall, 35.5% (696 cases) of gram-negative isolates produced ESBL. Figure 4-5 also shows the abundance of broad-spectrum beta-lactamase-producing strains among gram-negative bacteria.

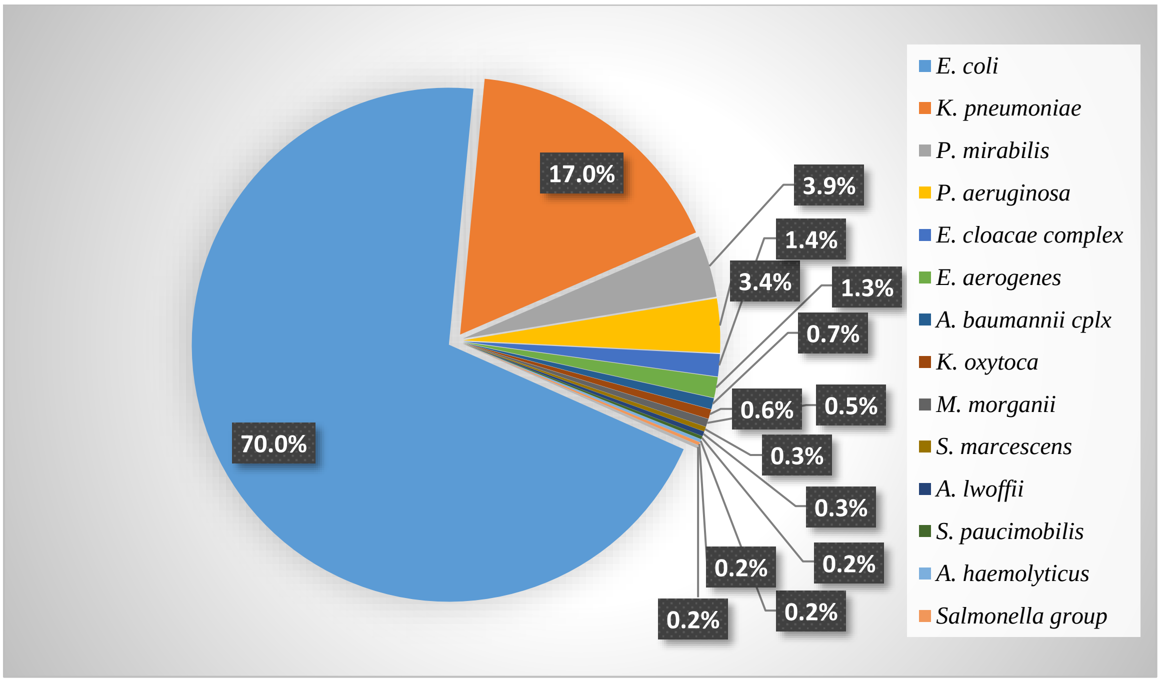

Figure 4-4: Prevalence of gram-negative bacteria in urine samples

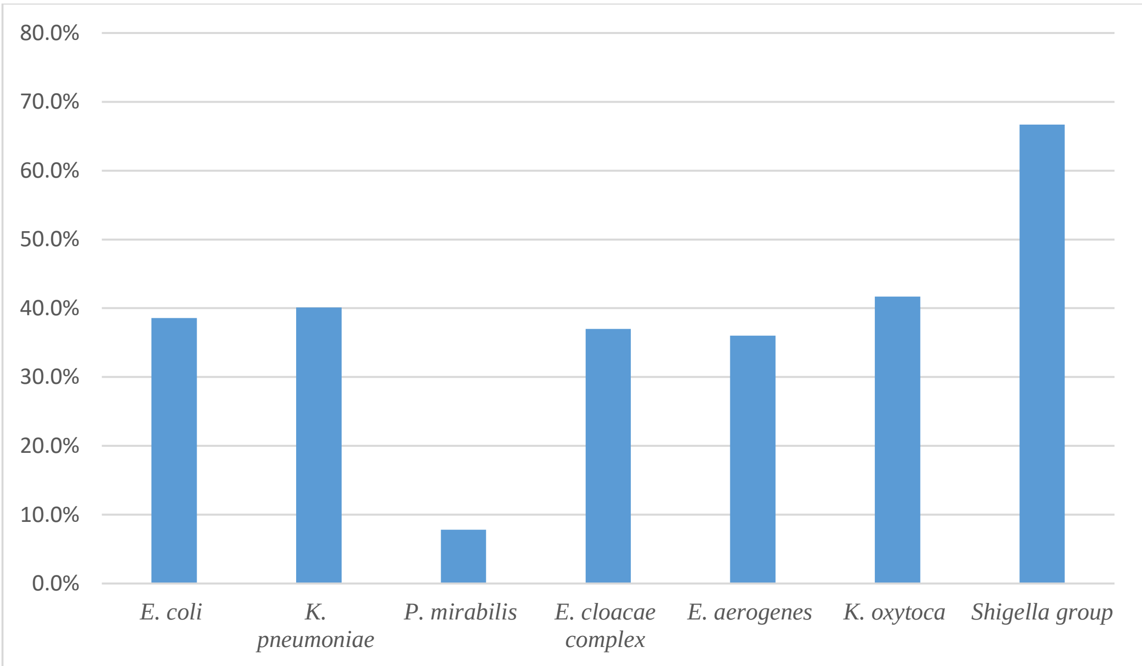

Figure 4-5: Prevalence of broad-spectrum beta-lactamase-producing strains among gram-negative bacteria

Table 4-5: Prevalence of antimicrobial resistance in gram-negative isolates (%).

	E coli	*K. pneumoniae*	*P. mirabilis*	*P. aeruginosa*	*S. paucimobilis*	*E. cloacae complex*	*A. baumannii*	*S. marcescens*	*Salmonella group*	*E. aerogenes*	*K. oxytoca*	*A. haemolyticus*	*A. lwoffii*	*M. morganii*	*Shigella group*
Ampicillin	929 (67.7)	250 (74.9)	46 (59.7)	20 (29.9)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (58.3)	0 (0)	0 (0)	5 (55.6)	1 (33.3)
Amoxicillin/Clavulanate	190 (13.8)	46 (13.8)	7 (9.1)	21 (31.3)	0 (0)	19 (70.4)	0 (0)	2 (40)	0 (0)	18 (72)	1 (8.3)	0 (0)	0 (0)	5 (55.6)	1 (33.3)
Amikacin	3 (0.2)	9 (2.7)	2 (2.6)	2 (3)	0 (0)	1 (3.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)
Aztreonam	81 (5.9)	23 (6.9)	1 (1.3)	0 (0)	0 (0)	1 (3.7)	0 (0)	0 (0)	0 (0)	2 (8)	2 (16.7)	0 (0)	0 (0)	0 (0)	1 (33.3)
Ceftazidime	343 (25)	111 (33.2)	3 (3.9)	7 (10.4)	0 (0)	13 (48.1)	4 (30.8)	0 (0)	0 (0)	11 (44)	2 (16.7)	0 (0)	0 (0)	1 (11.1)	2 (66.7)
Cefixime	431 (31.4)	105 (31.4)	6 (7.8)	21 (31.3)	1 (25)	13 (48.1)	0 (0)	1 (20)	0 (0)	13 (52)	0 (0)	0 (0)	0 (0)	1 (11.1)	0 (0)
Ciprofloxacin	364 (26.5)	31 (9.3)	8 (10.4)	4 (6)	1 (25)	1 (3.7)	4 (30.8)	0 (0)	0 (0)	1 (4)	2 (16.7)	1 (25)	1 (20)	1 (11.1)	1 (33.3)
Ceftriaxone	449 (32.7)	112 (33.5)	2 (2.6)	12 (17.9)	0 (0)	10 (37)	2 (15.4)	1 (20)	0 (0)	15 (60)	1 (33.3)	1 (25)	0 (0)	1 (11.1)	1 (33.3)
Cefotaxime	111 (8.1)	36 (10.8)	1 (1.3)	4 (6)	0 (0)	3 (11.1)	2 (15.4)	0 (0)	0 (0)	2 (8)	2 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
Ertapenem	6 (0.4)	3 (0.9)	1 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cefepime	55 (4)	15 (4.5)	2 (2.6)	2 (3)	0 (0)	1 (3.7)	1 (7.7)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)
Nitrofurantoin	29 (2.1)	26 (7.8)	48 (62.3)	17 (25.4)	0 (0)	0 (0)	1 (7.7)	2 (40)	1 (33.3)	3 (12)	0 (0)	0 (0)	0 (0)	3 (33.3)	0 (0)
Gentamicin	193 (14.1)	79 (23.7)	14 (18.2)	3 (4.5)	0 (0)	9 (33.3)	4 (30.8)	0 (0)	0 (0)	7 (28)	1 (8.3)	1 (25)	0 (0)	2 (22.2)	0 (0)
Imipenem	5 (0.4)	2 (0.6)	7 (9.1)	2 (3)	0 (0)	1 (3.7)	1 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (22.2)	0 (0)
Levofloxacin	46 (3.4)	5 (1.5)	0 (0)	2 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Meropenem	4 (0.3)	2 (0.6)	0 (0)	1 (1.5)	0 (0)	0 (0)	1 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TMP/SMX	714 (52)	156 (46.7)	43 (55.8)	20 (29.9)	1 (25)	14 (51.9)	2 (15.4)	0 (0)	0 (0)	9 (36)	4 (33.3)	1 (25)	0 (0)	6 (66.7)	1 (33.3)
Piperacillin/tazobactam	67 (4.9)	11 (3.3)	0 (0)	6 (9)	0 (0)	2 (7.4)	4 (30.8)	0 (0)	0 (0)	6 (24)	2 (16.7)	1 (25)	0 (0)	0 (0)	1 (33.3)

Table 4-5 shows the prevalence of antimicrobial resistance in gram-negative isolates. Of *Escherichia coli* isolates, 67.7% are resistant to Ampicillin, 52% to TMP / SMX, 32.7% to ceftriaxone and 31.4% to Cefixime. The lowest antibiotic resistance was reported to *Escherichia coli* for the antibiotics Amikacin (0.2%), Meropenem (0.3%), Imipenem (0.4%) and Ertapenem (0.4%). These four antibiotics also showed the highest sensitivity in other isolates. The pattern of resistance of antibiotics to *K. pneumoniae* was largely similar to that of *Escherichia coli*. In *Enterobacter cloacae* complex isolate, the highest resistance was related to Amoxicillin / Clavulanate.

Resistance to Ertapenem and Levofloxacin was reported in only three types of gram-negative urinary pathogens and the rest of the strains were quite sensitive. Only *Serratia marcescens* and *Salmonella* strains showed no resistance to Ciprofloxacin, and resistance to this antibiotic was observed in other strains.

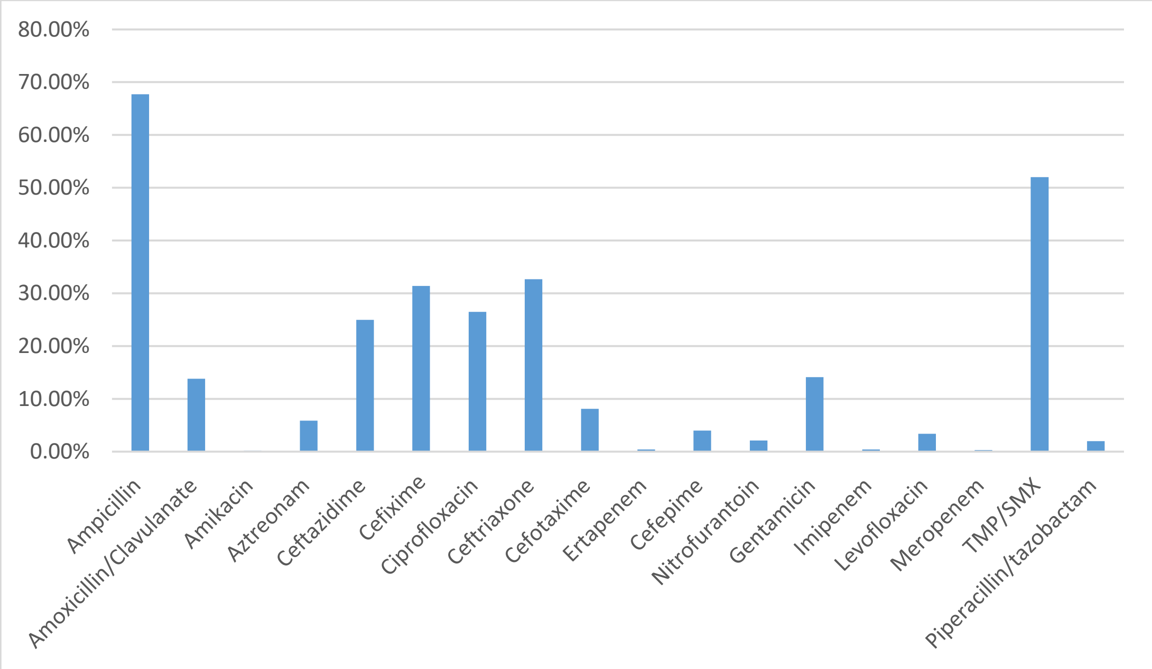

Figure 4-6: Resistance of *Escherichia coli* strains to different antibiotics

5. DISCUSSION AND CONCLUSION

5.1. DISCUSSION

In this study, the results of urine culture of patients with suspected UTI in Erbil were evaluated. The aim of this study was to evaluate the prevalence of gram-negative urinary pathogens and the prevalence of broad-spectrum beta-lactamase-producing strains. In general, the results of urine culture of 3380 suspected UTI cases were examined, of which 69.1% were female and 30.9% were male. The majority of them (44.1%) were in the age group of 18 to 45 years. The results of urine culture showed that in 3097 samples (91.6%) positive urine culture was reported while contamination and no growth cases were included in 2.8% and 5.6%, respectively. Out of 3097 positive cultures observed, a total of 1961 (63.3%) isolates were gram-negative bacteria and 1136 (36.7%) were gram-positive pathogens. Among 1961 gram-negative isolates, 93 (4.7%) were non-fermenters. The most common pathogen identified was *Escherichia coli*, which accounted for 70% of gram-negative isolates. *Klebsiella pneumoniae* (17%), *Proteus mirabilis* (3.9%) and *Pseudomonas aeruginosa* (3.4%) were the following most common pathogens, respectively. *Escherichia coli* strains showed the highest resistance to Ampicillin (67.7%), TMP/SMX (52%), Ceftriaxone (32.7%) and Cefixime (31.4%). The lowest antibiotic resistances reported for *Escherichia coli* were for the antibiotics Amikacin (0.2%), Meropenem (0.3%), Imipenem (0.4%) and Ertapenem (0.4%). The most volatile strains producing broad-spectrum beta-lactamase relative to the population of each strain were found among *Shigella*, *Klebsiella oxytoka*, *Klebsiella pneumoniae*, and *Escherichia coli*, respectively.

In the present study, the most common uropathogen is *Escherichia coli*, which accounted for 70% of gram-negative isolates, followed by *Klebsiella pneumonia* (17%), *Proteus mirabilis* (3.9%) and *Pseudomonas aeruginosa* (3.4%). Previous studies have reported similar results. In the study of Ahmed et al. (2019), the most common uropathogens were *Escherichia coli* (27%), *Klebsiella pneumoniae* (12.4%), *Proteus mirabilis* (4.5%) and *Pseudomonas aeruginosa* (4.5%) (Ahmed, Shariq, Alsalloom, Babikir, and Alhomoud, 2019). Aktaş and Denktaş (2020) identified *Escherichia coli* as the most common strain (48%) among gram-negative pathogens, followed by *Klebsiella* (Aktaş and Denktaş, 2020). Abujnah et al. (2015) reported similar results in Libya. Osman (2019), gupta et al. (2007) and Giwa et al. (2018) identified the most common gram-negative uropathogens as *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa* (Giwa et al., 2018; Gupta, Kundra, Sharma, Gautam, and Arora, 2007; Osman, 2019). In some studies, *Proteus mirabilis* was more common than *Pseudomonas*(Giwa et al., 2018), and in others(Gupta et al., 2007), vice versa. Therefore, our findings were consistent with other studies and showed that *Escherichia coli* is the most common uropathogen. The above studies reported the prevalence of uropathogens as a whole positive culture results, but the present study examined their prevalence among gram-negative bacteria, so numerical differences can be justified. The present study evaluated a larger sample than others, which increases the validity of the results.

In the present study, Imipenem, Meropenem, Ertapenem and Amikacin were the most effective antibiotics against gram-negative uropathogens (especially *Escherichia coli*). In the study of Aktaş and Denktaş (2020), *Escherichia coli* strains showed the lowest resistance to these four antibiotics (Aktaş and Denktaş, 2020). A study by Ali et al. (2017) in Erbil showed the lowest resistance of *Escherichia coli* to imipenem (1.25%), meropenem and amikacin (1.9%) and Ertapenem (3.8%) (Ali, Merza, and Aula, 2017). These findings were consistent with our results. The only difference was in the order of antimicrobial susceptibility. For example, in the study of Mohammed et al. (2016), amikacin was the most effective antibiotic (Mohammed, Alnour, Shakurfo, and Aburass, 2016), while Ullah et al. (2018) named meropenem as the most sensitive and appropriate antibiotic for the treatment of UTI caused by gram-negative pathogens (Ullah, Shah, Almugadam, and Sadiqui, 2018). Thus, the most sensitive antibiotics were almost identical in all studies, indicating that the four antibiotics amikacin, imipenem, meropenem, and ertapenem could be effective treatments for bacterial infections resistant to conventional therapies. On the other hand, in the present study, *Escherichia coli* strains showed the highest resistance to Ampicillin (67.7%), TMP /

SMX (52%), Ceftriaxone (32.7%) and Cefixime (31.4%). Consistent with these findings, Edlin et al. Showed that *Escherichia coli* strains in UTI patients were most resistant to ampicillin and trimethoprim / sulfamethoxazole (Edlin, Shapiro, Hersh, and Copp, 2013). A study by Abujnah et al. (2015) in Libya showed that the resistance to ampicillin in *Escherichia coli* and *Klebsiella* species was 69.2% and 100%, respectively (Abujnah et al., 2015). Similarly, the study of Osman (2019) and Mohammed et al. (2016) reported the highest antimicrobial resistance to ampicillin (Mohammed et al., 2016; Osman, 2019). Some studies have reported different results. Ali et al. (2017) reported the highest resistance of *Escherichia coli* to Cefepime (66.9%), Trimethoprim / Sulfamethoxazole (60%), Ciprofloxacin (54.4%) and Gentamycin (40.6%) (Ali et al., 2017). This difference is due to the assessment of different samples (blood, urine, pus, sores) in the above study and these results cannot be considered inconsistent with this study. Gupta et al. (2007) reported resistance of cotroprimoxazole, ampicillin and ciprofloxacin to the three uropathogens of *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas* between 90% to 96%, 92% to 98% and 55% to 65%, respectively (Gupta et al., 2007). The resistance of these three pathogens in the present study to cotrimoxazole was between 29.9 to 52%, to ampicillin between 29.9 to 74.9%, and to ciprofloxacin between 6 to 26.5%. Although there was considerable agreement in the report of the most common gram-negative urinary pathogens between the two studies, the level of resistance to antibiotics do not match, and the level of resistance in the above study conducted in India was much higher than the findings of the present study.

This discrepancy is probably due to the high prevalence of infectious diseases and ineffective use of antibiotics in India, which have been reported in various studies (Ganguly et al., 2011). Findings from previous studies have shown that resistance to antibiotics varies in different parts of the world. Developing countries such as India and Libya have reported very high resistance to conventional antibiotics. However, in the present study, antibiotic resistance was relatively high and it seems that widespread and careless use of antibiotics has caused this resistance. However, due to the high sensitivity of other antibiotics, there are currently no specific issues in the treatment of urinary tract infections with gram-negative pathogens, but prevention of unnecessary antibiotic use is a good approach to prevent increased antimicrobial resistance.

ESBL-producing bacteria are resistant to many common antibiotics, and the increasing prevalence of these bacteria is an indicator of increased antimicrobial resistance. In the present study, 38.6% of *Escherichia coli* strains were ESBL positive. Aktaş and Denktaş (2020) reported 27.8% of *Escherichia coli* samples as extended-spectrum beta-lactamase-producing strains (Aktaş and Denktaş, 2020). Given the novelty of the above study, it can be concluded that the prevalence of EBSL-producing strains of *Escherichia coli* in Erbil, Iraq is higher than in Turkey. It appears to be because of the unscrupulous use of antibiotics in Erbil. According to previous studies, the treatment of ESBL-producing *Escherichia coli,* which is commonly observed in community-acquired UTIs, is a challenge (Hertz et al., 2016). In the study of Giwa et al. (2018), ESBL-producing strains generally accounted for 34.3% of cases (Giwa et al., 2018). These findings were consistent with the results of present study with a 35.5% prevalence of ESBL-positive bacteria.

The problem of antimicrobial resistance in bacterial pathogens is described as a growing global crisis. The reported resistance to common pathogens in many parts of the world has reached a level where the experimental use of many of the strongest and most reliable antimicrobial agents available has been ineffective (Martens and Demain, 2017). The present study is unique because no research has been conducted with this large sample size in Erbil. In general, the level of antimicrobial resistance among gram-negative uropathogens in Erbil is relatively high, which is a warning to prevent unnecessary use of antibacterial. Also in the present study, compared to others, the ratio of *Escherichia coli* to other pathogens was higher. Therefore, the prevalence of *Escherichia coli* is increasing compared to previous studies in Erbil. Fortunately, antibiotics such as amikacin and meropenem are highly sensitive to this pathogen and can effectively treat urinary tract infections.

5.2. CONCLUSION

The most common gram-negative urinary pathogen determined in this study was *Escherichia coli*. The highest resistances of gram-negative urinary pathogens were against the antibiotic ampicillin, Trimethoprim / Sulfamethoxazole and ceftriaxone, and the lowest resistances were for amikacin, meropenem, ertapenem and imipenem. The results of this study also show that Gram-negative uropathogens show significant resistance to Trimethoprim/Sulfamethoxazole and ciprofloxacin, which are uncomplicated first-line therapies for UTI, and are unlikely to be ineffective. One of the best options for antibiotic treatment is fluoroquinolones, which can be replaced by ciprofloxacin, that show very little resistance. Some cephalosporins, such as cefepime and ceftazidime, were also highly sensitive.

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APPENDIX

Ethics Committee approval

Evrak Tarih ve Sayısı: 30.06.2021-40035

T.C.
SAKARYA ÜNİVERSİTESİ REKTÖRLÜĞÜ
Tıp Fakültesi Dekanlığı
Fakülte Girişimsel Olmayan Etik Kurulu

SAKARYA ÜNİVERSİTESİ

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Konu : Girişimsel Olmayan Etik Kurul Başvuru Dosyası Hk.

Sayın Prof. Dr. Mustafa ALTINDİŞ

Sakarya Üniversitesi Tıp Fakültesi
Tıbbi Mikrobiyoloji Anabilim Dalı

İlgi : 21.06.2021 tarihli 381 sayılı değişiklik başvurunuz.

Destekleyicisi olduğunuz **"Erişkin Hastalarda İdrar Yolu Enfeksiyonu Etkeni Gram Negatif Bakterilerde Antimikrobiyal Direnç: Erbil"** isimli çalışmanın ilgili belgeler araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş olup; Çalışmanın Sorumlu Araştırmacısının **Dr. Öğr. Üyesi Tayfur DEMİRAY**, **Prof Dr Mustafa ALTINDİŞ'** in ise Yardımcı Araştırmacı olarak değiştirilmesinde etik ve bilimsel açıdan sakınca bulunmadığına etik kurul üyelerince karar verilmiştir.

Bilgilerinize rica ederim.

Prof. Dr. Hasan Çetin EKERBİÇER
Etik Kurulu Başkanı

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RESUME

I- Personal Information

Name-Surname: Mohammed Sadeq Saleh SALEH

Birth Place and Date: Erbil/ 15.04.1987

Nationality: IRAQI

Marital Status: Married

Contact address: Zheyan quarter, Kirkuk Road/ Erbil

Foreign language: English, Arabic, Turkish (B1)

II- Education

University of Sakarya Institute of Health Science Medical Microbiology Post Graduate degree 2019-2021

University of Salahaddin/ Collage of Science/ Biology Department 2007-2010

III- Addresses

Laboratory technician in Pirmam general hospital 2012 to 2019

Laboratory technician in CMC private hospital 2016 to present

IV- Professional Experience

Medical laboratory technology, in vitro diagnosis of bacteria

V- Scientific Interests

Medical Microbiology

Publications:

A. Journal of Biotechnology and Strategic Health Research/ Case Report

A1. Ayhancı T., Demiray T., İnce B., Özmen E., Sadeq M., Aydın A., Yaylacı S. A Rare Case of Bacteriemia Due to Comamonas testosteroni, J Biotechnol and Strategic Health Res. 2021;5(1):64-68

VII- Scientific Activities

Mycobacterium tuberculosis course for T.B. identification in chest and respiratory hospital/Erbil-Iraq 2013