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Molecular Study of Some Virulence Genes in Pathogenic Bacteria Isolated from Urinary Tract Infection Patients in The North of Thi-Qar Province

A thesis

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Master Degree in Veterinary Medicine / Microbiology

By

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1447 H.A

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

((يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ
دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ))

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Declaration

I hereby declare that the thesis entitled **(Molecular Study of Some Virulence Genes in Pathogenic Bacteria Isolated from Urinary Tract Infection Patients in The North of Thi-Qar Province)** is my original work except for quotations and citations, which have been fully acknowledged. Also, I declare it is not previously and currently submitted for other degrees at the University of Shatrah or other institutions.

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We certify that the preparation of this thesis (**Molecular Study of Some Virulence Genes in Pathogenic Bacteria Isolated from Urinary Tract Infection Patients in The North of Thi-Qar Province**) was made under our supervision and conducted by (**Karrar Fadhil Hassan**) at the Department of Microbiology, College of Veterinary Medicine, University of Shatrah, in partial requirement for Master Degree in Veterinary Medicine / Microbiology.

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Dedication

To my beloved parents,

****Father ** and ** Mother****

Your unconditional love, sacrifices, and constant support have been the guiding light throughout my journey. You have shaped not only my education but also the person I have become. For that, I am forever grateful.

To my dear

****Family and friends****

Thank you for your encouragement, patience, and belief in me—even when I doubted myself. Your presence made the hard days bearable and the good days even better.

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Summary

Urinary tract infections (UTIs) are the second most common infectious diseases, which may vary from mild to severe life-threatening urosepsis. UTIs can affect people of all ages and demographics but is particularly common in women, the elderly, and people with underlying urological or immunological conditions.

From September 2024 to February 2025, 150 midstream urine samples were collected from patients with symptoms of UTIs, from healthcare centers, clinics and hospitals in the north of Thi-Qar province. The patients' ages ranged from 11 to 80 years, and from both sexes. Bacterial identification was performed using culture on blood and MacConkey agars, followed by biochemical tests. PCR was used to detect the presence of virulence genes such as *fimH* and *KpsMTII* for *Escherichia coli* and *mdeA* and *hla* genes for *Staphylococcus aureus*.

This study investigated bacterial UTIs among 150 patients, of which only 43 samples (28.7%) yielded positive bacterial cultures. Females were more susceptible to UTIs, comprising 60.5% of positive cases, compared to males (39.5%). The most prevalent uropathogen was *E. coli* (34.9%), followed by *Klebsiella pneumoniae* (25.6%), *Pseudomonas aeruginosa* (18.6%), and *Proteus mirabilis* (11.6%). The least frequently isolated pathogen was *S. aureus* (9.3%). Many antibiotics from different categories were used to assess antimicrobial susceptibility for main bacterial isolates using disk diffusion test. More than 60% of *E. coli* isolates were resistant to trimethoprim (73.3%), tetracycline and trimethoprim/ sulfamethoxazole (66.7% for each). *S. aureus* exhibited significant resistance rates to erythromycin (100%), tobramycin (100%), tetracycline (75%), trimethoprim (75%) and trimethoprim/sulfamethoxazole (75%). The resistance rate of *S. aureus* to ciprofloxacin was 50%. Antimicrobial resistance testing also revealed high resistance among *K. pneumoniae* isolates to tetracycline (100%), trimethoprim (81.8%), ciprofloxacin (63.63%), trimethoprim/sulfamethoxazole (63.63%) and

tobramycin (63.63%). Similarly, most *P. aeruginosa* and *P. mirabilis* isolates were resistant to tetracycline (100% and 80%, respectively), trimethoprim (100% for each), and trimethoprim/sulfamethoxazole (100% and 80%, respectively). All *P. aeruginosa* isolates exhibited resistance to nitrofurantoin and ceftiofex (100%). *FimH* and *KpsMTII* genes for *E. coli* were detected, with high prevalence at 86.7% and 80%, respectively. The prevalence of *mdeA* and *hla* genes in *S. aureus* isolates was 50% for each, with only 25% of the isolates harboring both of them.

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List of Abbreviations

Abbreviations	Meanings
ABU	Asymptomatic bacteriuria
ADAM10	A-disintegrin and metalloprotease 10
CFU/mL	Colony-forming units per milliliter
DNA	Deoxyribonucleic Acid
EAEC	Enteraggregative <i>Escherichia coli</i>
eDNA	Extracellular DNA
ESBLs	Extended Spectrum B-Lactamase
FPR2	Formyl peptide receptor 2
IBCs	Intracellular Bacterial Communities
kDa	kiloDalton

LPS	Lipopolysaccharide
MDR	Multidrug Resistant
MFS	Major Facilitator Superfamily of efflux pumps
Mg	Milligram
mL	Milliliter
NK	Natural killer cells
Nm	Nanometer
No.	Number
OD600	Optical density at 600 nm
P fimbriae	Pyelonephritis-associated fimbriae
PCR	Polymerase Chain Reaction
pEC14-114	a plasmid of the uropathogenic <i>E. coli</i> strain EC14
PH	Potential Of Hydrogen
pUTI89	Plasmid of uropathogenic <i>E. coli</i> strain UTI89
Spp.	Species
TLRs	Toll-like receptors
TolC	Tolerant colicin protein
UTIs	Urinary Tract Infections
UTI-ST	Urinary tract infection-derived-sequence type
UV	Ultraviolet
V	Volt
VF _s	Virulence factors

Chapter One

Introduction

1.1. Introduction

Urinary tract infections (UTIs) are a serious public health concern that can be caused by a variety of organisms. Annually, over 150 million people worldwide receive a UTI diagnosis (Sujith *et al.*, 2024). UTIs can be classified into upper and lower tract infections based on anatomy of infected part of urinary tract (Dobrek, 2021). Lower UTIs are referred to as bladder infections or cystitis, while upper UTIs are referred to as kidney infections or pyelonephritis (Asadi Karam *et al.*, 2019). More than 95% of UTI cases are caused by bacteria, despite the fact that a variety of pathogens, including viruses and fungi, can cause UTIs (Tia and Lal, 2016). The most common pathogens associated with UTIs were *E. coli* (51.5%) and *Klebsiella* spp. (28.5%), followed by *P. aeruginosa* (10.6%), *S. aureus* (5.2%) and *Proteus* spp. (5.2%) (Luma Hikmat Kareem, 2023).

UTIs can be either complicated or uncomplicated, based on underlying host factors and underlying uropathogens (Behzadi *et al.*, 2010). UTIs in healthy people who have no anatomical or neurourological abnormalities are known as uncomplicated (Ondari, 2020). Uncomplicated UTIs are also associated with patients with a healthy urinary tract system and no use of medical devices, which are frequently observed in outpatients (community-acquired infections) (Asadi Karam *et al.*, 2019). Complicated infections may also refer to infections that occur in the presence of underlying conditions or factors that increase the likelihood of therapeutic failure. Although acute cystitis is typically classified as an uncomplicated infection, certain circumstances may render it complicated. Similarly, although acute pyelonephritis involves the upper urinary tract, is generally considered as uncomplicated when occurring in otherwise healthy individuals (Hooton, 2000). A study conducted by Assafi *et al.* (2022) reported that females (88.9%) were more susceptible to UTIs than males (55.2%).

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Hematogenic and ascending infections are the two ways that UTIs can be developed. In ascending route, the uropathogen can ascend from rectal region and pass through urethra into urinary bladder. Rarely, bacteria from nearby organs may migrate through lymphatics to enter the urinary tract, in which called lymphatic route (Davis and Flood, 2011). The most common mechanism of UTIs, with the exception of the neonatal period, is ascending urinary tract contamination caused by intestinal flora (Guglietta, 2017). The presence of a positive urine culture with 10^5 CFU/mL with no symptoms is known as asymptomatic bacteriuria (ABU). Alternatively, these infections can manifest as symptomatic infections, which cause dysuria with or without pain, urgency, and frequency (Martínez-Santos *et al.*, 2021). With involvement of lower urinary tract, ABU is the most common cause of UTI during pregnancy, while acute pyelonephritis is manifested as symptomatic bacteriuria. Symptomatic UTIs affect 17.9% of pregnant women, whereas asymptomatic infections affect 13% of them (Shakoor, 2023).

Chapter One Introduction

1.2. Aim of Study

This study aimed to use molecular-approach in order to detect some of virulence genes for predominant bacterial species associated with UTIs in the northern region of Thi –Qar province.

1- Isolation and identification of main bacterial isolates associated with UTIs in patients from northern region of Thi-Qar province. Morphological and confirmed diagnosis by biochemical reactions.

2- Antimicrobial sensitivity test for main bacterial isolates from patients.

3- Molecular detection of some virulence genes (*fimH* and *kpsMTII* for *E. coli*, and *mdeA* and *hla* for *S. aureus*) associated with UTIs.

Chapter Two

Literatures Review

Chapter two Literatures Review

2.1. Literatures Review

2.1.1. Urinary Tract Infections

A UTI occurs when microorganisms are present in the urinary tract and its symptoms range from mild discomfort during urination to severe conditions like bacteremia, sepsis, or fatal septicemia (Kaur and Kaur, 2021). UTI is the most frequent healthcare-associated infection and 78% of UTIs are linked to catheterization (Peng *et al.*, 2018). In USA, UTI is responsible for 3 million US hospitalizations, and it costs more than \$3.5 billion per a year (Zilberberg *et al.*, 2022). It has been demonstrated that individuals with symptomatic UTIs show a notable immune response when the microbial density reached a threshold of 10,000 cells/mL or higher (Parnell *et al.*, 2023). UTIs caused by *Chlamydia* and *Mycoplasma* can be sexually transmitted disease and treatment for both partners is required (Kareem and Rasheed, 2016). The diagnosis of UTI remains challenging, with clinical criteria alone having a 33% error rate (Schmiemann *et al.*, 2010). The traditional criterion of 10^5 colony-forming units (CFU)/mL for significant bacteriuria is being reconsidered, as recent studies show that one-third of confirmed UTIs have only 10^2 to 10^4 CFU/mL. UTI symptoms include dysuria, frequency, urgency, and suprapubic pain, with hematuria strongly suggesting bacterial cystitis (Stamm, 1988).

2.1.2. Epidemiology

2.1.2.1. Age

Age is significantly positively correlated with symptoms of UTIs, while educational level is significantly negatively correlated with symptoms (Atiahy, 2011). UTI prevalence increases with age, and it is roughly twice as common in women over 65 as it is in the general female population. In this age group, the etiology varies according to health status, with factors like catheterization influencing the risk of infection (Medina and Castillo-Pino, 2019). Age, but not gender or education level, was significantly associated with UTIs in diabetic patients

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(Mageto *et al.*, 2020). According to a study conducted in 26 countries around the world, the global pooled incidence of UTIs is 1.6%, with the highest incidence of 3.6% in the African region (Mengistu *et al.*, 2023). Despite the high frequency of UTIs, diagnosing them in elderly persons can be challenging. Elderly patients frequently exhibit ABU (Gravey *et al.*, 2017). Aging impairs bladder immunity and epithelial homeostasis, leading to increased susceptibility to recurrent UTIs in the elderly (Ligon *et al.*, 2023).

UTIs represent major source of morbidity among women of all ages, older men, and infant boys (Flores-Mireles *et al.*, 2015). According to a study, the incidence rate of UTIs among children between 2.5–7 years old was 7%, with *E. coli* being the most common causative pathogen (Amin *et al.*, 2020). By the age of seven, approximately 2% of boys and 8% of girls experience UTIs, and around 7% of infants with a fever are diagnosed with UTIs. During one year, recurrent UTIs range from 12% to 30% in children at age 7 (Desai *et al.*, 2016). During childhood, 2-4 years old girls exhibited the highest incidence rates of cystitis and pyelonephritis (40.3/1000 person-years, 8.1 /1000 person-years, respectively) compared to boys at the same age (Boon *et al.*, 2022). Throughout childhood, females are more likely to have UTIs (77.7%) than males (Hanna-Wakim *et al.*, 2015). The prevalence of UTIs in children was highest in the age group (1 month- 1 year), followed by age group (3-6 years), accounts for 27.72% and 25.74 respectively in Baghdad-Iraq (Al-Baqer *et al.*, 2021).

2.1.2.2. Sex

The incidence rate of UTIs was calculated to be approximately 2400 cases per 100,000 patients, with a range between 1800 and 3000 per a year in women due to antibiotic-resistant *E. coli* (Rossignol *et al.*, 2017). Because of shorter urethra and short distance between anus and urethra, women tend to have more UTIs compared to men (Mwang'onde and Mchami, 2022). Every year, 7 million women are scheduled to visit outpatient clinics for simple UTIs in USA alone and the annual

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cost is approximately 1.6 billion US dollars (Öztürk and Murt, 2020). One study showed that hospitalization rates for female patients were slightly higher (85%) than those for male patients (15%) (Kumar *et al.*, 2023). In 2000, incidences of cystitis in the USA were 12.6% among women and 3.0% among men annually (Wagenlehner *et al.*, 2020). Sexually active women are more likely to experience UTIs, as sexual intercourse ascends the pathogens to urethra (Burrows, 2024).

The statistical analysis of one study showed that the distribution of sexes and ages among the four seasonal groups was not significantly different. However, *Enterococcus faecium* was responsible for significant prevalence during the spring, accounting for 22.0% of isolates. This study also revealed that men were more likely than women to have infections associated with Gram-positive bacteria, especially, *Enterococcus faecalis* and *S. aureus* demonstrated notable sex differences, with both being more prevalent in men (Zhan *et al.*, 2024). The prevalence of UTIs is considerably higher in menopausal females than in males at the same age (Deltourbe *et al.*, 2022). As women age, the population of lactobacillus colonizing the vagina decreases due to the decline in estrogen level, therefore postmenopausal women are more susceptible to UTIs (Jung and Brubaker, 2019).

2.1.2.3. Pregnancy and Diabetes

Bacterial UTIs are the most frequent infections during pregnancy and occur in 2% to 15% of the pregnant women. Increased progesterone levels during pregnancy reduce ureteric peristalsis and expand bladder capacity, promoting conditions like physiological hydronephrosis and urine retention (Weber and Ansaldi, 2023). Asymptomatic bacteruria can lead to pyelonephritis in 20– 40% of pregnant women and 67% of them develop pyelonephritis during the second and third trimesters of pregnancy (Le and Diego, 2015). The prevalence of ABU in pregnancy was 16.9%, higher than the 1-2% prevalence of symptomatic bacteriuria, and the patients exhibited the highest prevalence in the second trimester of pregnancy (9.5%) (Amala

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et al., 2021). The incidence rates of UTIs in pregnant women were at the highest rate in the second and third trimester (43.4%, 33.96%, respectively) in Nasiriyah city south Iraq (Mousa and Abd Al-Amir, 2023).

The combination of diabetes and pregnancy is a critical risk factor for UTI, and the incidence of UTIs in diabetic pregnant women was 26.7% (Ovalle and Levancini, 2001). Diabetes increases the risk of bacterial UTIs, especially by drug-resistant uropathogens with significant risk at >2-fold, due to factors like hyperglycemia and impaired immunity (Paudel *et al.*, 2022). Given its ability to provide a favorable environment for growth of uropathogenic bacteria, glycosuria has also been suggested to increase UTI risk in diabetic people (Confederat *et al.*, 2023). It has been observed that 13.67% of diabetic patients developed UTIs in which Individuals with diabetes were found to have twice risk of experiencing UTIs compared to those without diabetes (Kumar *et al.*, 2019). Females with type 1 diabetes were more susceptible to UTIs (60%) compared to males, while half of both sexes with type 2 diabetes experienced UTIs (50% for each) in Thi-Qar Province (Beden and Mousa, 2022).

2.1.2.4. Others

Factors associated with sexual activity (its frequency per week, use of spermicidal agents that change pH of the vagina which impact vaginal microbiota, and sexual encounter with a new partner), a history of childhood or family UTIs, and blood type may increase risk of UTI in premenopausal women (Storme *et al.*, 2019). Long-term use of a urinary catheter increases the incidence of UTIs, mostly because bacteria can form a biofilm on the catheter that is resistant to medications and human defense (McLellan and Hunstad, 2016). Up to 21.6% of patients with catheter developed UTIs, and the most nosocomial UTI cases occurred 7 days after catheterization, and many isolates showed MDR bacteria (Nandini and Madhusudan, 2016). The prevalence of bacteriuria associated with *S. aureus* in bacteremic patients ranges

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from 7.8% to 39%, with urinary catheterization being a primary risk factor (Schuler *et al.*, 2021). Numerous factors, such as defects in neutrophil function and enhanced bacterial adhesion to uroepithelial cells, are probably responsible for the increased risks of UTIs in diabetic patients (Mnif *et al.*, 2013). UTIs are more likely to occur in children with urinary obstructions because stagnant urine encourages uropathogens to proliferate (Shaikh and Hoberman, 2024). Throughout infancy, the prevalence of UTIs was found to be four to eight times higher in uncircumcised male infants with fever than in circumcised males (Shaikh and Hoberman, 2024). A study concluded that being overweight/obese, poor fluid intake, and infrequent voiding are risk factors for UTIs in children, while breastfeeding and circumcision are protective (Renko *et al.*, 2022). Geriatric age, immobilization, urinary catheter, urolithiasis, and hyperglycemia are risk factors for UTIs in hospitalized patients (Setyorini *et al.*, 2019). At the age of 16 following a spinal cord injury (SCI), 80% of individuals are at high risk of UTIs. Additionally, urinary system diseases rank as the fifth most frequent primary or secondary cause of death among this population (Shekelle *et al.*, 2016).

2.1.3. Pathogenesis

2.1.3.1. Adherence and Colonization

Uropathogenic enteric microorganisms colonizing the periurethral region is the initial stage of UTIs. Glycosphingolipid receptors on the surface of epithelial cells mediate the active process by which pathogens adhere to the uroepithelial cells (Shaikh and Hoberman, 2024). Bacterial adhesion causes the urethra and bladder to be colonized after the perineum has been colonized for a variety of lengths of time (Roberts, 1999). The gut, vaginal, and urinary microbiomes play a role in UTI pathogenesis, with vaginal dysbiosis potentially leading to *E. coli* colonization and recurrent UTIs (Meštrović *et al.*, 2021). Uropathogenic *Escherichia coli* (UPEC) strains produce numerous adhesins, each differing in their receptor specificity and

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whether they form pili (or fimbriae). Among these, the type 1 pilus-associated protein *fimH* is one of the most extensively studied adhesins and is found in almost all UPEC isolates. *FimH* has the ability to attach to various mannose-containing glycoproteins on host cell membranes, as well as to elements of the extracellular matrix (Barber *et al.*, 2016). In both humans and mice, catheterization damages the bladder, causing the host protein fibrinogen (Fg) to be released. *S. aureus* uses interactions mediated by the Fg-binding protein ClfB to take advantage of the presence of Fg in order to colonize the bladder and the catheter and infect mice and humans with a persistent infection (Walker *et al.*, 2017).

2.1.3.2. Ascension of The Uropathogens

Once bacteria enter the ureter, they can ascend toward the kidney. This progression is greatly assisted by any factor that impairs the normal peristaltic function of the ureter. Gram-negative bacteria and their endotoxins, as well as factors like pregnancy and ureteral obstruction, have a substantial impact in reducing or disrupting normal peristaltic movement. While cystitis is localized to the bladder, around 50% of UTIs can ascend to the upper urinary tract (Altarac, 2015). It is believed that swimming helps in transmission through the urethra, between the kidneys and from the bladder to the kidneys. Therefore, immunological activation that results in the production of antibodies that immobilize *P. mirabilis* cells stops bacteria from spreading to the opposite kidney from the medullary tissue of the kidney (Yuan *et al.*, 2021). Because they prevent ureteral peristalsis, circumstances like pregnancy and ureteral blockage facilitate bacterial ascent. When bacteria get to the renal pelvis, they can damage the renal tubules by penetrating the renal parenchyma through the collecting ducts (Davis and Flood, 2011).

2.1.3.3. Formation of Biofilm and Biofilm-like Structures

Uropathogenic *E. coli* (UPEC) can form intracellular bacterial communities (IBCs), which are clusters of genetically identical bacterial cells that reside inside

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the cytoplasm of the bladder's superficial facet cells. These communities are surrounded by a biofilm-like structure and represent active, replicating, and metabolically functional groups of bacteria (Tamadonfar *et al.*, 2019). As a part of host defense mechanism, IBCs and bladder surface facet cells are exfoliated into the urine. Subsequently, remaining structures can be developed into biofilm-like appearances capable of evading immune system and resistant to antibiotics. Therefore antibiotics either cannot diffuse into the biofilm matrix or take longer time to penetrate the biofilm than the antibiotic's lifespan or treatment duration (Shrestha *et al.*, 2022). UPEC bacteria can then bind and invade other naive bladder cells and reform IBCs (Conover *et al.*, 2016).

As *P. mirabilis* migrate, the pathogens undergo differentiation from small, rod-shaped "swimming cells" into larger, elongated, multicellular "swarming cells". This process involves a rise in the number of flagella and nucleoid-like structures, which help form cohesive bacterial communities essential for kidney colonization. After adhering to surfaces, *P. mirabilis* can create a crystalline biofilm, which often forms on host tissues or medical devices such as catheters (Yang *et al.*, 2024). The formation of *K. pneumoniae* biofilms is commonly linked to catheter-associated urinary tract infection (CAUTIs), and the mechanisms that influence this process are probably crucial to pathogenesis (Clegg and Murphy, 2016). According to the in vitro phenotypic assays, UTI-ST1 in *S. aureus* clearly shows less hemolysis of human red blood cells and more biofilm and adhesion in the urea-supplemented medium than in the urea-free medium. In contrast, UTI-ST5 and nUTI-ST1 did not demonstrate any appreciable differences in their capacities for adhesion and biofilm formation (Xu *et al.*, 2023).

2.1.3.4. Host-immune Response

A critical aspect of host-pathogen interactions is the host's capacity to distinguish between foreign pathogens and its own cells, triggering a suitable immune response.

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Pattern recognition receptors (PRRs) play a vital role in this process by detecting specific molecular patterns associated with pathogens (PAMPs) or cellular damage (DAMPs), which in turn stimulate the innate immune system. These PRRs are typically found on immune cells that present antigens, such as dendritic cells and macrophages (Ching *et al.*, 2020). The two ways for innate immune to be triggered, first, recognition and binding to pathogen-associated molecular patterns (PAMPs) and second, reacting to molecules derived from damaged or dying cells (danger/damage-associated molecular patterns; DAMPs) (Terlizzi *et al.*, 2017). The pathogens attract inflammatory cells, which release chemokines and cytokines. To counteract UPEC, host cells employ various defense mechanisms, including the action of lactoferrin, Tamm-Horsfall protein (THP), immunoglobulin A (IgA), cathelicidin, and defensins (Choi and Chang, 2015).

The outflow of urine, which may eliminate microorganisms attached to the bladder, is considered one of the most significant defense mechanisms (Ma and Shortliffe, 2004). The bacteriostatic defenses rely on biophysical forces like urine flow and peristalsis, strange decoy chemicals, chelators that try to deprive bacteria of nutrients, and cellular processes that change the urine's composition (Munoz *et al.*, 2022). Both β -defensins from the local renal epithelium and α -defensins from the infiltrating neutrophils are secreted as part of the innate immune response during UTIs. Since all defensins have direct antibacterial activity, they can eradicate invasive pathogens (Weichhart *et al.*, 2008). Defensins can also improve innate responses by, for example, triggering mast cell degranulation then encouraging neutrophil chemotaxis. Additionally, there is evidence that defensins bring immature dendritic cells and naive T cells to the infection site, potentially bridging innate and acquired immune responses through TLRs or chemokines (Selsted and Ouellette, 2005). Neutrophils interact with pathogenic bacteria at the site of infection by a number of concurrent mechanisms, including phagocytosis (internalization and

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intracellular death), degranulation (extracellular discharge of granules containing antibacterial chemicals), and release of Extracellular traps of neutrophils (NETs) (Kuhn *et al.*, 2023). NK cells provide host defense against uropathogenic *E. coli*, but the bacteria counteract this by using hemolysin A to kill the NK cells (Gur *et al.*, 2013).

2.1.4. Main Causative Agents

2.1.4.1. *Escherichia coli*

E. coli is resident micro flora in gastrointestinal tract of human and animal, and the leading cause of most UTIs (Bien *et al.*, 2012). Uropathogenic *E. coli* is part of a group has ability to cause infections outside of intestinal tract called extra intestinal pathogenic *E. coli* (ExPEC) which also includes UPEC, sepsis-associated *E. coli* and neonatal meningitis-associated *E. coli* (Al-Hamdani and Ismael J. Abas, 2013). Ability to adhere and haemolysis, are among crucial criteria to distinguish UPEC strains from other *E. coli* strains (Forsyth *et al.*, 2018). *E. coli* strains from faecal source colonize perineal, vaginal, and periurethral area and then ascend to urethra and bladder, result in establishment UTIs (Timothy kudinha, 2016).

E. coli is well known for its possession of specific antigen, particularly surface O-antigens which classified into serogroups ranging from O1 to O180 based on the antigenic structure of the lipopolysaccharide (LPS). *E. coli* serogroups responsible for 75% of UTIs are : O1, O2, O4, O6, O7, O15, O18ac and O75 (Sayed *et al.*, 2024). UPEC is also characterized by presence of specific adhesins include P, S or Dr which promote colonization of the urinary tract, as well as toxins such as hemolysin and cytotoxic necrotizing factor 1 which trigger the host immune response and develop symptoms of UTIs (Zhang and Foxman, 2003). Some studies reported that the diarrheagenic pathotype EAEC, which is responsible for travelers' diarrhea in people who visit developing countries, can also cause UTIs (Martínez-Santos *et al.*, 2021).

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UTIs caused by UPEC can be disseminated to bloodstream and leading to urosepsis and death. *E. coli* utilizes and tolerate high concentrations of urea, creatinine, amino acids, organic acids, inorganic ions include ammonia, sodium and potassium, and many water-soluble toxins in urine (Mann *et al.*, 2017). UPEC strains have ability to form biofilms associated with chronic UTIs which protect these microorganisms from innate immunity and antibiotics (Whelan *et al.*, 2023). Virulence factor genes, which distinguish UPEC from other *E. coli* and linked to its pathogenesis, are found on integrated mobile elements called pathogenic island (PAI). *E. coli* strains were classified into eight major phylogroups: A, B1, B2, C, D, E F and G, and the vast majority of the UPEC belongs to phylogroup B2 (Tanabe *et al.*, 2022).

2.1.4.2. *Staphylococcus aureus*

Gram-positive opportunistic pathogen, belonging to Staphylococcaceae with three important human pathogenic species: *S. aureus*, *Staphylococcus epidermidis*, and *Staphylococcus saprophyticus* (Kuroda *et al.*, 2005). While urinary colonization with *S. aureus* may also be the cause of staphylococcal bacteremia, UTIs caused by *S. aureus* can also be associated with staphylococcal bacteremia (Megged, 2014). *S. aureus* is responsible for 0.5-6% of UTI, and if patients with Staphylococcal UTIs are not receiving any therapy they may develop serious, life-threatening infection (Yousefi *et al.*, 2016). *S. epidermidis* is able to attach to both living and inanimate surface such as urinary catheters by producing slime layer, therefore it can cause nosocomial UTIs (Fadhel *et al.*, 2013). *S. aureus* is the most common pathogen in both hospital and community sitting, it causes 5-40% of hospital acquired infections (Baba-Moussa *et al.*, 2008). *S. aureus* is responsible for formation of biofilm on biologically derived materials, which increases its resistance to host defence mechanism and antimicrobial agents (Ando *et al.*, 2004). Many strains of *S. aureus* harbour many multi-drug resistant genes located on their plasmids, which are

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associated with increased antibiotic resistance (Onanuga and Awhowho, 2012). *S. saprophyticus* is the most frequent cause of acute UTIs in young sexually active females (Hur *et al.*, 2016).

2.1.4.3. *Klebsiella pneumoniae*

It is negative to Gram stain and appears as rod. *K. pneumoniae* colonizes mucosal surfaces of mammals and the gastrointestinal tract, eyes, respiratory tract and genitourinary tract of healthy people (Abdelwahed Jaheel Al-Kaaby, 2017). It is resident microflora of gastrointestinal tract in human and animal, but can spread to different areas, resulting in a variety of infectious diseases including blood, respiratory, urinary tract, and burns. It is facultative anaerobic, motile pathogen with large antiphagocytic capsule, and has ability to ferment lactose (Khazaal, 2017). It is the second most common pathogen associated with community-acquired UTIs and significant pathogen in conditions such as sepsis, soft tissue infections and respiratory tract infections (Khalaf and Al-hashimy, 2022). *K. pneumoniae* possesses several virulence genes encode factors mediate *K. pneumoniae* infectivity such as yersiniabactin, aerobactin, the regulators of mucoid phenotype and type-1 fimbriae (Marques *et al.*, 2019). It causes Infections associated with insertion of medical devices such as urinary catheters and it can form biofilm on them. *K. pneumoniae* is classified into more than 77 serotypes based on distinct antigenic types of capsule and most infections with *K. pneumoniae* involve more than one serotype (Clegg and Murphy, 2016)

2.1.4.4. *Pseudomonas aeruginosa*

P. aeruginosa, Gram-negative rod, opportunistic bacterium thrives in diverse environments such as soils, marshes, river waters, coastal and marine areas and do not ferment most sugars (Laibi Chelab and Jala Taima, 2019). *P. aeruginosa* is associated with 51,000 nosocomial infections in the USA per year and considered as MDR uropathogen (Attalah, 2023). One study reported that *P. aeruginosa* was the

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second leading cause of UTIs (26.9%) and was most common in females and also was higher among those aged 18 or more (Habibu A. U, 2014). Genetic materials of *P. aeuroginosa* harbour many virulence genes associated with its pathogenesis including drug resistance and biofilm formation genes and they can obtain genes resistant to antibiotics from other different bacteria (Ahmad *et al.*, 2024). An outer membrane with low permeability, ability to produce antibiotic-inactivating enzymes and possession of the various efflux pumps all contribute to intrinsic resistance of *P.aeuroginosa* to antibiotics (Badamchi *et al.*, 2017).

P. aeuroginosa may develop fatal Septicemia associated with UTIs in elderly patients or people with weakened immune system due to either medical condition such as diabetes or therapy such as steroid and cancer treatment (Shigemura *et al.*, 2006). *P. aeuroginosa* is also the fourth most common causative agent of surgical site infection and it also causes (2-6%) of septicaemia (Badamchi *et al.*, 2017). *P. aeuroginosa* can cause recurrent UTIs in elderly patients who have been received antimicrobial therapy (Newman *et al.*, 2022). *P. aeuroginosa* is non-fastidious pathogen which does not require any special nutrition supplement or conditions to grow, therefore it thrives on inanimate objects such as hospital room sinks, toilets, showers and health care equipment such as catheters and respiratory ventilators (Moore *et al.*, 2011). *P. aeuroginosa* is responsible for producing pigments such as fluorescent pigment (fluorescein) and a blue pigment (pyocyanin), as well as sweet grape-like odor. It produces many exotoxins such as exotoxin A, which inhibits protein synthesis and some strains have capsule with antiphagocytic activity (Mohammed T. and Almahde, 2017).

2.1.4.5. *Proteus mirabilis*

It's motile Gram-negative enteric bacteria with peritrichous flagella. *P. mirabilis* can be found as hyperflagellated swarmer cells and vegetative swimmer cells (Coker *et al.*, 2000). *P. mirabilis*, belonging to the class Gammaproteobacteria and family

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Enterobacteriaceae, is well-known for its swarming motility on the agar plates (Armbruster *et al.*, 2018). *P. mirabilis* is primarily found in soil, water and the intestinal tracts of mammals (Jacobsen and Shirtliff, 2011). Bacteriuria, kidney stones, catheter obstruction, acute pyelonephritis, fever and the majority of complicated UTIs are associated with *P. mirabilis* (Hussein E. I. *et al.*, 2020). *P. mirabilis* is widely recognized for producing urease, which results in producing ammonia and raising the pH of urine to >7.2. Acute urinary retention, bacteriuria, and other ascending infections are caused by catheter obstruction linked to calcium and magnesium crystallization in urine with an alkaline pH (Chen C. Y. *et al.*, 2012). Raised pH in urine causes salt to precipitate and crystallize, which leads to the formation of stones. Struvite stones are the result of the crystals depositing on the catheter (Mancuso *et al.*, 2023). Urolithiasis was more common in the *P. mirabilis* bacteremic group (44.8%) than in the nonbacteremic cases (24.2%) (Chen C. Y. *et al.*, 2012). *P. mirabilis* is a prevalent cause of bacteremia in the elderly, severe UTIs, and UTIs linked to long-term indwelling catheters (Burall *et al.*, 2004). *P. mirabilis* also causes UTIs in prepubescent males and girls and is more common in older adults. Uncircumcised males have been found to have a higher frequency (Coker *et al.*, 2000).

Among Gram-negative bacteria, *P. mirabilis* had the strongest adherence to catheters, particularly on the inside and outside of silicone and red rubber catheters, in the presence of urine and serum (Yuan *et al.*, 2021). *P. mirabilis*, on the other hand, showed no adhesion to polytetrafluoroethylene catheters when serum was present. It is believed that *P. mirabilis* infections do not spread through the hematogenous route. Swarmer cells are notably characterized by an overproduction of flagella, which contributes significantly to facilitating the pathogen ascension from the urethra to the bladder (Coker *et al.*, 2000). *P. mirabilis* is able to differentiate from a single short, rod-like "swimming cell" into multicellular,

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elongated "colony cells" that are stacked in a certain order to create rafts of cells that can move quickly and cooperatively across solid surfaces (Yuan *et al.*, 2021). *P. mirabilis* prevalence was found to be the highest at the age 17-37 in both men and women (Ibrahim A. *et al.*, 2023). *Proteus* spp has ability to produce biofilms on indwelling catheters (Jacobsen and Shirtliff, 2011).

2.1.5. Virulence Factors

Genes for virulence factors that promote host invasion and infection distinguish pathogenic bacteria from non-pathogenic ones (Sengupta and Austin, 2011). VFs can be classified as cytosolic, membrane-associated, or secretory. The bacterium is capable of rapidly adapting by changing its morphology, metabolism, and physiology associated with the cytosolic factors (Sharma *et al.*, 2017). Membrane-associated factors that contribute to adhesion, colonization, and invasions are the cause of antibiotic resistance and facilitating intercellular communication (Wu *et al.*, 2008). Pili is one of protein-containing adhesion factors, whereas lipopolysaccharide is one of non-protein-containing adhesion factors (Abdulateef *et al.*, 2023). Adhesins are one of the first virulence factors to be involved in the development of a UTIs. Additionally, adhesins may act as invasins, encourage the formation of biofilms, and send signals to epithelial cells that cause inflammation (Oelschlaeger *et al.*, 2002). By penetrating host cells and then evading destruction within degradative lysosomes, bacteria can improve their access to limited resources and gain the protection against antibiotics and host defences (Lewis *et al.*, 2017). Toxins as secreted VFs help the bacteria penetrate into deeper tissues by impairing cell judgment, allowing them to absorb nutrients inside their cells, or destroying safe effector cells in order to defeat their potential antibacterial function (Mitiku and Lata, 2025). VFs are either carried by mobile genetic elements include plasmids, viral prophages, and transposons or encoded by the host chromosome (Sengupta and Austin, 2011).

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2.1.5.1. Plasmids

The extra-chromosomal, self-replicating components known as bacterial plasmids are important agents in microbial communities. They encourage the spread of certain characteristics, such as virulence factors, increased fitness, resistance to antibiotics, and rare substance metabolism (Johnson T. J. and Nolan, 2009). In order to lessen the metabolic load on their host, plasmids are kept at low copy numbers. Plasmids with a low copy number face the danger of being lost during cell division. Therefore, plasmid-encoded systems, which guarantee that every cell receives at least one plasmid copy, combat this (Sengupta and Austin, 2011). Antimicrobial resistance to the major classes, such as β -lactams, aminoglycosides, tetracyclines, chloramphenicol, sulfonamides, trimethoprim, macrolides, and quinolones, can be transferred by plasmids (Carattoli, 2013).

Plasmids are a superior way for transferring (vertically and horizontally) specific characterization than a specific bacterial clone (Farshad *et al.*, 2012). Plasmids that encode virulence factors are frequently passed from one bacterium to another by conjugation, either by another plasmid (helper plasmid) in the same cell or by systems encoded on the plasmid itself (Pilla and Tang, 2018). A UPEC isolate called UTI89, possesses a big F-like plasmid called pUTI89, which is similar to other Enterobacteriaceae plasmids and contains around half genes related with virulence and/or unknown functions. Recently, it was shown that a plasmid called pEC14_114, which is almost the same as pUTI89, appears to be widely distributed in UPEC strains that cause cystitis, indicating that it may boost UPEC fitness and/or virulence (Cusumano *et al.*, 2010).

2.1.5.2. *Escherichia coli*

UPEC expresses virulence factors like fimbriae, outer membrane proteins, and toxins that contribute to successful UTIs. Because they are engaged in the secretory apparatus, outer membrane proteins also contribute to virulence. TolC, for instance,

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is a protein that transports α -hemolysin across *E. coli*'s outer membrane (Alam Parvez and Rahman, 2019). Aerobactin (aer), hemolysin (hly), outer membrane protein T (ompT), pap-related fimbriae (prj), S fimbrial adhesin (sfa), and Dr-binding adhesins (drb) are among the bacterial VFs that convert commensal *E. coli* to uropathogen (Foxman *et al.*, 1995). At least two adhesins of *E. coli*, type 1 and P fimbriae, are known to be crucial to the development of cystitis and pyelonephritis, respectively (Kau *et al.*, 2005). Lipopolysaccharide (LPS), polysaccharide capsule, flagella, outer-membrane vesicles, pili, curli, non-pilus adhesins, and outer-membrane proteins (OMPs) are examples of surface structural VFs of UPEC. Other elements include secreted toxins, secretion systems, and TonB-dependent iron-uptake receptors, including siderophore receptors (Terlizzi *et al.*, 2017). Hemolysin, cytotoxic necrotizing factor 1 (CNF1), and secreted autotransporter toxins are the three major toxins that UPEC produce and release into their environment. (Zhou *et al.*, 2023). In order to keep iron away from invasive pathogens, the host's reaction to infection involves increased expression of a number of iron-binding proteins, such as lactoferrin and lipocalins. Bacterial pathogens have developed a number of genes that encode siderophores in order to prevent this (Klein and Hultgren, 2020).

Type 1 fimbriae (fimH) and P fimbriae (papC, papAH, papG allele III, papG allele II, papG allele I, and papG allele II and III) are among the organelles that colonize the surface of the host cells with *E. coli* due to the adhesion genes (Khalifeh and Obaidat, 2022). In type 1 fimbriae, the distal tip fibrillum is formed by the subunits FimF, FimG, and FimH, whereas the pilus rod is constructed by up to 3,000 copies of the subunit FimA. The fimbrial tip adhesin (FimH) selectively binds in a catch-bond mechanism to the terminal α -D-linked mannoses of N-linked glycans of the urinary epithelial membranes' receptor uroplakin 1a (Sauer *et al.*, 2016). Because of the terminal sialic acid residues' capacity to prevent the alternative complement pathway from being activated, the K1 capsule offers *E. coli* an antiphagocytic barrier

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(Vann *et al.*, 2004). The K1 capsule polysaccharide has been frequently linked with pyelonephritis, neonatal meningitis, and bloodstream infections (Arredondo-Alonso *et al.*, 2023). All the information required for capsular polysaccharide expression is contained in the *kps* gene cluster of *E. coli* K1 capsule (Pavelka *et al.*, 1994). Cloned gene clusters (especially K1 and K5) that code for the group II capsules K1, K4, K5, K7, K12, and K92 share three functional regions; they are regions 1, 2, and 3 (Russo *et al.*, 1998). Two genes (*kpsM* and *kpsT*) that produce members of the ATP-Binding Cassette (ABC)-transporter protein family are encoded in region 3 of the cluster. In *E. coli*, the export of capsular polysaccharide is mediated via the KpsMT system (Pavelka *et al.*, 1994).

2.1.5.3. *Staphylococcus aureus*

S. aureus strains isolated from UTI patients exhibit high levels of VFs and multi-drug resistance. Common virulence genes include *hla*, *sea*, *mecA*, and *clfB*, with *mecA* conferring resistance to methicillin and similar antibiotics. (Aubais aljelehawy *et al.*, 2021). Surface proteins are among the most significant virulence factors because they facilitate the bacterium's adherence and binding activities to the surfaces of host cells. Protein A, found in *S. aureus*'s cell wall, is an essential component that precisely attaches to the peptidoglycan pentaglycine bridges of the bacteria (Malak *et al.*, 2020). MSCRAMM (microbial surface component recognizing adhesive matrix molecules) expression and biofilm formation are both increased when *S. aureus* is exposed to human plasma in vitro, indicating the significance of their function in in vivo biofilm formation. Clumping factor A (ClfA), clumping factor B (ClfB), and the Sdr proteins are a part of the Clf-Sdr family (Paharik and Horswill, 2016). Hemolysins, Staphylococcal binding of IgG, aerolysin, phenol-soluble modulins, nuclease, leukocidins, FPR2 inhibitory proteins, staphylococcal complement inhibitor, chemotaxis inhibitory protein of *Staphylococcus*, extracellular adherence protein, and staphylococcal superantigens

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are just a few of the proteins that *S. aureus* produces in order to evade the host immune defences (Arunachalam *et al.*, 2009) .

Numerous cytolytic exotoxins, including alpha-hemolysin (hla) and leukotoxins, as well as cytolytic peptides, are secreted by *S. aureus* strains that contribute to staphylococcal pathogenesis by encouraging tissue injury, immune evasion, and dissemination (Paudel *et al.*, 2021). After attaching itself to its receptor, ADAM10, Alpha-hemolysin (hla) forms a heptameric pore. By using ADAM10's metalloprotease activity, hla can alter the activity of immune cells, such as neutrophils, or cause epithelial cell lysis (Thammavongsa *et al.*, 2015). One significant mechanism of resistance in pathogenic bacteria is antibiotic efflux. Multi-drug efflux A protein (mdeA) gives *S. aureus* resistance to antibiotics and a variety of quaternary ammonium compounds, but not fluoroquinolones (Huang *et al.*, 2004). Increased resistance to the biocides benzalkonium chloride, dequalinium, and tetraphenylphosphonium, as well as to the dye ethidium bromide and the antibiotics virginiamycin, novobiocin, mupirocin, and fusidic acid, was linked to the overexpression of *mdeA* gene (Koch *et al.*, 2016). By affecting physical-chemical interactions, motility, gene regulation, quorum sensing (QS), extracellular polymeric substances (EPS), and the extrusion of hazardous compounds, efflux pumps also contribute to the formation of biofilms (Hajiagha and Kafil, 2023).

2.1.6. Antibiotic Sensitivity and Resistance

Antimicrobial resistance is consider a major serious health issue and has raised among patients with UTIs as they are managed without performing bacterial culture and antibiotic susceptibility testing (Nuha Abd Al Rheem Saad *et al.*, 2022). Bacterial resistance mediated by β -lactamases has been linked to overuse of β -lactam antibiotics, especially the third generation of cephalosporins, which has resulted in the development of ESBLs producing Bacteria. Extended spectrum β -lactamases produced by these bacteria have the ability to hydrolyze third-generation

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cephalosporins (e.g. cefotaxime, ceftazidime, and ceftriaxone) and monobactam, but have no ability against β -lactamase inhibitors such clavulanic acid and tazobactam, as well as cephamycins and carbapenems (Abd Al-Mayahi and Almohana, 2014). According to Abbas Atyia Hammoudi, imipenem demonstrated significant activity against all bacterial isolates associated with UTIs, while tetracycline was ineffective (Atyia, 2017).

Amikacin showed the highest susceptibility uropathogenic bacteria include *E. coli*, *Klebsiella* spp, *Enterobacter* spp, *Proteus* spp, *Pseudomonas* spp, *Staphylococcus* spp, and *Streptococcus* spp 27.6%, while cephalothin exhibited the highest resistance to these isolates (32.6%) (Ibrahim S. A. *et al.*, 2020). According to study conducted in Baghdad-Iraq, between March 1, 2019, and September 1, 2020, *E. coli* exhibited the highest resistant rate among uropathogens to trimethoprim, ciprofloxacin, gentamycin, and ceftriaxone accounts for 57.1%, 56%, 33.3% and 29.7% respectively (Jawad *et al.*, 2022). The resistance rates of *E. coli* against ciprofloxacin, tetracycline, novobiocin, cefotaxime, ceftazidime, rifampin and carbenicillin were (60%, 64%, 72%, 80%, 88%, 92% and 96%, respectively) (Abbood, 2024). *E. coli* showed significant resistance against ampicillin, cefixime, ceftriaxone, cefotaxime, tetracycline, cefepime, ceftazidime and gentamicin (accounting for 74%, 76%, 82%, 78%, 78%, 68%, 74% and 52%, respectively) (Al-Jubouri and Shami, 2023). More than 88% of UPEC isolates were resistant to amoxycillin/clavulanic acid, ceftazidime, ceftriaxone, cefotaxime, cefpodoxime, cefepime, while more than 57% of isolates were susceptible to nitrofurantion, meropenem, imipenem and amikacin (Al-Hasnawy H. *et al.*, 2019).

Gram-positive pathogens including *E. faecalis*, *Staphylococcus haemolyticus*, *Streptococcus Agalactiae* were significantly resistant to erythromycin, while *S. agalactiae* demonstrated high sensitivity to vancomycin. Ardalan Abdulhamid Osman claimed that ampicillin and other penicillins such as amoxycillin, azidocillin,

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amoxycillin/clavulanic acid, bacampicillin, cloxacillin, dicloxacillin, flucloxacillin, mezlocillin, oxacillin, penicillin G, penicillin V, propicillin, piperacillin, piperacillin tazobactam, sulbactam are no longer suitable for treatment of UTIs (Ardalan Abdulhamid Osman, 2019). All isolates of *S. aureus* were resistant to novabocin, while *S. epidermidis* exhibited fully resistant to gentamicin, azithromycin and novabocin (100%) (Nidaa wasmy Shahab *et al.*, 2023). According to the urine cultures' sensitivity tests, the majority of the urine cultures were susceptible to norfloxacin (25.4%), amikacin (27.2%), and gentamycin (23.4%). The cultures that showed the highest resistance to trimethoprim (31.2%), cephalothin (32.6%), and cefixime (21.6%) (Ibrahim S. A. *et al.*, 2020). All isolates of *K. pneumoniae* were sensitive to amikacin and sulphamethoxazole showed resistance against 61.1% of them (Alashoury, 2024). 60% and more of *Klebsiella aerogenes* isolates were resistant to cotrimoxazole, nitrofurantoin, gentamycin and amoxicillin (account for 84.1%, 78.3%, 66.7%, 60.7%, respectively, while susceptibility rates of these bacteria to imipenem, augmentin and ciprofloxacin were 73.9%, 63.0%, 57.2% (Hassan A.O *et al.*, 2023).

The resistance rates of *K. pneumoniae* in infants and young children against ampicillin, penicillin, trimethoprim/sulfamethoxazole, amoxycillin/clavulanic acid, gentamicin, cephalexin, cefotaxime, cephalothin, amikacin and nalidixic acid were (100%, 100%, 100%, 57.1%, 71.4%, 100%, 100%, 100%, 57.1% and 57.1%, respectively) (Saeed *et al.*, 2015). *P. aeruginosa* isolates were sensitive to amikacin, ciprofloxacin, levofloxacin, and meropenem, while antibiotics such as amoxicillin and erythromycin exhibited less antimicrobial activity against *P. aeruginosa* (Saleem Salman, 2024). Antibiotics such as ciprofloxacin, nalidixic acid, nitrofurantoin, gentamicin were active against *P. aeruginosa* isolates (the percentages were 59%, 46%, 47%, 57%, whereas oxacillin exhibited no activity against them (Al-nasrawi and Mousa, 2009). Susceptibility of *P. aeruginosa* to ceftazidime, cefotaxime,

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piperacillin, ciprofloxacin, tobramycin, and gentamicin were 81%, 78%, 76%, 74%, 72%, respectively. Resistance rate of *P. aeruginosa* to amikacin, meropenem, ofloxacin, and imipenem were 70%, 66%, 65%, respectively (Ayad Daher, 2024).

All isolates of *P. aeruginosa* were resistant to cephradine, amoxicillin, rifampin, amoxycillin/ clavulanic acid, cefixime, streptomycin and ceftizoxime (100% for each), while 50% or more resistant to cefotaxime, , ceftriaxone, ciprofloxacin, ceftazidime, trimethoprim/ sulfatomexazole (50% for each) and gentamicin (75%) (Mahmood *et al.*, 2021). A study conducted in Iran reported that resistance rate of *P. mirabilis* to cotrimoxazole was 59.1% and to amoxicillin was 44.5%, and more than 95% of *P. mirabilis* isolates were sensitive to meropenem and amoxicillin (Mirzaei *et al.*, 2019). 90% or more of *Proteus* strains (polish group) were resistant to tetracycline and nitrofurantoin, and almost 50% of these strains showed resistance to carbenicillin, ampicillin, imipenem and aztreonam (Adamus-Bialek *et al.*, 2013). *Proteus* isolates were susceptible to 78.1% of trimethoprim / sulfatomexazole, 94.5% of nalidixic acid and gentamicin, 96.7% of norfloxacin and ciprofloxacin, 99.5% of amikacin and amoxicillin / clavulanic acid , 80.3% of ampicillin, 97.8% of cephalothin, 98.4% of efuroxime, ceftriaxone, and cefepime and 100% of ertapenem, meropenem, piperacillin / tazobactam (Danilo de Oliveira *et al.*, 2021).

Chapter Three

Materials and Methods

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3. Material and methods

3.1. Materials

3.1.1. Equipments and Instruments

There were several instruments used in the current study described in Table 3-1.

Table (3-1): General laboratory equipments and instruments in the present study.

NO	Instruments	Companies	Origins
1	Autoclave	Raypa	Spain
2	Beakers, Flasks and Cylinders	Superior	Germany
3	Burner	Memmert	Germany
4	Centrifuge	DLAB	China
5	Deep freeze	GFL	Germany
6	Disposable petri dishes	TRUST	China
7	DNA electrophoresis apparatus	Hettich	Germany
8	Dry microtubes incubator	Ae	UK
9	Electrophoresis system	Cleaver	UK
10	Eppendorf tube (2 ml)	Eppendorf	Germany
11	Hood-cabinet	LAMINAR	USA
12	Incubator	Froilabo	France
13	Inoculating loop	TRUST	China
14	Kern PFB balance	Kern and Sohn	Germany
15	Light microscope	Olympus	Japan
16	Microfuge IB Centrifuge	BeckmanCoulter	Germany
17	Optimus 96G thermal Cycler	QLS	UK
18	Oven	Onko	China
19	Pipettes	DARWELL	China
20	Plain Test tubes (10 ml)		China
21	Refrigerator	DAEWOO	Korea
22	Sensitivity balance	Sartorius	Germany
23	UVP	Analytik Jena	UK
24	Vortex	Fisher Scientific	USA

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3.1.2. Culture Medium

There were several culturing media used in the current study as described below in Table 3-2.

Table (3-2): Types of culture media were used in the current study.

NO	Media	Company	Origins
1	Aimes Transport medium	AFCO	Jordan
2	Blood Agar	Accumix	India
3	Brain Heart Infusion Broth	Biolab	Hungary
4	Buffered Glucose Broth	HIMEDIA	India
5	Chromogenic UTI Agar	HIMEDIA	India
6	MacConkey Agar	Accumix	India
7	Mannitol Salt Agar	Accumix	India
8	Mueller Hinton Agar	Accumix	India
9	Peptone Water	Liofilchem	Italy
10	Simmons Citrate Agar	Liofilchem	Italy

3.1.3. Chemical and Kits

There were several chemical materials and kits used in this study described in Tables (3-3 and 3-4).

Table (3-3): Chemical and materials used in the current study.

No	Material	Company	Origins
1	10X TAE (Tris borate EDTA) buffer	Promega	USA
2	Agarose LE	Intron	Korea
3	Antibiotic disks	Bioanalyse	Turkey
4	Catalase test	Mothalath Al-massy	Iraq
5	Oxidase test	HIMEDIA	India
6	Primers	Macrogen	Korea
7	RedSafe nucleic acid staining solution	Intron	Korea
8	Safe-Green 100bp Opti-DNA Marker	Abm	Canada

Chapter Three Materials and Methods

Table (3-4): list of the kits used in this study.

NO	Kits		Company	Origins
1	Gram stain	Crystal violet	Bio research	Jordan
		Iodine/ ethanol		
		Acetone		
		Sufranin		
2	GoTaq® G2 Green Master Mix		Promega	USA
3	IMViC tests	Indole test	HIMEDIA	India
		Methyl red test	HIMEDIA	India
		Voges proskauer 1 and 2	Mothalath Al-massy	Iraq
4	Presto Mini gDNA Extraction Kit for Bacteria		Geneaid	Taiwan

3.2. Methods

3.2.1. Sample Collection

Between September 2024 to February 2025, a total of 150 samples were collected from patients suffering from UTIs at hospitals, health centers and clinics in the districts and outskirts of Northern region of Thi-Qar governorate (Al-Refai, Al-Nasar, and Qalat Suker). 5-10 ml urine specimens collected in sterile screw capped tube and cultured within 1 hour after collection or stored in a refrigerator at 4°C for no more than 18 hours to be cultured later. Information such as the patient's name, age, residency and habitation were obtained from the patients and described in an educational worksheet with clear instructions called the "Questionnaire sheet. The patients' ages were from 11 to 80 years.

3.2.2. Preparation of Different Media

The culture media utilized in the present work (Blood , MacConkey, Brain Heart Infusion Broth, Mannitol Salt and Chromogenic UTI Agar) were prepared based on the instructions of manufacturer identified on containers and autoclaved for 15 mins at 121 °C and 15 pound Per Square Inch (Harrigan and McCance, 2014). Following the sterilization, blood agar base was supplemented by 5% blood, poured on petri dish or plain tubes, and incubated at 37 °C for 24 hours to ensure their sterility to be ready for culture and storage in refrigerator.

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3.2.3. Isolation and Identification of Bacteria

The midstream urine samples were collected from patient with UTI symptoms aged between (11-80) years. The samples were cultured on MacConkey and Blood agar, then incubated for 24 hours at 37 C in an aerobic environment (Bhatia and Ichhpujani, 2008). The bacterial cultures were identified by morphological examination and biochemical assays.

3.2.3.1. Gram Stain Method

A small sample from a bacterial colony was spread onto a clean slide using a drop of normal saline. The sample was heat-fixed and then stained sequentially with crystal violet, iodine, alcohol, and safranin. After staining, the slide was examined under oil immersion lens at 100X magnification (Leboffe and Pierce, 2013).

3.2.3.2. Identification by Biochemical Reactions

The main groups of Enterobacteriaceae were differentiated by analyzing their biochemical properties and enzymatic reactions to specific substrates. The IMViC tests include indole, methyl red, Voges-Proskauer, and citrate utilization test were used for this purpose, as described in Table (3-5). Additionally, Samples were tested for oxidase activity to differentiate oxidase positive *Neisseria* and *Pseudomonas* spp and oxidase-negative Enterobacteriaceae. Catalase test used to distinguish Gram positive *Staphylococcus* spp from *Streptococcus* spp (Cappuccino and Welsh, 2018).

Table (3.5): Biochemical tests for bacterial isolates linked to UTIs.

Isolates	Biochemical tests					
	Catalase	Oxidase	Indole	M.R	V.P	Simmon citrate
<i>E. coli</i>	+	-	+	+	-	-
<i>K. pneumoniae</i>	+	-	-	-	+	+
<i>P. aeruginosa</i>	+	+	-	-	-	+
<i>P. mirabilis</i>	+	-	-	+	-	+
<i>S. aureus</i>	+	-	-	+	+	+

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3.2.3.2.1. Catalase Test

The catalase test is a fundamental method for detecting the enzyme catalase in bacteria, which neutralizes hydrogen peroxide (H_2O_2) (Reiner, 2013). Catalase, present in most aerobic cells, catalyzes the conversion of H_2O_2 to oxygen and water, playing a crucial role in cellular detoxification (Havel, 2019). The test is essential for identifying Gram-positive and certain Gram-negative organisms, particularly in differentiating *staphylococci* and *streptococci* (Reiner, 2013).

3.2.3.2.2. Oxidase Test

The oxidase test is a crucial method for detecting cytochrome oxidase in microorganisms, primarily used to differentiate various bacterial species (Shields and Cathcart, 2013). It has applications in identifying potentially psychrophilic organisms in dairy products, particularly pseudomonads, which are strongly oxidase-positive (Hankin and Dillman, 1968). The test typically involves flooding agar plates with a reagent that causes oxidase-positive colonies to turn blue. A modified oxidase reagent using tetramethyl-p-phenylenediamine in dimethyl sulfoxide has shown superior results in detecting weakly oxidase-positive Gram-negative bacteria compared to the traditional aqueous solution (Tarrand and Groschel, 1982).

3.2.3.2.3. Indole

The indole test is a biochemical assay used to identify bacteria, particularly in UTIs (MacWilliams, 2009). It detects the ability of organisms like *E. coli* to produce indole from tryptophan (Dash *et al.*, 2012). Various reagents and methods have been developed for this test, including Kovacs' reagent, p-dimethylaminobenzaldehyde, and p-dimethylaminocinnamaldehyde (Miller and Wright, 1982).

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3.2.3.2.4. Methyl Red (MR)

The Methyl Red (MR) test is a biochemical assay used to differentiate bacteria based on their fermentation products when grown with glucose (Mcdevitt, 2009). It involves the production of acidic compounds and subsequent pH changes in the growth medium. Some bacteria, like *K. aerogenes*, can reverse the acidification through realkalinization, leading to negative results (Marica *et al.*, 1990). The test's effectiveness depends on factors such as cell suspension density, glucose-to-buffer ratio, and bacterial adaptation to glucose (Cowan, 1953).

3.2.3.2.5. Voges-Proskauer (V-P) Test

The Voges-Proskauer (V-P) test, developed in 1898, is a valuable method for identifying and differentiating microorganisms based on their ability to produce acetoin (acetylmethyl carbinol) during glucose fermentation (Werkman, 1930). The test involves adding potassium hydroxide to glucose peptone cultures, resulting in an eosin-like coloration in positive reactions (Paine, 1926). This color change is due to the oxidation of acetoin in the presence of strong alkali and peptone (Werkman, 1930).

3.2.3.2.6. The Citrate Utilization Test

The citrate utilization test is a key method for differentiating bacterial species, particularly within the Enterobacteriaceae family. Koser's citrate test, developed in 1924, demonstrated that *Aerobacter aerogenes* could grow in a synthetic citrate medium, while *E. coli* could not (Vaughn *et al.*, 1950). The citrate test is used to determine an organism's ability to utilize citrate as its sole carbon source. The final products of using an organic acid, like citrate, as a source of carbon and energy are alkaline carbonates and bicarbonates. An organism can import citrate if there is growth on the medium and the pH indicator color changes as a result of the elevated pH (MacWilliams, 2009).

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3.2.3.3. Identification by Differential Media

All positive bacterial cultures were also inoculated on Hicrome UTI agar and incubated at 37°C for 24 hours, for further identification. Culture characteristics such as shape and color of colony used to differentiate pathogens associated with UTI on the later media, according to manufacturer's instructions, as described in Table (3-6). Mannitol Salt Agar was used as a selective media for the isolation of pathogenic *Staphylococci* (Morello *et al.*, 2003). Table (3-7) shows culture characteristics of *Staphylococcus* strains according to Zimbro *et al.*, (2016).

Table (3.6): Cultural characteristics of uropathogens on CHROMagar UTI.

Organisms	Inoculum	Growth	Recovery	Colour of colony
<i>E. coli</i>	50-100	luxuriant	>70%	pink-purple
<i>P. mirabilis</i>	50-100	luxuriant	>70%	light brown
<i>K. pneumoniae</i>	50-100	luxuriant	>70%	blue to purple, mucoid
<i>P. aeruginosa</i>	50-100	luxuriant	>70%	colorless, greenish pigments
<i>S. aureus</i> subsp <i>aureus</i>	50-100	luxuriant	>70%	golden yellow

Table (3.7): Cultural characteristics of *Staphylococcus* strains on Mannitol salt agar.

Organisms	Inoculum (CFU/ml)	Recovery	Around the colony
<i>S. aureus</i>	$10^3 - 10^4$	Good	Yellow
<i>S. epidermidis</i>	$10^3 - 10^4$	Good	Red

3.2.4. Antibiotic Sensitivity Test

The antimicrobial susceptibility test was performed by the standardized Kirby-Bauer disc diffusion method, and the results were interpreted according to Clinical and Laboratory Standards Institute (CLSI, 2024). By measuring the turbidity of the test, the McFarland Standards were used to standardize the approximate number of bacteria in a liquid suspension. A sterile swab was dipped in the suspension for

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inoculation the Mueller-Hinton (MH) agar plate. The inoculum is applied to the dried surface of an Mueller-Hinton agar plate by streaking the swab three times across the entire agar surface, followed by rotating the plate approximately 60 degrees each time to ensure consistent and even distribution of the sample. 6-mm paper disks of appropriate antibiotics were placed on the surface of the agar by using forceps. The plate was examined after 18-20 hours of incubation at 35-37°C.

3.2.5. Maintenance of Bacterial Isolates:

Short-term Preservation

Pure cultures were successfully stored at 0-4°C for days in screw- capped tubes containing a brain heart infusion broth with 15% glycerol, after incubation at 37 °C for 18 hours (Rohman *et al.*, 2013).

Long-term Preservation

A loop of pure bacterial culture was used to inoculate a brain heart infusion broth in Screw-capped tube, and after 18 hours of incubation at 37C°. The inoculum was preserved at -20C° for 6 months by adding glycerol at the final concentration of 15% and normal saline (0.9 of Sodium Chloride) (Mahmmoud, 2020).

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3.2.6. Molecular Studies

3.2.6.1. DNA Extraction from Bacteria

Table (3-8) shows the components of the Bacterial DNA Extraction Kit Presto Mini gDNA Extraction.

Table (3-8): Components of the Bacterial DNA Extraction Kit.

Contents	100 COLUMN
Gram+ Buffer	30 ml
GT Buffer	30 ml
GB Buffer	40 ml
W1 Buffer	45 ml
Wash Buffer (Add Ethanol)	25 ml
Lysozyme, Lyophilized	110 mg
Proteinase K, Lyophilized	11 mg (1.1 ml)
Elution Buffer	30 ml

3.2.6.2. Protocol

Presto Mini gDNA Extraction Kit

1. 1-2 ml of cells (OD₆₀₀: 2.0-1.0) was harvested by centrifuging at 14,000 rpm for 1 min and remove supernatant.

2 A. 180 µl of G-Buffer solution with 20µl of proteinase K was added, and mixed well by inversion. **(For Gram-negative Bacteria)**

2 B. 200 µl of Gram + buffer (lysosome was added) transferred to 2 ml centrifuge tube. **(For Gram-positive Bacteria)**

3 A. The mixture was incubated at 65°C for 15 min.

Note: To help lysis cells, inverted mix the tube every 5 min during the incubation. **(For Gram-negative Bacteria)**

3 B. At 37°C for 30 min was incubated. The tube was inverted every 10 min during incubation. **(For Gram-positive Bacteria)**

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4. 200 µl of Binding Buffer with 20µl of proteinase K was added, and completely mixed well by pipetting (at least 10 times) or gently vortexing.
5. Cell lysates was loaded on column and centrifuged at 14,000 rpm for 1 min.
6. 400 µl of Washing Buffer A was added to column and centrifuged for 1 min at 13,000 rpm.
7. Solution was removed and centrifuged for 30 seconds at 14,000 rpm.
8. The spin column was placed in a clean 1.5 ml microcentrifuge tube and added 100 µl of Elution Buffer directly onto the membrane.
9. At room temperature was incubated for 1 min, and then centrifuged for 30 seconds at 14,000 rpm

3.2.6.3. Agarose Gel Electrophoresis of DNA

After the PCR program had been completed, electrophoresis was performed to visualize the size of the PCR result and evaluate the quality of the DNA extraction. Depending on the type of material, the gels had different concentrations. Though it varied from 1 to 2% for typical PCR results, the agarose gel concentration used to evaluate DNA quality was typically 1.5%.

3.2.6.4. Preparing of The Agarose Gel

The procedures described by (Sambrook and Green, 2012) were followed in the preparation of the agarose gel. In conclusion, a microwave was used to bring 1.5 of agarose to a boil after it had been dissolved in roughly 100 milliliters of 1X TBE buffer. A volume of 5 µl of RedSafe nucleic acid staining solution was added to the gel after it had been cooled to a temperature 50°C. After that, the gel was poured into the gel cast and left for roughly 30 min to be completely solidified. After inserting the gel plate into the gel tank, 1X TBE buffer was added until the entire gel surface was coated.

3.2.6.5. Loading The PCR Products

The center of the corresponding hole on the 1% gel was filled with around 5 µl of each PCR product. The first well of the gel lines was filled with 5 µl of Safe-Green

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100bp Opti-DNA Marker, which was used as a reference to measure the size of the PCR products.

3.2.6.6. Electrophoresis

After loading the samples and the Safe-Green 100bp Opti-DNA Marker, the electrophoresis apparatus was set up with a constant current of 80 volts for 70 minutes. Finally, a 320 nm UV light source was used to visualize the PCR products on the gel by placing it into the UVP system.

3.2.6.7. Preparation of Primers

To reach a final concentration of 100 $\mu\text{M}/\mu\text{l}$, the lyophilized primers were dissolved in distilled water according to the guidelines provided by the primer synthesiser company. After that, this solution was stored at -20°C as a stock solution. The stock primers, which used as a work primer, were diluted to a concentration of 10 $\mu\text{M}/\mu\text{l}$.

3.2.6.8. Primers Used in This Study

The primers used in this study are listed in the Table 3-9

Table (3-9): Primers used in this study.

Gene	Primer name	Sequence (5'-3')	PCR size	References
<i>FimH</i>	F	TGCAGAACGGATAAGCCGTGG	508	(Johnson and Stell, 2000)
	R	GCAGTCACCTGCCCTCCGGTA		
<i>kpsMTII</i>	F	GCGCATTTGCTGATACTGTTG	272	(Johnson and Stell, 2000)
	R	CATCCAGACGATAAGCATGAGCA		
<i>mdeA</i>	F	GCGAGAGGTGAAACGTTAGC	256	(Alves <i>et al.</i> , 2018)
	R	AGAACAGAGCAGCAGCAACA		
<i>Hla</i>	F	ACCGCCAATTTTCCAGAAT	167	(Alves <i>et al.</i> , 2018)
	R	CCTGGCCTTCAGCATTTAAG		

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3.2.6.9. GoTaq® G2 Green Master Mix

The GoTaq® G2 Green Master Mix is a pre-made mixture of reaction buffer, deoxynucleotides, and premium Taq DNA Polymerase at a 2X concentration. It contains every component needed for DNA amplification. The final products can be directly placed onto a gel for analysis due to the stabilizing agent and non-reactive green dye included in the GoTaq® G2 Green Master Mix.

3.2.6.10. Preparation of PCR Solutions

The following solutions were combined to prepare the PCR solution as listed in Table 3-10.

Table (3-10): PCR reaction.

Components	Concentration	Volume (50 µl)
GoTaq® G2 Green Master Mix	1X	25 µl
Forward primer	10 µM/µl	4 µl
Reverse primer	10 µM/µl	4 µl
ddH ₂ O	-	13 µl
DNA	40 ng	4 µl

3.2.6.11. PCR Conditions

The conditions of PCR that used for genes identification are listed in the Table 3-11.

Table (3-11): Conditions of PCR program that used for identification of virulence genes.

Phase	T _m (°C)	Time	Cycles
Initial denaturation	95°C	5 min	1X
Denaturation	95°C	45 sec.	35X
Annealing	55°C	45 sec.	
Extension	72°C	45 sec.	
Final extension	72°C	5 min	1X

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Statistical Analysis:

The Statistical Packages of Social Sciences-SPSS (2019) program was used to detect the effect of difference factors in study percentage (George and Mallery, 2019). Chi-square test was used to significant compare between percentage (0.05 and 0.01 probability) in this study.

Chapter Four

Results

4. Results**4.1. Urinary Tract Infections**

In this study, 150 patients diagnosed with UTIs were included with both sexes and aged between (11-80). Bacterial pathogens were detected in 43 patients (28.7%), whereas 107 patients (71.3%) tested negative for bacterial UTIs. The study indicated a significant difference at p. value < 0.05, as in Figure (4.1).

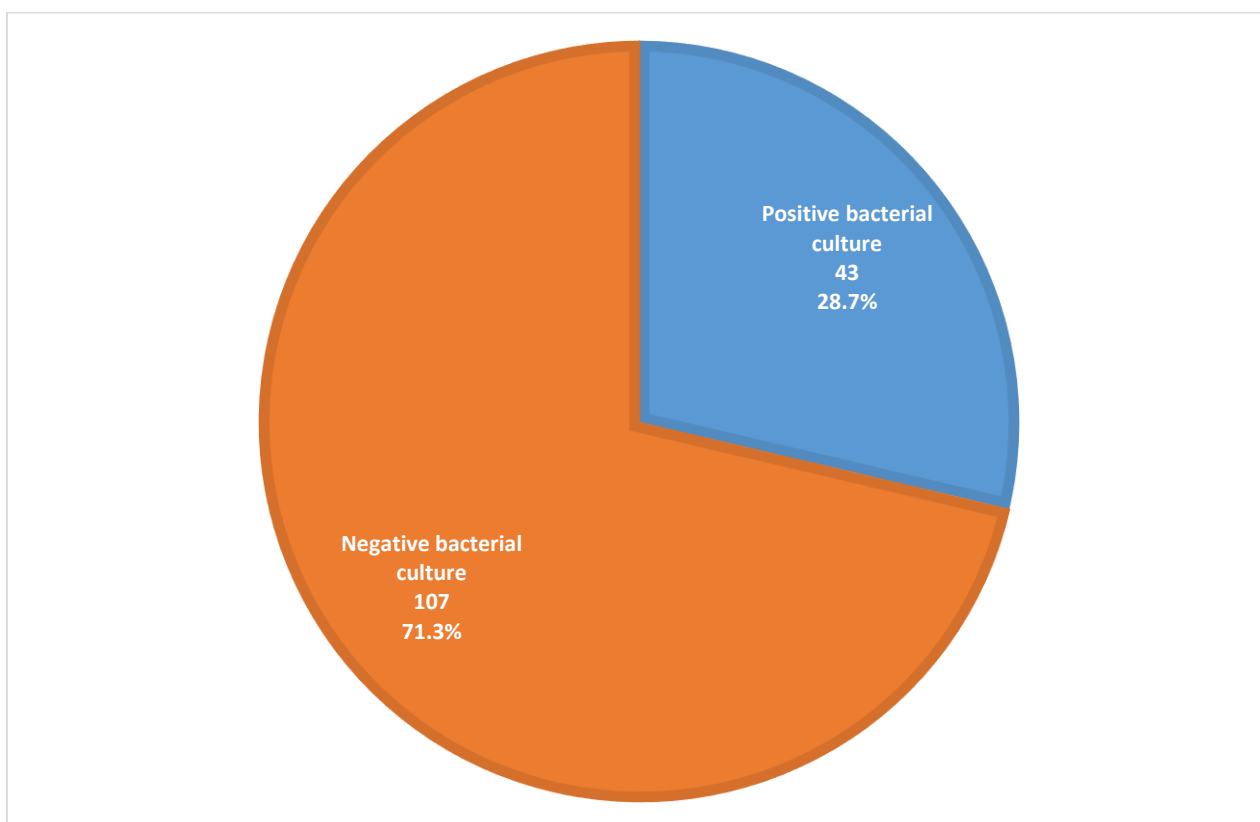


Figure 4.1: Prevalence of Bacterial infection in UTI patients

4.2. Distribution of UTI Patients According to Sex

In the current study, the highest rate of positive bacterial infections was observed among females, accounting for approximately 60.5% of the total. In comparison, the prevalence of bacterial infections in males was 39.5%. Data displayed a highly significant difference between male and female group at p. value < 0.01 (Table 4-1).

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Table (4-1): Distribution of UTI patients according to sex.

Sex	Positive Culture		Negative Culture		Total	
	No.	%	No.	%	No.	%
Male	17	39.5	85	79.44	102	68.00
Female	26	60.5	22	20.56	48	32.00
Total	43	28.67	107	71.33	150	100
Cal: $\chi^2 = 32.502$ Tab: $\chi^2 = 6.63$ DF= 1 P-value: 0.0001 ($P \leq 0.01$).						

4.3. Distribution of UTI Patients According to Residency

In the present study, the highest rate of UTI in northern region of Thi-Qar was in Qalat Suker district (41.9%), followed by Al-Refai district and Al-Naser district (32.5% and 25.6%, respectively) as shown in Figure (4.2). The current study showed highly significant difference between these residences at p. value ($P \leq 0.01$).

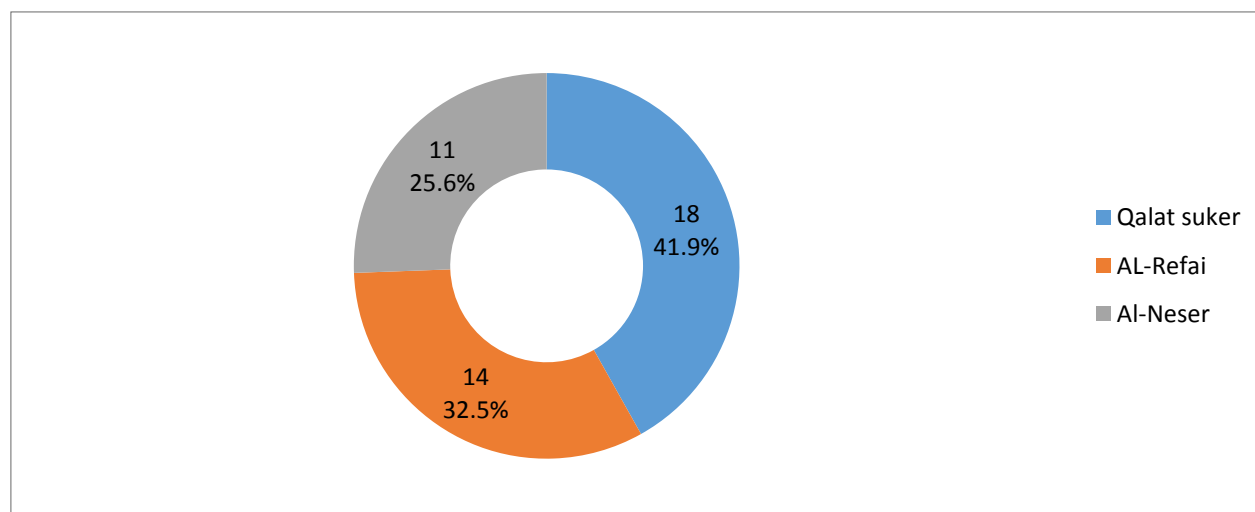


Figure (4.2): Distribution of UTI patients according to residency.

4.4. Distribution of UTI Patients According to Habitation

The results indicated that the residences of urban patients exhibited the highest positive bacterial infection rate (53.49%). On the other hand, the prevalence of UTIs in Rural group was 46.51%. The present study exhibited a significant difference between rural and urban group at p. value < 0.05 (Table 4-2).

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Table (4-2): Distribution of UTI patients according to habitation.

Habitation	Positive Culture		Negative Culture		Total	
	No.	%	No.	%	No.	%
Rural	20	46.51	67	62.62	87	58.00
Urban	23	53.49	40	37.38	63	42.00
Total	43	28.67	107	71.33	150	100
Cal: $\chi^2 = 4.392$ Tab: $\chi^2 = 3.84$ DF= 1 P-value: 0.0388 ($P \leq 0.05$).						

4.5. Distribution of UTI Patients According to Age Group

This study revealed that the highest incidence of positive bacterial infections was observed in the sixth age group (61 -70 years), accounting for 23.26%, followed by the second age group (21 -30 years) with 20.93% and the fifth (51 -60 years) with 16.28%. In contrast, the first age group exhibited the lowest incidence rate of UTIs at just 4.65%. Furthermore, it was noted a highly significant difference according to age groups at p. value < 0.01 (Table 4-3).

Table (4-3): Distribution of UTI patients according to age group.

Age Groups	Positive Culture		Negative Culture		Total	
	No.	%	No.	%	No.	%
11 -20 years	2	4.65	35	32.71	37	24.67
21 -30 years	9	20.93	20	18.69	29	19.33
31 -40 years	5	11.63	18	16.82	23	15.33
41 -50 years	6	13.95	10	9.34	16	10.67
51 -60 years	7	16.28	11	10.28	18	12
61 -70 years	10	23.26	9	8.41	19	12.67
≥ 71 years	4	9.30	4	3.74	8	5.33
Total	43	28.67	107	71.33	150	100
Cal: $\chi^2 = 52.782$ Tab: $\chi^2 = 16.81$ DF= 6 P-value: 0.0001 ($P \leq 0.01$).						

Chapter four Results

4.6. Identification of Bacterial Species in UTI Patients

The study demonstrated that the highest isolated bacteria were *E. coli* (34.9%), and the second isolated bacteria were *K. pneumoniae* (25.6%), followed by *P. aeruginosa* (18.6) and *P. mirabilis* (11.6%). On the other hand, the lowest isolated bacteria were *S. aureus* (9.3%). The study exhibited a highly significant difference according to species of isolated bacteria at P. value < 0.01 (Table 4-4).

Table (4-4): Identification of bacterial species in UTI patients.

Bacterial Species	No.	%
<i>E. coli</i>	15	34.9
<i>K. pneumoniae</i>	11	25.6
<i>P. aeruginosa</i>	8	18.6
<i>P. mirabilis</i>	5	11.6
<i>S. aureus</i>	4	9.3
Total	43	100
Cal: $\chi^2 = 9.442$ Tab: $\chi^2 = 9.49$ DF= 4 P-value: 0.0001 ($P \leq 0.05$).		

4.7. Antibiotics Sensitivity Test

Many antibiotics with different mechanisms of action were tested against different types of pathogens associated with UTI. Many *E. coli* isolates exhibited high resistant to cefotaxime, ciprofloxacin, tetracycline, trimethoprim, tobramycin and trimethoprim/sulfamethoxazole, accounting for 60%, 53.3%, 66.7%, 73.3%, 46.7% and 66.7%, respectively (Table 4-5). Susceptibility rates of *E. coli* for cefoxitin, gentamicin, imipenem, nitrofurantoin and amikacin were 53.3%, 40%, 53.3%, 46.7% and 46.7%, respectively. *K. pneumoniae* isolates showed high resistance rates to ciprofloxacin, tetracycline, tobramycin, trimethoprim and trimethoprim/ sulfamethoxazole (were accounting for 63.6%, 100%, 63.6%, 81.8%, and 63.6%, respectively) (Table 4-5). Regarding antibiotic susceptibility testing for Enterobacteriaceae, the current study showed highly significant difference ($P \leq 0.01$).

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Table (4.5): Antibiotic susceptibility test for Enterobacteriaceae.

List	<i>E. coli</i>			<i>K. pneumoniae</i>			<i>P. mirabilis</i>		
	S	I	R	S	I	R	S	I	R
AK	7(46.7)	2(13.3)	6(40)	5(45.45)	1(9)	5(45.45)	3(60)	1(20)	1(20)
CTX	5(33.3)	1(6.7)	9(60)	3(27.3)	2(18.2)	6(54.54)	3(60)	0(0)	2(40)
Fox	8(53.3)	3(20)	4(26.7)	6(54.54)	1(9)	4(36.46)	3(60)	1(20)	1(20)
Cip	6(40)	1(6.7)	8(53.3)	4(36.4)	0(0)	7(63.6)	1(20)	1(20)	3(60)
CN	6(40)	2(13.3)	7(46.7)	5(45.45)	1(9)	5(45.45)	1(20)	2(40)	2(40)
IMI	8(53.3)	1(6.7)	6(40)	3(27.3)	2(18.2)	6(54.54)	0(0)	1(20)	4(80)
Net	5(33.3)	2(13.3)	8(53.3)	6(54.54)	1(9)	4(36.36)	3(60)	1(20)	1(20)
F	7(46.7)	2(13.3)	6(40)	7(63.63)	1(9)	3(27.3)	0(0)	0(0)	5(100)
TZP	5(33.3)	1(6.7)	9(60)	4(36.36)	2(18.2)	5(45.45)	2(40)	1(20)	2(40)
TE	4(26.6)	1(6.7)	10(66.7)	0(0)	0(0)	11(100)	0(0)	1(20)	4(80)
Tob	6(40)	2(13.3)	7(46.7)	2(18.2)	2(18.2)	7(63.63)	3(60)	2(40)	0(0)
Tm	3(20)	1(6.7)	11(73.3)	1(9)	1(9)	9(81.8)	0(0)	0(0)	5(100)
SXT	4(26.7)	1(6.7)	10(66.7)	3(27.3)	1(9)	7(63.63)	0(0)	1(20)	4(80)
Cal: $\chi^2 = 78.66$ Tab: $\chi^2 = 50.89$ DF= 24 P-value: 0.0001 ($P \leq 0.01$).									

Abbreviations: **AK:** Amikacin , **CTX:** Cefotaxime, **Fox:** Cefoxitin, **Cip:** Ciprofloxacin, **CN:** Gentamicin, **IMI:** Imipenem, **Net:** Netilmicin, **F:** Nitrofurantoin, **TZP:** Piperacillin/tazobactam, **TE:** Tetracycline, **Tob:** Tobramycin, **Tm:** Trimethoprim, **SXT:** Sulfamethoxazole-Trimethoprim.

All isolates of *P. aerogenosa* were resistant to nitrofurantoin, trimethoprim, tetracycline, cefoxitin and trimethoprim /sulfamethoxazole (100%). *P. aeruginosa* showed high resistance to tobramycin, imipenem, and gentamicin (accounting for 75%, 50%, and 62.5%, respectively), as shown in Figure (4.3). The susceptibility

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rates of *P. aeruginosa* isolates to ciprofloxacin, netilmicin, piperacillin-tazobactam and amikacin were 50%, 50%, 75% and 50%, respectively. The data associated with antibiotic susceptibility patterns for *P. aeruginosa* exhibited highly significant difference at ($P \leq 0.01$). Resistance rates of *P. mirabilis* to cefotaxime, trimethoprim/sulfamethoxazole, ciprofloxacin, gentamicin, imipenem, nitrofurantoin, tetracycline, and trimethoprim were 40%, 80%, 60%, 40%, 80%, 100%, 80%, and 100%, respectively (Table 4-5).

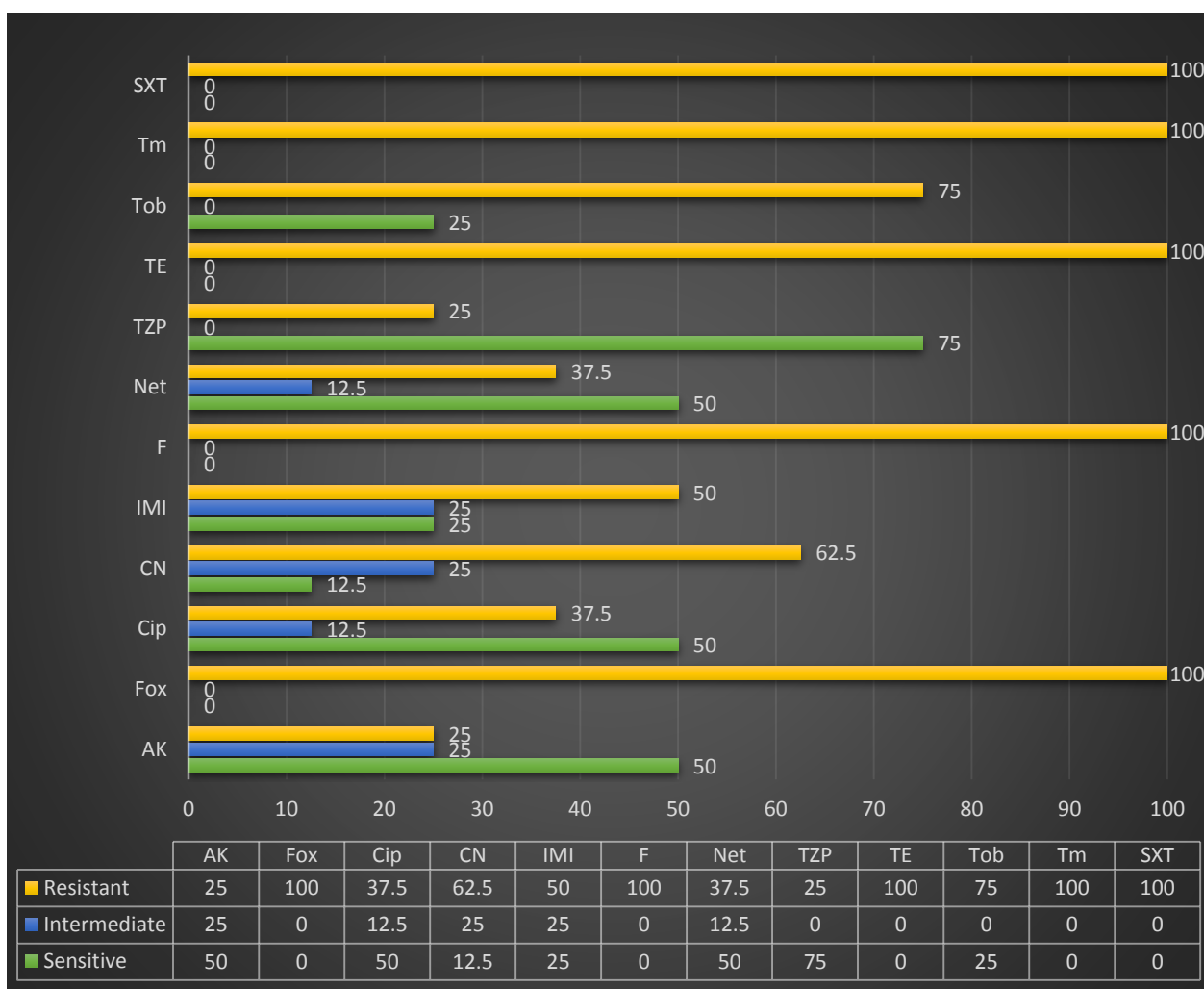


Figure (4.3): Antibiotic susceptibility test for *P. aeruginosa*.

Abbreviations: *SXT*: Sulfamethoxazole-Trimethoprim, *Tm*: Trimethoprim, *Tob*: Tobramycin, *TE*: Tetracycline, *TZP*: Piperacillin / Tazobactam, *Net*: Netilmicin, *F*: Nitrofurantoin, *IMI*: Imipenem, *CN*: Gentamicin, *Cip*: Ciprofloxacin, *Fox*: Cefoxitin, *AK*: Amikacin.

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Antibiotics like erythromycin and tobramycin were ineffective against all isolates of *S. aureus* (100%), and most of these isolates exhibited significant resistance against tetracycline, trimethoprim and trimethoprim/ sulfamethoxazole (75% for each), as shown in the Figure (4.4). The data indicate that susceptibility rates of *S. aureus* for cefoxitin, chloramphenicol, gentamicin, ciprofloxacin, clindamycin, amikacin, nitrofurantoin and vancomycin were 50%, 75%, 75%, 50%, 50%, 100%, 100% and 50%, respectively (with highly significant difference at $P \leq 0.01$).

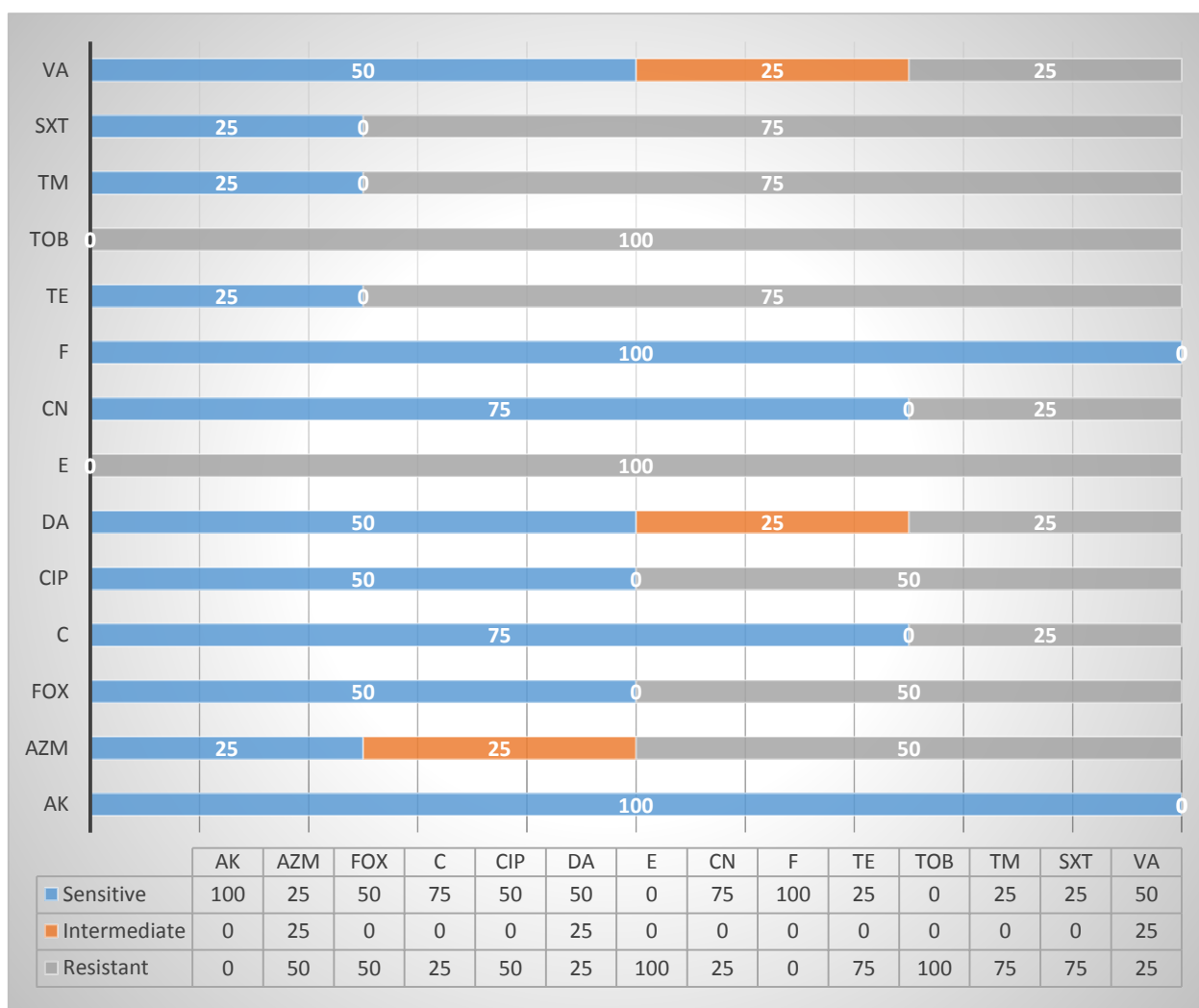


Figure (4.4): Antibiotic susceptibility test for *S. aureus*

Abbreviations: *VA:* Vancomycin, *SXT:* Sulfamethoxazole-Trimethoprim, *Tm:* Trimethoprim, *Tob:* Tobramycin, *TE:* Tetracycline, *F:* Nitrofurantoin, *CN:* Gentamicin, *E:* Erythromycin, *DA:* Clindamycin, *Cip:* Ciprofloxacin, *C:* Chloramphenicol, *Fox:* Cefoxitin, *AZM:* Azithromycin, *AK:* Amikacin.

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4.8. Molecular Detection of Virulence Genes of *E. coli* and *S. aureus*

Isolates of the leading cause of UTIs among Gram- negative bacteria (*E. coli*) and the most common Gram positive bacteria (*S. aureus*) were tested for harboring particular virulence genes by PCR. Fifteen isolates of *E. coli* isolated and identified by biochemical reactions were examined for the presence of virulence genes (*FimH* and *KpsMTII* genes). Meanwhile, 4 isolates of *S. aureus* were tested by PCR for detection of *mdeA* and *hla* genes, as shown in Table (4.6).

Table 4.6: prevalence rate of virulence genes for *E. coli* and *S. aureus*.

Bacteria	Gene	Positive results		Total	
		No.	%	No.	%
<i>E. coli</i>	<i>FimH</i>	13	86.7	15	100
<i>E. coli</i>	<i>KpsMTII</i>	12	80	15	100
<i>S. aureus</i>	<i>mdeA</i>	2	50	4	100
<i>S. aureus</i>	<i>Hla</i>	2	50	4	100
Cal: $\chi^2 = 15.275$ Tab: $\chi^2 = 11.34$ DF= 3 P-value: 0.0016 ($P \leq 0.01$).					

4.8.1. Molecular Detection of *FimH* of *E. coli*

Out of the 15 *E. coli* isolates, the bacteria were identified using biochemical tests. All isolates of *E. coli* were detected by PCR amplification via *fimH*, and only 13 isolates (86.67%) were positive for molecular detection of *fimH* gene (Figure 4-5).

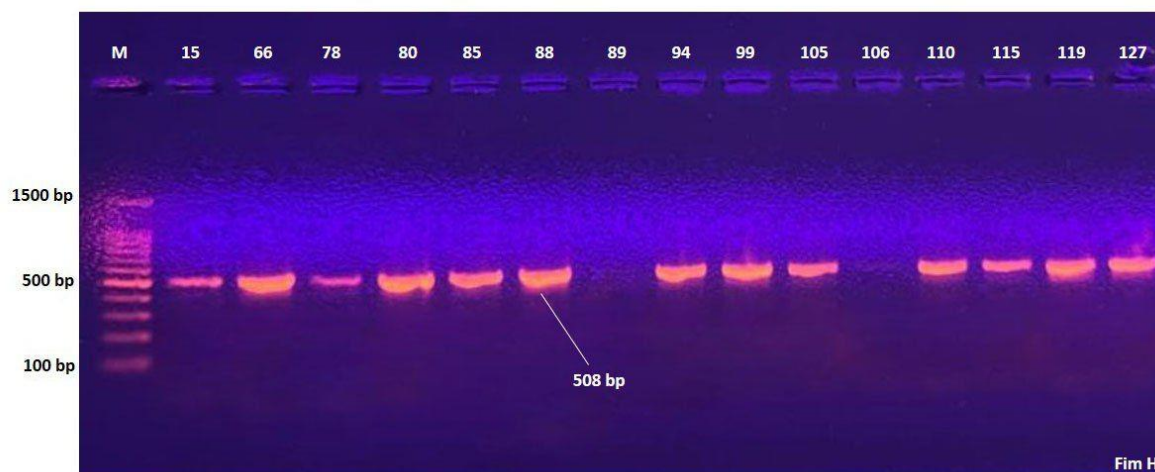


Figure (4.5): PCR products of the amplification of partial region of gene *fimH* of *E. coli*. The size of the PCR product is 508 bp. The gel was 1.5%. V: 80, Time: 70 minutes. M: DNA ladder (100 bp).

4.8.2. Detection of *KpsMTII* Gene of *E. coli*.

All 15 isolates of *E. coli* were detected by PCR amplification via *KpsMTII*, only 12 isolates were examined positive for *KpsMTII* (80%). The *KpsMTII* gene was amplified successfully, and the bands on the gel were located at 272 bp in size (Figure 4.6).

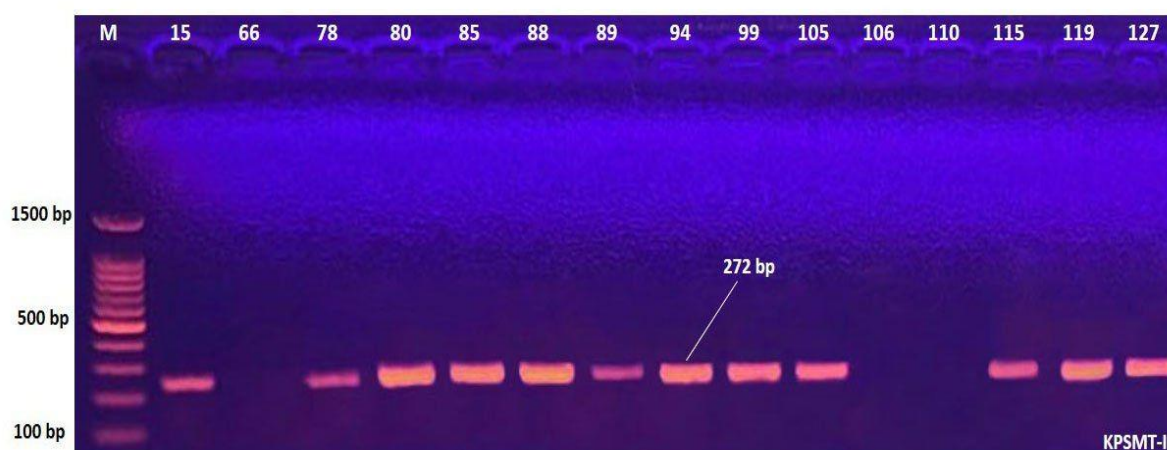


Figure (4.6): PCR products of the amplification of partial region of gene *KpsMT-II* in the isolates of *E. coli*. The gel was 1.5%, V: 80, Time: 70 minutes. M: DNA ladder (100 bp).

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4.8.3. Detection of *mdeA* Gene of *S. aureus*.

Only 2 out of 4 isolates (50%) of *S. aureus* in the current investigation tested positive for *mdeA* gene, as shown in the figure below.

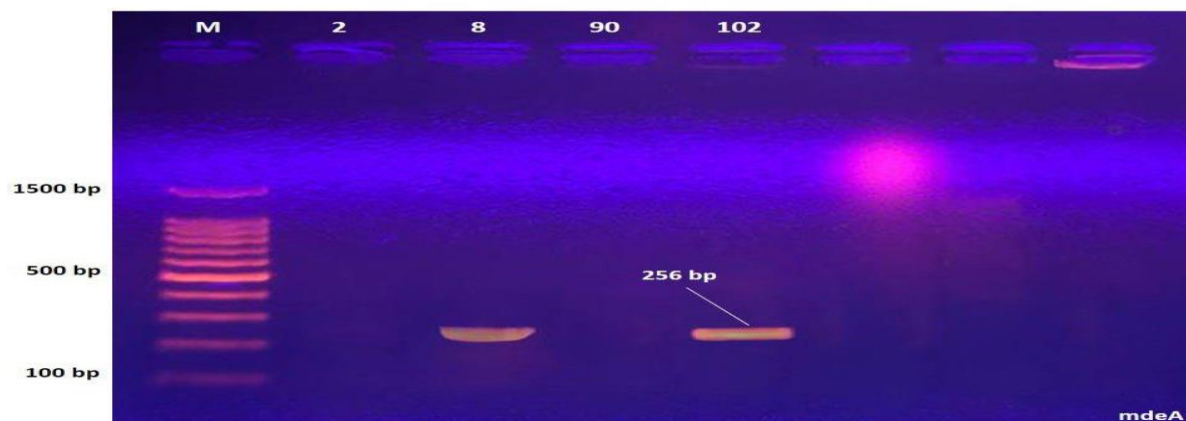


Figure (4.7): PCR products of the amplification of partial region of gene *mdeA* in the isolates of *S. aureus*. The gel was 1.5%. V: 80, Time: 70 minutes. M: DNA ladder (100bp).

4.8.4. Detection of *hla* Gene of *S. aureus*

All four isolates of *S. aureus* were examined for *hla* gene by PCR (Figure 4.8), and only two isolates (50%) were positive. Data showed that the *hla* gene was expressed and located at 167 bp in size.

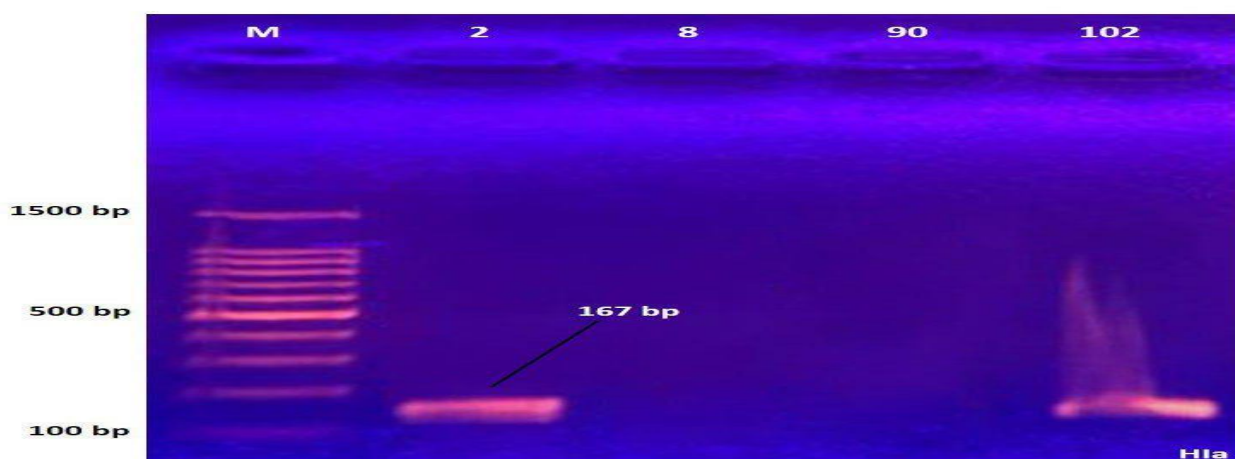


Figure (4.8): PCR products of the amplification of partial region of gene *hla* in the isolates of *S. aureus*. The size of the PCR product is 167 bp. The gel was 1.5% and. V: 80, Time: 70 minutes. M: DNA ladder (100bp).

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Discussion

5. Discussion**5.1. Urinary Tract Infections**

In the current study, 150 patients who showed symptoms of UTIs were included. However, only 43 patients (28.7%) showed positive bacterial culture on blood and MacConkey agars. These results align with previous studies conducted in Iraq. A study carried out in Maysan between January 2018 and January 2019, showed that 216 out of 830 patients exhibited bacterial UTIs (accounts for 26%) (Allami *et al.*, 2021). In Baghdad, only 63 out of 237 patients with UTI symptoms visited Medical City Hospital showed positive bacterial growth accounting for (26.58 %) (Al-Gasha'a *et al.*, 2020). A study conducted in Ebril by Ekrem Kîreççi *et al.*, reported that out of 120 midstream urine samples diagnosed with UTIs, only 70 patients (58.3 %) were positive for bacterial culture (Kîreççi *et al.*, 2015).

5.2. Incidence of UTIs According to Sex

In the present study, females exhibited higher incidence of UTIs compared to males (60.5% vs. 39.5%, respectively). The higher incidence of UTI in female compared to males may be due to anatomical and physiological differences, including a shorter urethra and short proximity to the anus (Burrows, 2024). Similar results were reported by previous studies that showed a high frequency of UTIs occurred in females compared to males. It has been reported that females exhibited a significantly greater rate of UTI s (77%) compared to males (23%) (Saleem Salman, 2024). The current study agrees with Sinha *et al.* (2013) who stated that out of 1239, only 745 patients (60.13%) were females and 494 patients (39.87%) were male. As a result of factors such as sexual activity, urinary incontinence, a less acidic vaginal pH, and unhygienic living conditions, females in Baghdad were more susceptible to UTIs than males (accounting for 81.8 % and 18.8%, respectively) (Alwan *et al.*, 2023).

5.3. Incidence of UTIs According to Residency

The present study recorded the highest positive bacterial infection in Qalat Suker district, followed by Al-Refai district (accounting for 41.9% and 32.5%, respectively). The lowest positive bacterial infection was in Al-Neser district (25.6%). These findings disagree with a study conducted in the north of Thi- Qar province between September and December 2023, which reported that the residents of Al-Refai (33.85%) had the highest frequency of bacterial infections, while the residents of Qalat Suker district had the lowest (16.15%). The results showed that there was no significant difference in the $P\text{-value} < 0.05$ according to residency (Shuwaili and AL-Maliky, 2024). Numerous reasons, including low socioeconomic standing, low sanitation status, inadequate personal hygiene, and population density, may be responsible for the high frequency of microbial infections in the presents study (Mousa H. M. and Qasim, 2021).

5.4. Incidence of UTIs According to Habitation.

In this study conducted in the northern region of Thi-Qar, urban patients showed the highest rate of positive bacterial infections, accounting for 53.49%. In comparison, rural residents had a lower infection rate of 46.51%. The current study disagrees with a study, which found that the incidence rates of UTIs were higher in rural (61.54%) than urban areas (38.46%), suggested that some factors such as lack of health education, limited access to healthcare services, and poor preventive measures in rural areas are the contributing factors for these differences (Al-hakak, 2025). Another study reported that the percentage of urban-dwelling women who experienced UTIs was higher than that of rural-dwelling women (43.6% versus 56.4%) (Almukhtar, 2018). The present study is in consistent with a study conducted in Erbil, which reported that urban areas had a greater frequency of UTIs among females (76.1%) compared to rural areas (57%) (Hussein S. *et al.*, 2014). According to Ibrahim M. S. *et al.*, (2021), UTI patients in Zakho City had the highest prevalence of UPEC (40.56%) when compared to patients in villages and camps (13.89% and

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12.20%). The average annual incidence was higher for children, adolescents, and young people in urban regions than in rural ones, with rates of 439 per 100,000 and 211 per 100,000, respectively (Ibrahim M. S. *et al.*, 2021). Increased population density, closer living quarters, and more interpersonal encounters are the outcomes of rapid urbanization, which is characterized by a large migration of people into metropolitan areas (Chen L. *et al.*, 2024).

5.5. Incidence of UTIs According to Age

The current study revealed that the age group (61-70) exhibited the highest infection rate among patients with UTIs. This may be because elderly people face higher risks for UTIs due to factors like diabetes, kidney stones, stroke, dementia, and bowel and bladder incontinence (Marshall and Hale, 2013). In contrast, a study reported that the highest rate of bacterial UTIs was observed in younger people who aged between (21-30), followed by the age group 31-40 years (Isma'il, 2021). The current study found that the second highest infection rate was in the age group (21-30), followed by people aged between (51-60), which accounts for 20.93% and 16.28%, respectively. Sexual active women are at increased risk for UTIs, with recent coitus and frequency of intercourse more than three times per week being independent predictors. Other risk factors in sexually active women are swabbing from back to front, history of UTI, and delayed voiding (Seid *et al.*, 2023).

5.6. Identification of Bacterial Species in UTI Patients

E. coli was the predominant pathogen among Gram-negative bacteria associated with UTIs, followed by *K. pneumoniae* and *P. aeruginosa* (accounted for 34.9%, 25.6% and 18.6%, respectively). The less common pathogen among Gram-negative bacteria linked to UTIs was *P. mirabilis* (11.6%). The results agrees with different local studies. A study conducted in Thi-Qar province reported that the most frequent bacterial species associated with UTIs in Diabetic people was *E. coli*, accounted for 48%, followed by *K. pneumoniae* (15%) (Beden and Mousa, 2022). A study that

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was done by Salwa Muhsin Hasan and Khalid S. Ibrahim, which found that *E. coli* was the first most common pathogen associated with UTIs (accounts for 44.7%) (Hasan S. M. and Ibrahim, 2022). The prevalence of UPEC reported in Zakho city was 35.25% (Ibrahim M. S. *et al.*, 2021), in Basra city was 60% (Hadi *et al.*, 2014), and in Baghdad was 38% (Nuha Abd Al.rheem Saad *et al.*, 2022). According to a study carried out in Thi-Qar province, the prevalence rate of *E. coli* isolated from patients with UTIs was 42.85% (Aya Talib jawad *et al.*, 2024). In contrast, a study carried out in AL-Nasiriyah City stated that the predominant bacterial species was *Staphylococcus* spp (40.69%) followed by *E. coli* (18.60%) (Jihad and Salih, 2024). *S. aureus* in the present study was the only Gram-positive bacteria was identified recording the lowest bacterial pathogen related to UTIs at 9.3%. The results disagree with the data reported by Naji and Awadh, who stated that Gram-positive bacteria were the leading cause of UTI (66.7%), while Gram-negative bacteria were stated 33.3% (Naji and Awadh, 2023). The present study is in agreement with a study conducted in Basra city- Iraq, which reported that the leading cause of UTIs was *E. coli* (*E. coli* was responsible for 60% of UTIs) (Hadi *et al.*, 2014).

5.7. Antibiotic Sensitivity Testing

Up to 66.7% of *E. coli* isolates were resistant to tetracycline and trimethoprim/sulfamethoxazole. *E. coli* isolates were highly resistant to trimethoprim (accounts for 73.3%). This study corresponded with the data reported by Nuha Abd Al Rheem Saad *et al.*, (2022), who found that UPEC isolates were highly resistant to trimethoprim/ sulfamethoxazole and tetracycline (65.0% and 57% respectively). A study conducted in Baghdad was investigating disturbance antibiotic resistance genes of UPEC in teen pregnant women stated that the *dfrA1* gene, which associated with trimethoprim resistance, was found in 74% of UPEC isolates (Mohammed and Ibrahim, 2022). In the current study, the majority of *K. pneumoniae* were resistant to tetracycline and trimethoprim (100% and 81.8%, respectively). These findings are consistent with a previous study in Kirkuk City, which showed that the isolates of *K.*

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pneumoniae exhibited significant resistance to tetracycline and trimethoprim (accounting for 100% and 76%, respectively) (Mohammed S. A. H. *et al.*, 2024). A study carried out in Wasit province, reported that the resistance percentages of multi-drug resistant *K. pneumoniae* isolates against tetracycline and trimethoprim were 27.27 and 33.76%, respectively (Alquraishi *et al.*, 2022). High rates of antibiotic resistance, including to tetracycline, in *K. pneumoniae* isolates from UTIs in Iraq, were associated with high prevalence of class 1 and 2 integrons (*intl-1* and *intl-2* genes) (Omar and Ibrahim, 2023). In the present study, all isolates of *P. mirabilis* and *P. aeruginosa* were 100% resistant to nitrofurantoin and trimethoprim. This study disagrees with data reported by Rashid Rahim Hateet who found that nitrofurantoin showed good effectiveness against isolates of both *P. aeruginosa* and *P. mirabilis* (Hateet, 2022). Erythromycin and tobramycin in the current study showed no activity against all isolates of *S. aureus*. *S. aureus* biofilms enhance antibiotic resistance and protect bacteria from hostile conditions (Idrees *et al.*, 2021). The sluggish diffusion of antibiotics through the biofilm matrix may sustain the development of multidrug resistance, maybe through the selection of highly tolerant strains that are momentarily exposed to sub-inhibitory dosages of antimicrobial therapy (Hami and Ibrahim, 2023).

5.8. Molecular Detection of Virulence Genes of *E. coli* and *S. aureus*

5.8.1. Molecular Detection of The *fimH* Gene of *E. coli*

The *fimH* adhesin gene plays a crucial role in UPEC virulence, mediating bacterial attachment to uroepithelial cells and contributing to colonization and invasion (Moubayed *et al.*, 2023). *FimH* enters the superficial umbrella cells of the bladder lumen by attaching itself to mannosylated uroplakin proteins. Following the invasion, UPEC either escapes into the cytoplasm or is expelled from the cell in a process that is dependent on TLR4. Intracellular bacterial communities (IBCs), have unique morphological structures and biofilm properties that shield UPEC from the immune system, are created when bacteria multiply quickly inside cells via intricate

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routes (Foroogh *et al.*, 2021). Out of 15 isolates of *E. coli* were examined for identification of *fimH* gene by PCR, we found that only 13 (86.67%) of these isolates were positive. Studies in Iraq have employed PCR-based methods to detect *fimH* and other virulence genes in UPEC isolates. The prevalence of the *fimH* gene in UPEC isolates from Iraqi patients is consistently high, ranging from 94.8 % to 100% (Fadhil, 2022) (Hasan R. N. *et al.*, 2022).

5.8.2. Molecular Detection of The *KpsMTII* Gene of *E. coli*

Numerous UPEC strains produce a K polysaccharide capsule, which shields them from the host's innate immune defenses and enhances their ability to survive and persist during infections (Goh *et al.*, 2017). Most UPEC bacteria exhibit group II capsules (K1, K5), which are identified by *kps* operon. UPEC frequently uses capsules, which are more well-known for their ability to cause pyelonephritis than other UTIs (Tiba *et al.*, 2008). Kanamaru *et al.* (2003) reported that *kpsMTII*, along with other virulence factors like *iroN*, *iha*, *ompT*, and *usp*, was 2.0-4.3 times more prevalent in UTI isolates compared to fecal isolates. According to Ejrnæs *et al.* (2011) *E. coli* strains associated with persistent or relapsing UTIs have higher prevalence of certain VFs like *KpsM II*. The current study observed that *KpsMTII* gene was found in 80% of *E. coli*. This observation was close to a study conducted by Umran and Al-Khateeb (2020), which stated that the prevalence of *KpsMTII* in uropathogenic *E. coli* was (82.3%), 78.5% of these isolates harboring this gene were associated with mild UTIs and 100% of them were linked to urosepsis.

5.8.3. Molecular Detection of The *mdeA* Gene of *S. aureus*

In *S. aureus*, the *mdeA* gene encodes a multidrug efflux pump that provides resistance to a range of antimicrobial drugs, such as antibiotics and quaternary ammonium compounds (Huang *et al.*, 2004). A transmembrane helical structure made up of 479 amino acids, the *mdeA* protein belongs to the MFS family of efflux pumps. It is stated that fluoroquinolone has a poor affinity for this 52 kDa protein

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(Ahmed and Al-Daraghi, 2022). The *mdeA* transporter is known to provide resistance to structural derivatives of quaternary ammonium compounds and has 14 predicted transmembrane segments. Recently, serum resistance in clinical isolates from individuals with poor prognoses after *S. aureus* bacteremia was linked to the gene encoding *mdeA* (Stephen *et al.*, 2023). In the current study, the prevalence of *mdeA* gene in isolates of *S. aureus* associated with UTIs was 50%. A study conducted in Iran reported that *mdeA* gene was found in (61.7%) of *S. aureus* isolates, and it had a significant association with ciprofloxacin-resistant *S. aureus*, compared to those with high susceptibility to ciprofloxacin (Hassanzadeh *et al.*, 2017). According to Umran and Al-Khateeb (2020), *mdeA* showed the second most prevalent gene in *S. aureus* isolates in Iraqi patients (92.71%).

5.8.4. Molecular Detection of The *hla* Gene of *S. aureus*

The bacterium's virulence is enhanced by its ability to form biofilms on medical devices and express various VFs, including alpha-hemolysin (*hla*) and beta-hemolysin (*hly*) (Ando *et al.*, 2004). The *hla* gene has evolved alongside *S. aureus* genetic backgrounds, with community-associated strains showing higher expression levels than hospital-associated strains (Tavares *et al.*, 2014). The presence of virulence genes like *hla* and *hly*, along with biofilm formation capabilities, contributes to the pathogen's resilience and persistence in catheter-related infections (Jafari Fesharaki *et al.*, 2022). The present study has observed that *hla* gene was expressed by 50% of *S. aureus* isolates. A study carried out in Iran stated that the prevalence of *hla* in *S. aureus* was 93% (Jafari Fesharaki *et al.*, 2022). According to Saleem, (2018), the most second prevalent hemolysin gene in *S. aureus* isolated from different sites was *hla* (accounted for 95%).

Conclusions and Recommendations

Conclusions

1- The current study concluded that females were more susceptible to UTIs than males.

2- The individuals aged 61-70 represent the highest-risk group for UTIs, confirming that immunological changes and age-related conditions are significant contributing factors for UTIs.

3- The most effective drugs among antibiotics against *E. coli* were cefoxitin and imipenem, and for *K. pneumoniae* were cefoxitin and nitrofurantoin. Amikacin, cefoxitin, tobramycin and cefotaxime were more useful substances among antibiotics against *P. mirabilis*. Antibiotics such as amikacin and nitrofurantoin should be used as empirical therapy against *S. aureus*, as well as piperacillin / tazobactam against *P. aeruginosa*.

4- Erythromycin and Tobramycin were not useful for treating UTIs caused by *S. aureus*, as well as Nitrofurantoin, Cefoxitin, Tetracycline, Trimethoprim and Trimethoprim / Sulfamethoxazole for those with *P. aeruginosa*.

5- The majority of *E. coli* isolates in this study were found to carry the *fimH* (adhesion) and *KpsMTII* (capsular synthesis) virulence genes.

6- Half of the *S. aureus* isolates were confirmed to harbor each of *mdeA* and *hla* genes, and only 25% of these isolates possessed both of them at the same time.

Recommendations

- 1-Further research is needed to identify further patterns in bacterial infections related to UTIs.
- 2- Extend the investigation to incorporate more virulence genes related to *E. coli* and *S. aureus*
- 3- Efforts must be focused on patient education and antibiotic regulation to prevent resistance are required, particularly in Multi-drugs resistant bacteria like *S. aureus* and *P. aeruginosa*.
- 4- Identifying different *E. coli* and *S. aureus* strains that cause UTIs and studying further virulence factors linked to antibiotic resistance.
- 5- Use cefoxitin for treatment UTIs that caused by Enterobacteriaceae with prior antibiotic susceptibility testing, and amikacin and nitrofurantoin for those caused by *S. aureus*. Use piperacillin-tazobactam for treating UTIs caused by *P. aeruginosa*

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Appendices

Appendix:



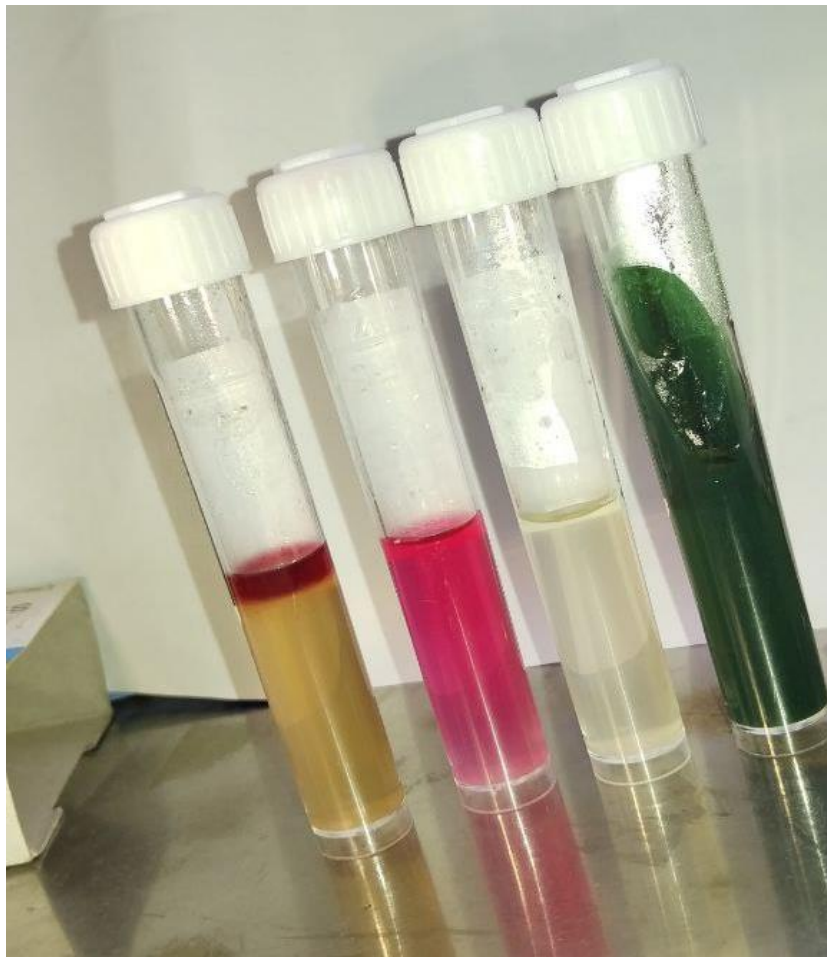
Gram negative rod bacteria on MacConkey agar



Gram positive bacteria on Blood agar



Staphylococcus aureus on Mannitol salt agar



IMViC test for *E. coli*



Disk diffusion test for *S. aureus* on Mueller Hinton Agar (MHA)

Ministry of Higher Education
& Scientific Research
AL- Shatrah University
Office of the dean assistant for
scientific affairs & postgraduate



وزارة التعليم العالي والبحث العلمي
جامعة الشطرة



أ/د مستشفى الرفاعي العام

أ/د مستشفى الشطرة العام

أ/د مستشفى النصر العام

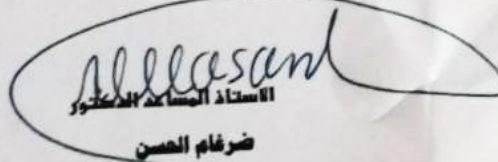
أ/د مستشفى مهمة

العدد : ٢٠٢١ / ٧ / ١٩
التاريخ : ٢٠٢١ / ٧ / ١٩

تحية طيبة ...

يرجى التفضل بالموافقة على تسهيل مهمة طالب الدراسات العليا (كرار فاضل حسن ، أحمد رشيد ساجت) لغرض جمع العينات التي تخص بحثهما .

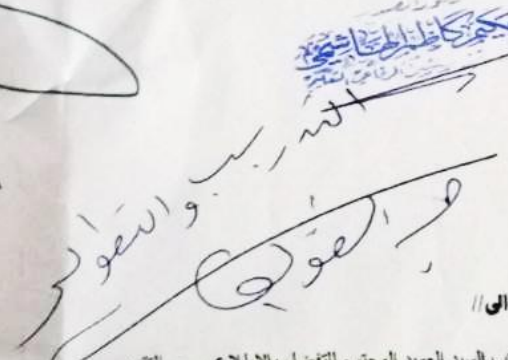
شاكرون تعاونكم معنا خدمة العلم والحياة .. مع التقدير...


الأستاذ المساعد الدكتور
زهرام الحسن

معاون العميد للشؤون العلمية والدراسات العليا

٢٠٢١/٧/١٩




الأستاذ المساعد الدكتور
زهرام الحسن

نسخة منه الى //

- مكتب السيد العميد المحترم للتفضل بالإطلاع ... مع التقدير
- الصادرة للحفظ

إملاء السيد الأستاذ المساعد الدكتور
زهرام الحسن
من جمع عينات الكا م ه بالبحث

Email: university.alshatrah@uq.edu.iq

العنوان : محافظة ذي قار - قضاء الشطرة

Questionnaires sheet

No.	Sex	Age	Residency	Habitation	Culture results
1	Female	19	Al-Refai	Village	<i>P. mirabilis</i>
2	Male	74	Al-Refai	City	<i>S. aureus</i>
3	Male	61	Al-Refai	City	<i>K. pneumoniae</i>
4	Female	23	Al-Refai	Village	<i>K. pneumoniae</i>
5	Male	49	Al-Refai	Village	<i>P. aeruginosa</i>
6	Male	54	Al-Refai	City	Negative
7	Male	56	Al-Refai	City	<i>P. aeruginosa</i>
8	Female	35	Al-Refai	City	<i>S. aureus</i>
9	Male	62	Al-Refai	City	Negative
10	Male	66	Al-Refai	Village	<i>K. pneumoniae</i>
11	Female	28	Al-Refai	City	<i>K. pneumoniae</i>
12	Male	77	Al-Refai	City	<i>P. aeruginosa</i>
13	Male	55	Al-Refai	Village	Negative
14	Male	62	Al-Refai	Village	Negative
15	Male	54	Al-Refai	City	<i>E. coli</i>
16	Male	77	Al-Refai	Village	Negative
17	Male	45	Al-Refai	City	Negative
18	Male	54	Al-Refai	Village	Negative
19	Male	63	Al-Refai	City	Negative
20	female	23	Al-Refai	City	<i>K. pneumoniae</i>
21	Male	55	Al-Refai	Village	Negative
22	Male	28	Al-Refai	Village	Negative
23	Male	47	Al-Refai	Village	Negative
24	Male	15	Al-Refai	Village	Negative
25	Female	18	Al-Refai	Village	Negative
26	Male	46	Al-Refai	City	Negative
27	Male	57	Al-Refai	Village	Negative
28	female	25	Al-Refai	City	<i>P. aeruginosa</i>
29	Female	19	Al-Refai	Village	Negative
30	Female	16	Al-Refai	City	Negative
31	Male	72	Al-Refai	Village	Negative
32	Male	43	Al-Refai	Village	Negative
33	Male	25	Al-Refai	Village	Negative
34	Male	12	Al-Refai	Village	Negative
35	Male	29	Al-Refai	Village	Negative
36	Male	54	Al-Refai	Village	Negative

37	Male	75	Al-Refai	Village	Negative
38	Male	15	Al-Refai	Village	Negative
39	Male	28	Al-Refai	City	Negative
40	Male	53	Al-Refai	Village	Negative
41	Male	23	Al-Refai	City	Negative
42	Male	16	Al-Refai	City	Negative
43	Male	52	Al-Refai	Village	Negative
44	Male	78	Al-Refai	Village	Negative
45	Male	19	Al-Refai	City	Negative
46	Male	20	Al-Refai	Village	Negative
47	Male	58	Al-Refai	City	Negative
48	Female	28	Al-Refai	Village	<i>K. pneumoniae</i>
49	Male	24	Al-Refai	City	Negative
50	Male	56	Al-Refai	City	Negative
51	Female	18	Qalat Suker	City	Negative
52	Female	33	Qalat Suker	City	Negative
53	Male	55	Qalat Suker	Village	Negative
54	Female	28	Qalat Suker	Village	Negative
55	Male	13	Qalat Suker	City	Negative
56	Female	38	Qalat Suker	Village	Negative
57	Female	16	Qalat Suker	Village	Negative
58	Female	27	Qalat Suker	City	<i>P. aeruginosa</i>
59	Female	65	Qalat Suker	Village	Negative
60	Female	35	Qalat Suker	City	<i>K. pneumoniae</i>
61	Male	57	Qalat Suker	Village	<i>K. pneumoniae</i>
62	Male	26	Qalat Suker	City	Negative
63	Male	15	Qalat Suker	Village	Negative
64	Female	42	Qalat Suker	Village	Negative
65	Female	25	Qalat Suker	Village	Negative
66	Female	22	Qalat Suker	City	<i>E. coli</i>
67	Female	43	Qalat Suker	City	<i>P. mirabilis</i>
68	Female	19	Qalat Suker	City	Negative
69	Female	49	Qalat Suker	Village	<i>K. pneumoniae</i>
70	Male	14	Qalat Suker	Village	Negative
71	Male	25	Qalat Suker	City	Negative
72	Female	35	Qalat Suker	Village	Negative
73	Female	28	Qalat Suker	Village	Negative
74	Female	36	Qalat Suker	Village	Negative
75	Male	67	Qalat Suker	City	<i>P. aeruginosa</i>
76	Male	19	Qalat Suker	Village	Negative

77	Female	20	Qalat Suker	Village	<i>P. mirabilis</i>
78	Male	53	Qalat Suker	City	<i>E. coli</i>
79	Male	17	Qalat Suker	Village	Negative
80	Female	45	Qalat Suker	Village	<i>E. coli</i>
81	Female	54	Qalat Suker	City	<i>P. mirabilis</i>
82	Male	37	Qalat Suker	City	Negative
83	Male	64	Qalat Suker	Village	<i>P. mirabilis</i>
84	Male	74	Qalat Suker	City	Negative
85	Female	25	Qalat Suker	Village	<i>E. coli</i>
86	Female	36	Qalat Suker	Village	Negative
87	Male	22	Qalat Suker	Village	Negative
88	Female	51	Qalat Suker	City	<i>E. coli</i>
89	Female	53	Qalat Suker	Village	<i>E. coli</i>
90	Female	69	Qalat Suker	City	<i>S. aureus</i>
91	Male	16	Qalat Suker	Village	Negative
92	Male	62	Qalat Suker	City	Negative
93	Male	25	Qalat Suker	Village	Negative
94	Female	64	Qalat Suker	City	<i>E. coli</i>
95	Female	48	Qalat Suker	Village	Negative
96	Male	18	Qalat Suker	Village	Negative
97	Female	45	Qalat Suker	Village	Negative
98	Female	38	Qalat Suker	Village	Negative
99	Female	33	Qalat Suker	Village	<i>E. coli</i>
100	Female	48	Qalat Suker	Village	Negative
101	Male	17	Al-Neser	City	Negative
102	Female	42	Al-Neser	City	<i>S. aureus</i>
103	Female	68	Al-Neser	City	Negative
104	Male	14	Al-Neser	Village	Negative
105	Female	62	Al-Neser	Village	<i>E. coli</i>
106	Female	39	Al-Neser	Village	<i>E. coli</i>
107	Female	46	Al-Neser	City	Negative
108	Male	17	Al-Neser	Village	Negative
109	Female	22	Al-Neser	City	<i>P. aeruginosa</i>
110	Male	47	Al-Neser	Village	<i>E. coli</i>
111	Male	19	Al-Neser	Village	Negative
112	Male	27	Al-Neser	City	Negative
113	Male	34	Al-Neser	Village	Negative
114	Male	17	Al-Neser	Village	Negative
115	Male	65	Al-Neser	City	<i>E. coli</i>
116	Male	19	Al-Neser	City	Negative

117	Male	80	Al-Neser	Village	<i>K. pneumoniae</i>
118	Male	35	Al-Neser	Village	Negative
119	Female	34	Al-Neser	City	<i>E. coli</i>
120	Male	16	Al-Neser	Village	Negative
121	Male	74	Al-Neser	Village	<i>K. pneumoniae</i>
122	Male	15	Al-Neser	City	Negative
123	Male	69	Al-Neser	Village	Negative
124	Male	33	Al-Neser	City	Negative
125	Male	63	Al-Neser	Village	<i>P. aeruginosa</i>
126	Male	14	Al-Neser	City	Negative
127	Male	69	Al-Neser	Village	<i>E. coli</i>
128	Male	16	Al-Neser	Village	Negative
129	Male	22	Al-Neser	City	Negative
130	Male	66	Al-Neser	Village	Negative
131	Male	17	Al-Neser	City	Negative
132	Male	61	Al-Neser	Village	Negative
133	Male	19	Al-Neser	City	Negative
134	Male	24	Al-Neser	Village	Negative
135	Male	37	Al-Neser	City	Negative
136	Male	26	Al-Neser	City	Negative
137	Male	29	Al-Neser	Village	Negative
138	Male	35	Al-Neser	Village	Negative
139	Male	39	Al-Neser	City	Negative
140	Male	22	Al-Neser	Village	Negative
141	Male	17	Al-Neser	Village	Negative
142	Male	28	Al-Neser	Village	Negative
143	Male	21	Al-Neser	City	Negative
144	Male	37	Al-Neser	Village	Negative
145	Male	17	Al-Neser	Village	Negative
146	Male	26	Al-Neser	City	Negative
147	Male	24	Al-Neser	City	Negative
148	Male	35	Al-Neser	Village	Negative
149	Male	27	Al-Neser	City	Negative
150	Male	24	Al-Neser	Village	Negative

الخلاصة

التهابات المسالك البولية هي ثاني أكثر الأمراض المعدية شيوعًا، وقد تتراوح حدتها بين إصابة معتدلة الى الانتان البولي المميت. يمكن أن تصيب التهابات المسالك البولية الأشخاص من جميع الأعمار ومختلف الفئات، ولكنها شائعة بشكل خاص لدى النساء وكبار السن والأشخاص الذين يعانون من مشاكل بولية أو مناعية.

في الفترة من ايلول 2024 إلى شباط 2025، تم جمع 150 عينة ادرار من مرضى يعانون من التهابات المسالك البولية، من مراكز الرعاية الصحية والعيادات والمستشفيات في شمال محافظة ذي قار. تراوحت أعمار المرضى بين 11 و80 عامًا، ومن كلا الجنسين. تم زرع العينات على وسط ماكونكي و وسط الدم، ثم تلاها عملية تشخيص البكتيريا بواسطة اختبارات كيميوكيوية. تم بعد ذلك استخدام اختبار تفاعل البوليميراز المتسلسل PCR للكشف عن تواجد جينات الضراوة في كل من بكتيريا الإشريكية القولونية وبكتيريا المكورات العنقودية الذهبية.

من بين 150 عينة، فقط 43 عينة اظهرت نتائج ايجابية للزرع البكتيري (28.7%)، كما أظهرت الدراسة ان الإناث أكثر عرضة للإصابة بالتهابات المسالك البولية، حيث شكلن نسبة 60.5% مقارنة بالذكور (39.5%). وكانت بكتيريا الإشريكية القولونية أكثر المسببات البكتيرية شيوعًا في مرضى التهابات المسالك البولية (34.9%)، أما أقل المسببات البكتيرية المعزولة من هؤلاء المرضى فكانت بكتيريا المكورات العنقودية الذهبية (9.3%). وجدت الدراسة ان اعلى نسبة للإصابة البكتيرية كانت في المناطق الحضرية (53.49%)، بينما كانت بنسبة 46.51% في المناطق الريفية. كما وجدت الدراسة ان اعلى نسبة إصابة بكتيرية كانت في الاعمار بين 61-70 سنة بمعدل وصل الى (25.23%).

تم استخدام عدة مضادات حيوية من فئات مختلفة لتقييم حساسية المضادات الحيوية لل عزلات البكتيرية الرئيسية باستخدام اختبار انتشار القرص. أظهرت أكثر من 60% من عزلات بكتيريا الإشريكية القولونية مقاومة عالية للنتراسايكلين (66.7%) والتريمثوبريم (73.3%) و التريمثوبريم/سلفاميثوكسازول (66.7%). لاحظت الدراسة ان معظم عزلات بكتيريا المكورات العنقودية الذهبية كانت مقاومة لاليرثروميسين (100%) وللتوبراميسين (100%) و التريمثوبريم (75%) و التريمثوبريم/سلفاميثوكسازول (75%) و للنتراسايكلين (75%). توصلت الدراسة الى ان معدل مقاومة عزلات بكتيريا المكورات العنقودية الذهبية للسيبروفلوكساسين كان 50%. كما كشف اختبار مقاومة المضادات الحيوية عن ارتفاع مقاومة عزلات بكتيريا الكلبسيلا الرئوية للسيبروفلوكساسين (63.63%) و

التتراسايكلين (100%) و التوبراميسين (63.63%) و الترايمثوبريم (81.8%) و الترايمثوبريم/سلفاميثوكسازول (63.63%). كما كانت معظم عزلات بكتيريا الزائفة الزنجارية و المتقلبة الرائعة مقاومة للتتراسايكلين (100% و 80% على التوالي) و الترايمثوبريم (100% لكل واحدة منهما) و الترايمثوبريم/سلفاميثوكسازول (100% و 80% على التوالي). أظهرت كل عزلات بكتيريا الزائفة الزنجارية مقاومة للنيتروفورانتوين و السفوكستين. تم الكشف عن جينات الضراوة *fimH* و *KpsMTII* لبكتيريا الإشريكية القولونية حيث كان معدل تواجدها في البكتيريا مرتفعا جدا بلغ 86.7% و 80% على التوالي. كانت نسبة تواجد الجينات *mdeA* و *hla* في بكتيريا المكورات العنقودية الذهبية هي 50% مع احتواء 25% فقط من العزلات على كلاهما.



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دراسة جزيئية لبعض جينات الضراوة في البكتريا المرضية المعزولة من مرضى التهابات المسالك البولية في شمال محافظة ذي قار

رسالة ماجستير

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مقدمة من قبل

كرار فاضل حسن

بكالوريوس طب وجراحة بيطرية (2019)

تحت اشراف

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