University of Kerbala

Correlation of Lipopolysaccharide Binding Protein, Mannose Receptor, IL-1β and IL8 among UTI Patients

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيم

وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ ۚ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا (١١٣)

صدق الله العلي العظيم

سورة النساء الآية ١١٣

Dedication

To the candle that lights my path, to my support who was the source of my inspiration and courage to continue "special person in my world ."

To the great man who does the impossible for me " My father."

To the greatest women in the existence, Every step I takes is just to see the sparkle in her eyes as she is proud of her only daughter " My Mother."

For those who share the same blood with me " My brothers."

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Aia, 2024

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Supervisor certification

I certify the thesis entitle **(Correlation of Lipopolysaccharide Binding Protein, Mannose Receptor, IL-1β and IL8 among UTI Patients)** was prepared under my supervision at the department of Clinical Laboratories, at the College of Applied Medical Sciences, University of Kerbala, as a partial requirements for the degree of Master in Clinical Laboratories.

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We, the examining committee, certify that we have read the thesis entitled " **Correlation of Lipopolysaccharide Binding Protein, Mannose Receptor, IL-1β and IL8 among UTI Patients**" and have examined the student (**Aia Haider Qahtan**) in its content and that in our opinion it is accepted as a thesis for degree of Master of **Clinical Laboratories.**

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Approval certification

We Certify that the thesis entitled " **Correlation of Lipopolysaccharide Binding Protein, Mannose Receptor, IL-1β and IL8 among UTI Patients**" fulfills partial requirements of the degree of Master in Clinical Laboratories.

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List of Abbreviations

Abbreviations	Items
ABU	Asymptomatic Bacteriuria
AMP	Antimicrobial peptides
ANC	Absolute Neutrophil Count
ASM	American Society for Microbiology
AST	Antibiotics Susceptibility
BC	Before Christmas
BMI	Body Mass Index
BSAC	British Society for Antimicrobial Chemotherapy
bUTI	Bacterial Urinary Tract Infection
CBC	Complete Blood Count
CD14	Cluster of Differentiation 14
CD206	Cluster of Differentiation 206
CD8	Cluster of Differentiation 8
CDC	Community Diagnostic Centers
CFU/ml	Colony Forming Units per milliliter
CLEC	C-type Lectin
CoNS	Coagulase-Negative *Staphylococci*
CoPS	Coagulase-Positive S*taphylococci*
CRP	C-Reactive Protein
CTLDs	C-Type Lectin Domains
cUTI	Complicated UTI
CXCL-8	Interleukin-eight
CXCR1	Receptor of Interlukin-8 alpha
CXCR2	Receptor of Interlukin-8 beta
DW	Distilled water
E. faecalis	*Enterococcus faecalis*
E. faecium	*Enterococcus faecium*
EDTA	Ethylene Diamine Tetra Acetic Acid
ELISA	Enzyme Linked Immunosorbent Assay
EMB	Eosin Mythlin Blue
ESBL	Extended-spectrum beta lactamase

Esp	*Enterococcal* Surface Proteins
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GBD	Global Burden of Disease
GBS	Group B *Streptococcus*
GBS	Group B *Streptococcus*
GN	Gram Negative
GP	Gram Positive
GUE	General Urine Examination
HPF	High Power Failed
HRP	Horseradish Peroxidase
HSPA1B	Heat Shock Protein Family A(Hsp70) Member 1B
ICE	1β-converting enzyme
ID	Identifications
IDSA	Infectious Disease Society of America
IL-1	Interleukin-one
IL-1R1	Interleukin-1 receptor
IL-1α	Interleukin- alpha
IL-1β	Interleukin-beta
IL-6	Interleukin-six
IL-8	Interleukin-eight
ILs	Interleukins
K.pneumoniae	*Klebsiella pneumoniae*
Kp	*Klebsiella pneumoniae*
LBP	Lipopolysaccharide Binding Protein
LCR	Lymphocyte Count Ratio
LE	leukocyte Esterase
LPS	Lipopolysaccharide
MDR	Multidrug Resistance
MR	Mannose receptor
MR-VP	Methyl Red-Voges Proskaur
NCR	Neutrophil Count Ratio

OD	Optical Density
P. aeruginosa	*Pseudomonas aeruginosa*
P. mirabilis	*Protus mirabilis*
PGCs	Pilin Gene Clusters
pH	Potential of Hydrogen
rPM	Revolutions per minute
S. aureus,	*Staphylococcus aureus*
SCFAs	Short-Chain Fatty Acids
SIRS	Systemic Inflammatory Response Syndrome
TcpF	Transparency Consent and Privacy Freamwork
TGF-β1	Transforming Growth Factor beta 1
Th1	T Helper cell 1
Th17	T Helper cell 17
Th2	T Helper cell 2
TLR2	Toll Like Receptor 2
TLR4	Toll Like Receptor 4
TMB	3,3,5,5-Tetramethylbenzidine
TNF-α	Tumor Necrosis Factor-alph
UC	Uncomplicated Cystitis
ucUTI	Un complicated UTI
UP	Uncomplicated Pyelonephritis
UPEC	Uropathogenic *Escherichia coli*
UTIs	Urinary tract infections
WBC	White Blood Cell
WGS	Whole-Genome Sequence
WHO	World Health Organization

Summary

One of the most common types of infections in the world is urinary tract infections, or UTIs. UTIs are associated with a significant clinical and financial burden as well as a reduced quality of life for patients. Both sexes can get a UTI at different ages, and women are usually more susceptible than men. The rationale stems from differences in the structure and physiology of the urinary system between the sexes.

This study was conducted during the period from October 2023 to February 2024 at Imam Hussein Hospital in the holy city of Karbala and the laboratories of the College of Applied Medical Sciences/University of Kerbala.

A case-control study design was conducted. The current study including collection urine samples (for use in general urine examination and bacteriological culture) and blood using blood directly to measure the complete blood count CBC and serum to measure C- reactive protein (CRP), interleukin one beta (IL-1β), interleukin eight (IL-8), and lipopolysaccharide binding protein (LBP), mannose receptor (MR) from 70 patients with UTI (35 patients with positive bacterial growth and 35 patients with negative bacterial growth) in addition to 70 control people. The following general criteria were also investigated: age, sex, BMI.

The age of the study subject ranged from 18 to 77 years, and the percentage of females for each group is significantly ($P<0.05$) greater than the percentage of males for each group (the percentage of females was 80% and males 20%). The majority of age groups with urinary tract infections were from 18 to 38 years. Gram-positive bacteria appeared at a rate of 52% and gram-negative bacteria at a rate of 48%. Eight bacterial species were obtained, distributed as follows: *Escherichia coli* (33%),

Staphylococcus saprophyticus (26%), *Staphylococcus haemolyticus*, *Staphylococcus aureus*, and *Klebsiella aurogenes* (10%), *Klebsiella pneumoniae* (5%) also *Enterococcus faecalis* and *Enterococcus faecium* (3%).

The most important concluded of the study is the increase in the following parameters: CRP, IL-1β, LBP, MR, and pus cells in patients with urinary tract infections compared to the control group. It was also found that the increase in the concentration of the LBP and MR in the group of patients who had positive bacterial growth was significant compared to the control group and the group of patients who had negative bacterial growth.

The current study also concluded that there is a significant direct correlation in the group of patients who had bacterial overgrowth between: (WBC and CRP) and (Neutrophils and IL-8). In addition to the presence of a negative correlation between (WBC and MR) and (LBP and IL-1β). Correlations between markers in the group of patients without bacterial growth indicate that there is a positive correlation only between (LBP and IL-8).

Chapter One
Introduction

Chapter One : Introduction

1.1. Introduction

Urinary tract infections (UTIs) are highly prevalent on a global scale. UTIs are linked to a decline in patients' quality of life and impose a substantial clinical and economic burden **(Ozturk and Murt, 2020).** UTIs affect both sexes and at different ages, and usually females are more susceptible to infection than males. The reason is due to some physiological and anatomical differences in the composition of the urinary system for both sexes **(Yang and Foley, 2020)**. UTIs are categorized according to the location of the infection: either in the lower urinary tract (known as cystitis) or in the upper urinary tract (known as pyelonephritis) **(Nicolle *et al* ., 2019).**

Along with some fungus, Gram-negative and Gram-positive bacteria are among the several microorganisms that might cause urinary tract infections. Un complicated and complicated urinary UTIs are mostly caused by *Escherichia coli*, sometimes called *E. coli*. Other bacteria which are linked to acute infections are *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, group B *Streptococcus* (GBS), *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Candida* spp**. (Flores-Mireles *et al* ., 2015).**

With a worldwide incidence of roughly 424 million clinical cases in 2019 **(Yang *et al.*, 2022)**, urinary tract infections (UTIs) are rather common bacterial infections found worldwide. From mild, simple infections to more severe cases including complicated UTIs (cUTIs), pyelonephritis, and severe urosepsis, the clinical symptoms of urinary tract infections (UTIs) differ greatly **(Wagenlehner *et al* ., 2020).**

The exact knowledge of the host defensive systems preventing invasive bacterial infection is lacking. Recent studies showed that different natural immune responses defend the urinary system against

invading uropathogens. Understanding the natural mechanisms controlling the balance of the immune system in the kidney and urinary tract has made great advancement in past ten years. The chance of acquiring a pathogen rises when the body's natural defenses are compromised or disturbed **(Ching *et al.*, 2020).**

There are several limits in the identification of suitable biomarkers for UTIs. Many conditions including chronic, metabolic, or malignant diseases as well as intercurrent infections constantly influence the immune system. These diseases could influence biomarker expression **(Alidjanov *et al* ., 2020).**

Interleukins (ILs) which are important members of cytokines—consist of a vast group of molecules, including a wide range of immune mediators that contribute to the immunological responses of many cells and tissues. ILs are immune-glycoproteins,which directly contribute to the growth, activation, adhesion, differentiation, migration, proliferation, and maturation of immune cells; and subsequently, they are involved in the pro and anti-inflammatory responses of the body, by their interaction with a wide range of receptors **(Behzadi *et al* ., 2022).** Interleukin-1 is known as a proinflammatory and immunostimulatory cytokine, which plays important roles in inflammatory diseases **(Liu *et al*. 2021)**. IL-1 includes two agonists, IL-1α and IL-1β, which trigger signals via binding to IL-1 receptor 1 (IL-1R1) and recruitment of an accessory peptide chain **(Fields *et al* ., 2019).** IL-1β is primarily secreted by monocytes and macrophages. It induces tissue damage and infiltration of neutrophils. To avoid uncontrolled inflammation, secretion of the active-form of IL-1β is tightly regulated and modulated by a molecular complex called inflammasome **(Ambite *et al* ., 2016).**

Inflammation accompanying UTIs is mediated by several cytokines, including TNF-α, interleukin (IL)-1β, IL-6, and IL-8 **(Sundac**

***et al*. 2016)**. Multiple Uropathogenic *E.coli* virulence factors directly affect the release of IL-1β and can activate inflammasome response. Particularly hemolysin, the pore-forming poison has been found to induce cell death in bladder tissue and stimulate IL-1β release **(Nagamatsu *et al* ., 2015).**

IL-8 (CXCL-8) is a chemokine of the CXC family and it is actively produced by monocytes/macrophages and other cell types like endothelial cells, epithelial cells and airways smooth muscle cells. IL-8 is a key regulator of the acute inflammatory response and it recruits and activates monocytes and neutrophils to the site of inflammation **(Marta and Giovanni, 2020)**. In the advanced phases of a urinary tract infection (UTI), both blood and urine may show higher cytokine levels **(Zarkesh *et al*., 2015).**

Produced in response to acute inflammation, lipopolysaccharide (LPS)-binding protein (LBP) functions in the first immunological reaction to LPS, a component of bacterial cell walls **(Ha *et al* ., 2021).**

Created in reaction to lipopolysaccharides (LPS) generated by gram-negative bacteria, lipopolysaccharide-binding protein (LBP) is a liver-derived acute-phase protein. It thus acts as a sign of systematic inflammation brought on by the infection of these bacteria, including gut dysbiosis **(Watanabe *et al*., 2020)**. Usually referred to as endotoxin, lipopolysaccharide is a major component of the outer membrane of gram-negative (GN) bacteria **(Gnauk *et al*. 2016)**. LPS causes endotoxinemia when it gets into the bloodstream **(Farhan and Khan, 2020).**

On macrophages, the Mannose receptor (MR, CD206) is a type of Immunological receptor rather widely present. It is absolutely important for immune response, glycoprotein clearance, and extracellular matrix turnover **(Hu *et al* ., 2019)**. Belining to the C-type lectin (CLEC) family, the mannose receptor can bind and internalize different ligands either

endogenous or linked with pathogens **(Van *et al*., 2021)**. The mannose receptor also functions as part of the innate immune system. Sugar structures on microorganisms targeted by the receptor include mannans on the surface of yeasts, mannosecapped lipo-arabinomannans on mycobacteria, and high-mannose oligosaccharides on the surfaces of viruses **(Monteiro *et al*., 2017)**.

1.2. The aim of study

The study aims to investigate about the correlation and relationship among IL-1β, IL-8, LBP and MR with urinary tract infection patients and compare to them control group by achieving the following study objectives:

1. Recorded the general facts for the control group and UTI patients (age, sex, height, weight).
2. To be used in general urine examination and bacteriological culture, the urine samples taken from control and UTI patients.
3. CBC, CRP is among the clinical and laboratory tests that will be conducted using the blood samples taken from UTI patients and control group.
4. The serum levels of IL-1β, IL-8 , LBP and MR will be ascertained using ELISA technique.

Chapter Two
Literatures Review

Chapter Two: Literatures Review

2.1. Urinary Tract Infections

2.1.1. Definition of Urinary Tract Infections

Urinary tract infection (UTI) are inflammation of the renal system characterized by frequent and painful urination and caused by the invasion of microorganisms, usually bacteria, into the urethra and bladder. Infection of the urinary tract can result in either minor or major illness**(Rogers and Kara , 2024).**

The urinary system has a crucial function in eliminating the waste products of metabolism from the bloodstream. The system also plays a crucial role in maintaining the balance of ions and solutes in the blood, as well as controlling blood volume and blood pressure. Urine in healthy individuals is either sterile or includes a minimal amount of germs that have the potential to produce an infection **(Mancuso *et al* ., 2023).** UTIs rank as the second most prevalent kind of bacterial infection globally, with an annual diagnosis of 120-150 million cases. UTIs can be differentiated based on the anatomical site of the bacterial infections. When the infection affects the upper part of the urinary tract, It is classified as pyelonephritis or a kidney infection. This condition can cause severe symptoms including abdominal pain, fever, chills, flank pain, nausea, and vomiting. If left untreated, it can result in irreversible kidney damage and sepsis **(Maisto *et al* ., 2023).**

UTIs are categorized as cystitis and urethritis when they affect only the bladder, urethra, or lower urinary tract. These disorders are distinguished by slight symptoms such as blood in the urine, painful urination, and soreness above the pubic bone. Moreover, in order to distinguish between infections that are harmless and those that are more likely to recurrence or progress to severe pathology, UTIs can be

classified clinically as uncomplicated UTIs (uUTIs) and complicated UTIs (cUTIs) **(González de Llano et *al* ., 2020).**

UTI refers to a plethora of clinical phenotypes**(Gupta *et al*., 2017)**. UTIs are the fifth most common type of healthcare-associated infection, with an estimated 62,700 UTIs in acute care hospitals in 2015. UTIs additionally account for more than 9.5% of infections reported by acute care hospitals. Virtually all healthcare-associated UTIs are caused by instrumentation of the urinary tract (**Magill *et al*.,2019**). UTIs are common, recurrent infections that can be mild to life-threatening (**Klein and Hultgren, 2020**).

UTIs is a common clinical problem that comprises 1–6% of medical referrals and includes urinary tract, bladder, and kidney infections **(Tegegne *et al*.,2023).** Urinary tract infections (UTIs) represent the most common bacterial illnesses that occur in various settings, including community and clinical environments. Bacteria are the primary etiological agents of these infections, however less frequently, other species, such as fungi and some viruses, have been documented as the causal agents of UTIs **(Mancuso *et al* ., 2023).**

UTI occurs when microorganisms enter the urinary tract and cause symptoms and/or an inflammatory response that needs to be treated. Asymptomatic bacteriuria is the condition where a specific amount of bacteria is found in a urine sample collected from an individual who does not show any clinical symptoms **(Klein and Hultgren, 2020**).

UTI is an immune response that occurs in the urothelium to combat a bacterial infection. UTI is typically linked to bacteriuria, which refers to the presence of bacteria in the urine, as well as pyuria, which refers to the presence of white blood cells in the urine. Bacteriuria may occur without the presence of pyuria, which can be attributed to either bacterial contamination or aseptic consider during urine collection. In contrast,

pyuria can occur without bacteriuria, which suggests an inflammatory condition of the urothelium, such as a urinary stone or a cancer **(Abou Heider *et al.*, 2019).**

2.1.2. History of Urinary Tract Infections

The existence of UTI has been recorded since ancient times, with the first documented description being in the Ebers Papyrus dating back to approximately 1550 BC. Effective treatment did not occur until the development and availability of antibiotics in the 1930s before which time herbs, bloodletting and rest were recommended **(AL-Achi , 2016).** It was described by the Egyptians as "sending forth heat from the bladder" **(Whiteman and Topley , 1990).** UTIs have afflicted humanity for a long time, predating the recognition of bacteria as the primary cause of disease and the establishment of urology as a medical specialty. Until date, there has not been an attempt to comprehensively analyze the recorded medical history of UTI from its first description in ancient Egyptian papyri to the present day **(Nickel, 2019).**

UTIs are some of the most common bacterial infections, affecting 150 million people each year worldwide **(Stamm and Norrby , 2020).** In 2007, in the United States alone, there were an estimated 10.5 million office visits for UTI symptoms (constituting 0.9% of all ambulatory visits) and 2–3 million emergency department visits**(Schappert and Rechtsteiner , 2011).**

2.1.3. Epidemiology

There are limited data on the global scale and long-term trends of UTIs. Comprehensive national- and regional-level information about the UTI burden is important for policymakers with regard to allotting the finite resources available and establishing effective public health policies. The Global Burden of Disease (GBD) 2019 study is a systematic global epidemiological study that quantified the incidence, mortality, disability,

and 87 risk factors for 369 diseases by sex, age, location, and year **(GBD, 2020).**

Urinary tract infections occur four times more frequently in females than males **(Salvatore *et al* ., 2021).**

2.1.4. Classification of UTI

In 1992, the Infectious Disease Society of America (IDSA) and the European Society of Clinical Microbiology and Infectious Diseases classified urinary tract infections (UTIs) into two categories: uncomplicated and complicated. This classification was created to provide a standard for participants in research studies **(Anger *et al*., 2019).** Classification of urinary tract infections (UTI) is important for clinical decisions, research, quality measurement and teaching. Current definitions of UTI are above all based on the concept of the two main categories, complicated and uncomplicated UTI. The category "complicated UTI" especially is very heterogeneous and not always clear **(Johansen *et al* .,2022).**

Uropathogenic *Escherichia coli* (UPEC) is the primary cause of both uncomplicated urinary tract infections (uUTIs) and complicated urinary tract infections (cUTIs). Other pathogenic bacteria, including *Klebsiella pneumoniae, Proteus mirabilis, Enterococcus faecalis, and Staphylococcus* spp., are also responsible for these infections. Furthermore, there is an increasing incidence of UTIs caused by multidrug resistance (MDR), leading to a substantial rise in the dissemination of antibiotic resistance and the financial burden associated with these diseases **(Mancuso *et al* ., 2023).**

2.1.4.1. Complicated Urinary Tract Infection

Complicated UTIs occurs in individuals with functional or structural abnormalities of the genitourinary tract**(Jindal *et al* ., 2022).**

A complicated UTI is any UTI other than a simple UTI. C-UTI incidence is associated with specific risk factors. For example, there is a 10% daily risk of developing bacteriuria with indwelling bladder catheters and up to a 25% risk of bacteriuria progressing to a UTI **(González *et al* ., 2020).** Complicated UTI are characterized by increased morbidity, a higher likelihood of treatment failure, and a need for longer antibiotic courses. These infections often necessitate extra diagnostic tests. Complicated urinary tract infections encompass a range of scenarios, such as infections in males, pregnant females (including those without symptoms), infections caused by obstruction, hydronephrosis, renal tract calculi, or colovesical fistula, infections in immunocompromised patients or the elderly, infections caused by atypical organisms, infections following instrumentation or involving urinary catheters, infections in renal transplant patients, infections in patients with impaired renal function, and infections after prostatectomies or radiotherapy **(Sabih and Leslie, 2024).**

In the United States, 70–80% of complicated UTIs are attributable to indwelling catheters **(Lo *et al.*,2019).**

The ranking of prevalence for causal agents in complicated UTIs, after *E. coli*, is as follows: *Enterococcus spp., K. pneumoniae, Candida spp., S. aureus, P. mirabilis, P. aeruginosa, and* ***group B*** *Streptococcus* (GBS). A separate investigation conducted on patients admitted to the hospital with complicated urinary tract infections (cUTI) revealed that the most often encountered pathogens, listed in descending order of occurrence, were *E. coli, K. pneumoniae, P. aeruginosa, P. mirabilis, Enterococcus spp, and Enterobacter* **(Zilberberg *et al* ., 2018).**

2.1.4.2. Uncomplicated Urinary Tract Infection

Uncomplicated urinary tract infections (UTIs) occur in patients with a normal and unobstructed genitourinary tract, who have not recently

undergone any medical procedures, and whose symptoms are limited to the lower urinary tract. Uncomplicated urinary tract infections (uUTIs) are most prevalent in young women who are sexually active. Patients typically experience symptoms such as painful urination, frequent urination, a strong need to urinate, and/or pain in the lower abdomen. The presence of fever or discomfort in the costovertebral angle suggests that the upper urinary tract is affected **(Stuart *et al*., 2019).**

Uncomplicated UTIs are generally self-limiting, but commonly treated with antibiotics as this therapy leads to a more rapid resolution of symptoms and is more likely to clear bacteriuria **(Flores-Mireles *et al* ., 2019).**

Several uncomplicated UTI (uUTIs) might cure spontaneously without any medical intervention. However, patients frequently seek treatment to alleviate their symptoms. The objective of therapy is to restrict the transmission of infection to the kidneys or the development of an upper tract condition like pyelonephritis. Pyelonephritis can cause damage to the delicate structures in the nephrons and finally result in hypertension **(Tang *et al* ., 2019).**

Uncomplicated UTI (uUTI) is divided into two categories: uncomplicated cystitis (UC) and uncomplicated pyelonephritis (UP) **(Wagenlehner *et al* ., 2020).** Following *E. Coli*, the most common causes of uncomplicated UTIs, in order of prevalence, are *Klebsiella pneumoniae (K. pneumoniae), Staphylococcus saprophyticus, Enterococcus faecalis,* GBS, *Proteus mirabilis, Pseudomonas aeruginosa (P. aeruginosa), Staphylococcus aureus (S. aureus), and Candida* spp. **(Zilberberg *et al* ., 2018).**

2.1.5. Symptoms and Signs

The clinical symptoms of this condition can vary from a mild fever with chills to a severe case of sepsis with septic shock. These symptoms

can include inflammation of the urethra, bladder, kidneys, and presence of bacteria in the urine. Additional symptoms may include frequent urination, painful urination, cloudy and foul-smelling urine, pain in the lower abdomen and flank, and potential long-term illness or even mortality, depending on the individual's health and risk factors **(AL-khikani *et al* ., 2019).**

Common indications of UTI consist of lower urinary tract symptoms include painful urination, frequent and urgent need to urinate (cystitis), discomfort in the back or flank area, and tenderness at the costovertebral angle (pyelonephritis). Pyelonephritis may manifest with fever as a clinical condition **(Lee, 2019).**

Urine turbidity, sediment color, and odor do not consistently indicate the presence of infection and may be associated with excessive use of antibiotics. It should be emphasized that alterations in urine properties, such as color and smell, can be caused by factors such as lack of hydration, kidney stones, specific foods (like asparagus), or medications (such as multivitamins) **(Mayne *et al* ., 2019).**

UTI cases can be categorized as either asymptomatic or symptomatic. An asymptomatic UTI is identified by analyzing the findings of a urinalysis. Accurate sample collection is essential due to the location of the external urethral opening in women. The leukocyte count is the primary criterion used in diagnosing UTIs. A leukocyte count greater than 10 leukocytes per cubic millimeter indicates an infection. In pregnant women, the threshold is set at a higher level, specifically greater than 20 leukocytes per cubic millimeter. Urinalysis results without concurrent patient symptoms are inadequate to commence treatment. A urine culture can be employed to validate or invalidate a hypothesis regarding a UTI. An infection is confirmed when there are at least 105 colony forming units per milliliter (CFU/mL). To determine the

effectiveness of a certain treatment, an antibiogram can be used **(Van den Boom *et al* ., 2021).** Bacteria growth urine in the absence of urinary tract symptoms (i.e. asymptomatic bacteriuria) is most common and represents a commensal colonization **(Bonkat *et al* ., 2020).**

Although even if the urine has significant bacteria without any symptoms, that would be termed as asymptomatic bacteriuria, on the other hand with symptoms it is symptomatic bacteriuria **(Givler and Givler , 2021).**

2.1.6. Clinical Manifestations

Urethritis, Cystitis, Pyelonephritis , Bacteremia, and Septic shock.

UTIs are heterogeneous with regard to their etiology, clinical manifestations, and disease course, which range from simple (e.g., urethritis and cystitis) to severe (e.g., pyelonephritis, bacteremia, and septic shock) **(Tandogdu and Wagenlehner, 2016).**

I. Urethritis

Urethritis refers to inflammation of the urethra and is classified as gonococcal (caused by *Neisseria gonorrhoeae*) or nongonococcal in origin (most commonly caused by *Chlamydia trachomatis, Mycoplasma genitalium, or Trichomonas vaginalis)* **(Sell *et al* ., 2022).**

Urethritis is a sexually transmitted disease generally characterized by urethral discharge or other symptoms such as itching, tingling, and apparent difficulties in having a regular urinary flow **(Bartoletti *et al* ., 2019).**

II. Cystitis

Cystitis refers to infection of the lower urinary tract, or more specifically, the urinary bladder **(Goldman and Julian , 2019).** Cystitis usually develops due to the colonization of the periurethral mucosa by bacteria from the fecal or vaginal flora and the ascension of such pathogens to the urinary bladder. Uropathogens may have microbial

virulence factors that allow them to escape host defenses and invade tissues in the urinary tract**(Tyagi *et al* ., 2018).** Several risk factors are associated with cystitis, including sex , a prior UTI, sexual activity, vaginal infection, diabetes, obesity and genetic susceptibility **(Foxman , 2014).**

III. Pyelonephritis

Pyelonephritis is a bacterial infection causing inflammation of the kidneys. Pyelonephritis occurs as a complication of an ascending urinary tract infection that spreads from the bladder to the kidneys**(Belyayeva and Jeong , 2023).**

The incidence of acute pyelonephritis is higher in young women than in men but the incidence in men over 65 is similar to that in older women**(Shields and Maxwell ,2020).** *Escherichia coli* is the predominant bacterium responsible for acute pyelonephritis, mostly because of its distinctive capacity to attach to and establish colonies in the urinary system and kidneys. *E.coli* possesses sticky molecules known as P-fimbriae, which engage in interactions with receptors located on the surface of uroepithelial cells. Infection of the kidneys with *E. coli* can result in an immediate and intense inflammatory reaction, leading to the formation of scar tissue in the renal parenchyma **(Belyayeva and Jeong, 2023).**

IV. Bacteremia

In the strictest sense, refers to viable bacteria in the blood**(Smith and Nehring , 2023).** Understanding the clinical symptoms of bacteremic urinary tract infection (bUTI) is crucial, as it is a severe infection that required immediate diagnosis and antibiotic treatment. Most patients with *E. coli* bacteremia had a urinary origin. A considerable percentage of patients of bacterial urinary tract infection (bUTI) did not exhibit any urinary symptoms during the medical history assessment. Older and

confused patients had a higher likelihood of getting urinary tract infections (UTIs) without displaying urine symptoms. When dealing with older patients who are experiencing delirium and sepsis according to the criteria of Systemic Inflammatory Response Syndrome (SIRS), but without a clearly identifiable source of infection, doctors should consider, examine, and provide treatment for urinary tract infections (bUTI) **(Bai *et al* ., 2020).**

In bacteremia the majority of bacterial species are killed by oxidation on the surface of erythrocytes and digested by local phagocytes in the liver and the spleen **(Minasyan , 2019)**.

V. Septic shock

The most severe complication of sepsis, carries a high mortality. Septic shock occurs in response to an inciting agent, which causes both pro-inflammatory and anti-inflammatory immune system activation **(Mahapatra and Heffner , 2023).**

2.1.7. Risk Factor for UTIs

2.1.7.1. Inheritance

There is increasing data suggesting that genetic variables can add to the risks of UTIs **(Ambite *et al* ., 2016).** Genetics significantly influences common disorders such as urinary tract infections, as genetic variations regulate gene expression in bacterial diseases **(Samer, 2023).**

The vulnerability to UTIs was verified to be inherited in a study conducted on a family spanning three generations. The individuals who were prone to UTIs in these families exhibited low levels of CXCR1 expression. Unlike traditional human immunodeficiencies, the UTI susceptibility determinants that have been found do not largely impact structural genes. Instead, they modify regulators that control transcriptional efficiency **(Ragnarsdottir *et al* ., 2015).**

Genetic predisposition is essential, not just for rare monogenetic disorders but for common infections such as UTI, The risk increased with the number of affected individuals, especially if a sister, mother or daughter had a history of UTI and the influence of behavioural factors was increased **(González *et al* ., 2020).** Recent developments indicate that an absence of regulation in specific genes in humans could make patients more susceptible to recurring urinary tract infections (UTIs). Identifying a genetic component of UTI recurrences will enable the diagnosis of people who are at risk and the prediction of genetic recurrences in their children. Out of the 14 genes examined, six have been found to potentially contribute to the vulnerability of humans to recurrent UTIs. The HSPA1B, CXCR1 & 2, TLR2, TLR4, and TGF-β1 genes have been found to be linked to changes in the way the host responds to UTIs at different levels **(Zaffanello *et al* ., 2020).**

2.1.7.2. Age and sex

UTIs are common in the elderly, and cover a range of conditions from asymptomatic bacteriuria to urosepsis. Risk factors for developing symptomatic UTIs include immunosenescence, exposure to nosocomial pathogens, multiple comorbidities, and a history of UTIs(**Rodriguez-Mañas , 2020).**

UTIs is a prevalent ailment that impacts individuals of various age groups, with a higher incidence observed in women **(Badiger *et al*., 2021).** UTIs are prevalent and onerous, affecting approximately 50-60% of women at least once in their lives **(Yang *et al.*,2022).** Advancing age is an independent risk factor for UTIs. This risk is likely caused by multiple factors, including the rising prevalence of urine incontinence, urinary retention, hospitalizations, associated urinary catheterizations, long-term medical institutionalization, and weakened immune system due to aging. Possible factors that can be changed and contribute to UTIs include

structural abnormalities of the urinary tract, especially those that cause incontinence or urine retention (such as prostatic hyperplasia), and uncontrolled diabetes mellitus,vaginal atrophy in postmenopausal women, sexual intercourse a risk factor for both men , women , most critically in the elderly population, urinary catheterization **(Drekonja *et al* ., 2013) .**

It is estimated that 10-60% of all women will experience at least one symptomatic UTI in their lifetime **(Curtiss et *al* ., 2017).**

In younger women, increased sexual activity is a major risk factor for UTIs and recurrence within 6 months is common **(Medina and Castillo , 2019).** A older age (≥ 65 years, and especially ≥ 80 years) raises the likelihood of UTI in both females and males. UTI is infrequent in males before the age of 60. However, the occurrence of UTI significantly rises after this age, to the point where both males and females have similar rates of UTI by the time they reach 80 years old **(Schaeffer and Nicolle, 2016).**

2.1.7.3. Hormonal Factors

The primary factors contributing to the higher occurrence of urinary tract infections in peri- and postmenopausal women are hormonal changes, specifically a lack of estrogen, and the aging of connective tissue, which leads to urine incontinence and pelvic organ prolapse **(Bonkat *et al* ., 2020).**

Undoubtedly, alterations in vulnerability and occurrence of UTI in both women and men indicate that biological factors play a significant role in determining an individual's likelihood of infection. During the reproductive years, female vertebrate creatures, including humans, often experience elevated levels of estrogens, while male organisms normally have greater amounts of androgens, such as testosterone **(Amenyogbe *et al* ., 2020).**

The most noticeable disparities in UTI vulnerability are observed in adults over the age of 50, particularly in post-pubescent individuals. These variances coincide with the peak levels of estrogen in females and testosterone in males. The occurrence of UTIs in women specifically tends to rise after puberty, coinciding with an increase in estrogen levels. Conversely, adult males have the lowest risk of UTIs when testosterone levels are at their peak and estrogen levels are at their lowest. However, males who suffer from infection are more likely to develop chronic urinary tract infections (UTIs) and incur higher rates of illness and death from severe UTIs. **Deltourbe *et al* ., 2022).**

2.1.7.4. Obesity

Obesity is the excessive or abnormal accumulation of fat or adipose tissue in the body that may impair health. Obesity has become an epidemic which has worsened for the last 50 years **(Panuganti *et al* ., 2023).** More than two-thirds of the U.S. population is either overweight or obese**(Tiwari and Balasundaram , 2024).**

The body mass index (BMI) is determined by doing mathematical calculations using a person's height and weight information to assess their health state **(Oniszczenko and Stanisławiak, 2019).**

BMI is a measure of body mass that is determined by dividing weight in kilograms by the square of height in meters (kg/m^2). Overweight/obesity is a significant public health concern in the western world, and it is closely linked to a high prevalence of chronic autoimmune and inflammatory conditions. This has substantial social and economic consequences **(Feng *et al* ., 2019).**

Obesity is correlated with a higher likelihood of developing UTIs in both males and females. Individuals who were fat had a 2.5 times higher likelihood of being diagnosed with a UTI compared to those who were not obese **(Kim *et al* ., 2021).** The increased vulnerability to infectious

illnesses in individuals with obesity is mostly attributed to compromised innate and adaptive immunological responses, as well as a lack in vitamin D **(Pugliese *et al* ., 2022).**

In general, a high amount of fatty tissue is associated with an increase in the production of substances that cause inflammation. Conversely, a decrease in adipose tissue is linked to a decrease in the abundance of these inflammatory compounds and an increase in the number of molecules with anti-inflammatory properties. Therefore, obesity is presently acknowledged as a state that actively promotes inflammation **(Younis and Al-bustany, 2017).**

2.1.7.5 Patient with Catheter and other causes

The utilization of a urinary catheter is a significant contributing factor to the occurrence of urinary tract infections (UTIs)**(Li and Leslie , 2023).** The prevalence of UTI increases with age, and in women aged over 65 is approximately double the rate seen in the female population overall. Etiology in this age group varies by health status with factors such as catheterization affecting the likelihood of infection and the pathogens most likely to be responsible **(Medina and Castillo , 2019).** UTIs are frequently encountered in pregnant women. Pyelonephritis is the most common serious medical condition seen in pregnancy, Pregnancy increases the chances of urinary tract infection due to alterations in the urinary tract and immune system. The urinary system undergoes physiologic changes, which involve the expansion of the ureter and renal calyces. This expansion is caused by the relaxation of smooth muscles owing to progesterone and the compression of the ureter by the pregnant uterus. Ureteral dilatation can be significant. However, a reduction in bladder capacity often leads to increased urine frequency. Additionally, Vesicoureteral reflux may also be observed. These modifications elevate

the likelihood of developing urinary tract infections **(Habak *et al* ., 2023).**

UTIs occurs with increased frequency and severity in patients with diabetes mellitus. General host factors enhancing risk for urinary tract infection in diabetics include age, metabolic control, and long term complications, primarily diabetic nephropathy and cystopathy, The alterations in the innate immune system have been described and may also contribute **(Fünfstück *et al* ., 2022).**

A UK-based observational study evidenced a nearly 60% increase in the risk of developing urinary tract infections among patients with type 2 diabetes, with the possible risk factors being female sex, pregnancy, older age, UTI in the previous six months, and poor glycaemic control **(Confederat *et al* ., 2023).**

2.1.8. Pathogenies

When bacteria enter the urinary system and assault the mucosa in the bladder, ureters, and/or renal pelvis, urinary tract infections (UTIs) begin**(Godaly *et al* ., 2016).**The primary purpose of the urinary tract is to retain urine for an extended duration. However, urine contains a variety of poisons and microorganisms, therefore it must be kept securely contained. Therefore, the immune system must respond in a manner that specifically triggers the inflammatory response alone when the bacteria penetrate the urinary tract. However, let's assume that the inflammatory reaction is stopped before the bacteria leave the urinary system. Under those circumstances, there is a potential for the remaining bacteria to endure in the urinary system and result in illnesses**(Samer , 2023).**

Bacteria can reach the kidneys in two ways: hematogenous spread and through ascending infection from the lower urinary tract. Hematogenous spread is less common and usually occurs in patients with

ureteral obstructions or immunocompromised and debilitated patients **(Belyayeva and Jeong , 2023).**

Bacterial infections rely on the host immune system, which is influenced by their genetic makeup, as well as inherent and acquired weaknesses. The first elimination of microbes is carried out by the cellular innate and adaptive immune responses, while the liver and spleen serve as filters for actively circulating germs in the blood. Bacteria, in its simplest state, will initiate colonization in its primary location **(Woll *et al* ., 2018).**

Pathogenic bacteria ascend from the perineum and rectum, predisposing women to UTI , because women also have shorter urethras than men, which further contributes to their increased susceptibility to UTIs. Blood-borne bacteria cause few UTIs. *E.coli* is the most common organism in uncomplicated UTIs by a large margin, followed by *Klebsiella* **(Yamaji *et al* ., 2018).** Bacteria that are contributing to cause UTIs typically possess adhesins on their surface. These adhesins enable the bacteria to connect to the urothelial mucosal surface. Furthermore, a concise urethra also facilitates the infiltration of the uropathogen into the urinary system. Premenopausal women possess high numbers of lactobacilli in the vagina and maintain an acidic pH, which effectively prevents the colonization of uropathogens. Nevertheless, the administration of antibiotics can eliminate this defensive impact **(Bono *et al* ., 2023).** *Escherichia coli* is a primary bacterium responsible for causing urinary tract infections (UTIs) **(Tannupriye *et al* ., 2023).**

The term "Bacterial Translocation" refers to the movement of live bacteria, toxins, antigens, or other microbial products from the gut into the bloodstream, causing systemic inflammation and various diseases. Bacterial translocation can occur in two ways: paracellular, which is the

movement between cells, and transcellular, which is the movement through cells (intracellular trafficking) **(Nagpal and Yadav, 2017).**

In the figure (2-1) show the pathogenesis of UTI.

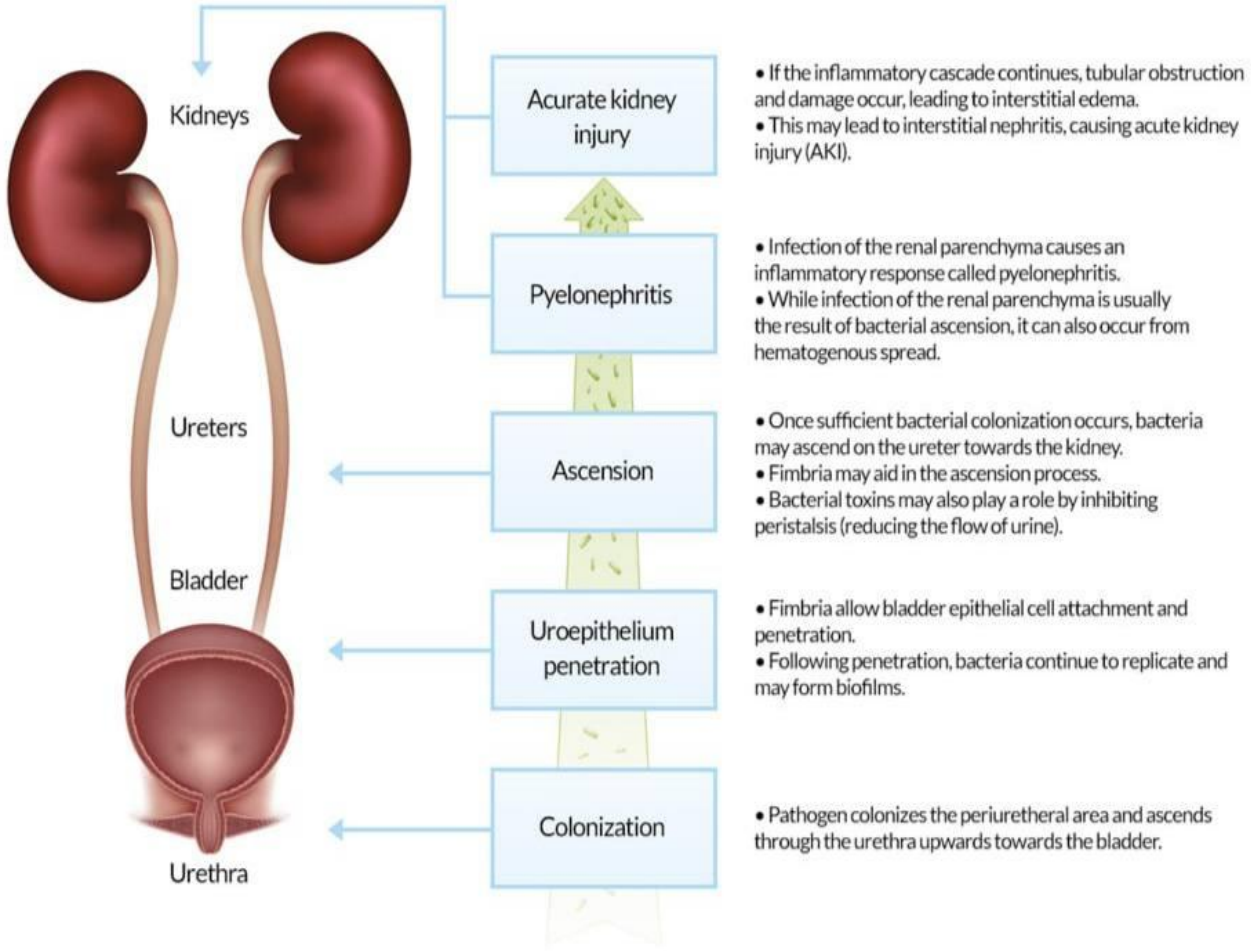


Figure (2-1): Pathogenesis of Urinary Tract Infections (Mancuso *et al* ., 2023).

2.2. Causative Agent of UTIs

2.2.1. Gram Positive Bacteria

Gram-positive bacteria frequently contribute to UTIs, especially in those who are elderly, pregnant, or have other risk factors for UTIs **(Kline and Lewis, 2016).**

2.2.1.1.Species of *Enterococcus*

Enterococcus species are Gram-positive cocci that are facultative anaerobes and form short to medium chains. These bacteria are known to

produce challenging-to-treat illnesses in healthcare settings. They are a frequent source of UTIs **(Said *et al* ., 2023).**

Unlike *staphylococci* and *streptococci, enterococci* do not secrete toxins. However, their capacity to cause disease is derived from other characteristics such as their resilience, structure, and resistance to antibiotics **(Miller *et al* ., 2016).** The outer layer are components consists of the polysaccharide capsule, adhesins, pili, and the aggregation material **(Fiore *et al* ., 2019).**

Urinary tract infections are primarily caused by *Enterococcus* species, with *E. faecalis* and *E. faecium* being the most common. These bacteria possess many mechanisms that enhance their ability to cause disease. These mechanisms encompass the processes of biofilm formation and the presence of virulence agents **(Dunny and Weaver., 2023).** Urinary isolates of *Enterococcus* spp. commonly possess several virulence factors, such as aggregation compounds, *enterococcal* surface proteins, pilin gene clusters (PGCs), collagen binding protein, TcpF, and gelatinase. *Enterococcal* surface proteins (Esp) are recognized as promoters of biofilm development and have demonstrated the ability to enhance initial adhesion. The presence of Esp has been detected in both *E. faecalis and E. faecium* **(García-Solach and Rice, 2019).**

When dealing with urinary infections caused by enterococcus, it is crucial to determine the susceptibility of the bacteria in order to select the most suitable antibiotic treatment, as enterococci are highly resistant to several drugs **(Kotagiri *et al.*,2020).** Although facing some opposition, ampicillin has demonstrated efficacy owing to its high concentration in urine. Intravenous ampicillin, fluoroquinolones, oxazolidinones, vancomycin, or daptomycin can be utilized for intricate infections. For severe infections, it is advisable to take ampicillin in combination with either streptomycin or gentamicin **(Richey *et al* ., 2023).**

2.2.1.2. Coagulase-Negative *Staphylococci*

Coagulase-negative staphylococci (CoNS) are often found bacteria in normal clinical care. Their prevalence continues to increase over the past few decades, in tandem with the progress in medicine, particularly in relation to the use of foreign body devices. In recent years, numerous unusual species have been identified, although there is limited clinical data available for most of these species **(Michels *et al.*, 2021).**

CoNS, or Coagulase-Negative Staphylococci, are the primary microorganisms that make up the skin's microbiota. These pathogens were overlooked and many microbiology laboratories did not include a specific species identification. Pathogenicity was attributed exclusively to the coagulase-positive strain of *Staph. aureus,* which led to significant attention and extensive analysis in several investigations. *Staph. saprophyticus,* a kind of CoNS, was identified in patients with UTIs during the late 1960s. Subsequently, the initial CoNS infections were discovered throughout the 1970s in individuals who had invasive and indwelling medical devices. The advancements in diagnostic protocols and molecular techniques have facilitated more precise identification of the various species within the genus *Staphylococci.* Researchers have noted a rise in the incidence of CoNS infections. From 1980 to 1989, the prevalence of CoNS-induced nosocomial bacteremia in the USA rose from 9% to 27%. The Staphylococci species form a highly cohesive group in terms of their evolutionary relationships. The average nucleotide identity values between *Staph. aureus* and CoNS, such as *S. epidermidis* and *S. haemolyticus,* are roughly 75%, indicating a strong genetic relationship **(Eltwisy *et al* ., 2022).**

2.2.1.2.1. *Staphylococcus Saprophyticus*

Staphylococcus saprophyticus is a type of bacteria that is Gram-positive, coagulase-negative, and non-hemolytic. It is frequently

responsible for simple UTIs, especially in young sexually active females. Additionally, it can lead to less frequent but nonetheless significant consequences such as acute pyelonephritis, urethritis, epididymitis, and prostatitis **(Argemi *et al.*, 2019).**

Staph. saprophyticus can be distinguished from other coagulase-negative staphylococci based on its resistance to Novobiocin. Similar to other bacteria that cause urinary tract infections, *Staph. saprophyticus* employs urease to generate ammonia. **(Ehlers and Merrill, 2023).**

2.2.1.2.2. *Staphylococcus haemolyticus*

Staph. haemolyticus is the predominant component of the microbiota found on human skin. It is prevalent in hospitals and among medical personnel, leading to its emergence as a microorganism that causes nosocomial infections. *Staph.haemolyticus*, particularly the strains responsible for nosocomial infections, exhibit greater antibiotic resistance compared to other coagulase-negative *Staphylococci***(Eltwisy *et al.*, 2022).**

An inherent attribute of *Staph. haemolyticus* is its capacity to generate biofilms, which are crucial in the initiation of infections. The exopolysaccharides synthesized have the capacity to impede the proliferation of other bacteria and concurrently reduce their capacity to generate biofilms **(Rossi *et al.*, 2016).**

2.2.1.3. *Staphylococcus aureus*

Staphylococcus aureus is Gram-positive bacteria (stain purple by Gram stain) that are cocci-shaped and tend to be arranged in clusters that are described as “grape-like”. These organisms can grow aerobically or anaerobically (facultative) and at temperatures between 18 C and 40 C. Typical biochemical identification tests include catalase positive (all pathogenic *Staphylococcus* species), coagulase positive (to distinguish *Staphylococcus aureus* from other *Staphylococcus* species), novobiocin

sensitive (to distinguish from *Staphylococcus saprophyticus*), and mannitol fermentation positive (to distinguish from *Staphylococcus epidermidis*) **(Taylor and Unakal , 2024).**

Staphylococcus aureus is a relatively uncommon cause of UTIs in the general population. Although rare, *Staph. aureus* induced UTIs are prone to potentially life-threatening invasive infections such as bacteremia **(Xu *et al* ., 2023).**

2.2.2. Gram Negative

UTIs are mainly caused by Gram-negative bacteria, which pose a challenge for diagnosis and treatment due to their increasing resistance to antibiotics.

2.2.2.1. *Escherichia coli*

Escherichia coli (E. coli) is a type of bacteria that is typically found in the intestines of humans. It is a gram-negative bacillus and can be both harmless as part of the normal intestinal flora, or it can cause illnesses in the intestines and other parts of the body. *E. coli* strains have been extensively studied and categorized, leading to a wide range of diseases that can be caused by this bacterium. These diseases can vary from minor cases of gastroenteritis that resolve on their own, to more severe conditions such as renal failure and septic shock. The virulence of *E. coli* allows it to avoid the host's immune system and acquire resistance to commonly used antibiotics **(Mueller and Tainter , 2023).**

The cell surface of many *E. coli* strains is enveloped in a gelatinous layer composed of tightly packed strands of long-chain polysaccharides called capsular polysaccharide or capsule **(Sande *et al* ., 2020).**

E. coli which are distinguished based on their O and H antigens. The O antigen is defined by a repetitive polysaccharide chain found in the outer membrane lipopolysaccharide (LPS), while the H antigen is determined by the flagellum **(Mueller and Tainter , 2023).** *E. coli* is

grow rapidly in and on a wide range of liquid or solid media, especially in the presence of oxygen (doubling time ~20 min), but can also grow under anaerobic conditions (facultative anaerobe) **(Tuttle *et al* ., 2022).**

Suspected colonies of *E. coli* (displaying a reddish tint on MacConkey agar and a metallic sheen on EMB were subsequently transferred to blood agar to observe colony features. Pure colonies obtained from the blood agar were then injected onto nutrient agar, which is a nonselective medium. conducted biochemical assays to verify the presence of *E. coli*. The tests conducted consisted of the catalase test, Indole Production test, and Methyl red-Voges proskaur (MR-VP) test and Simmon's Citrate test **(Geletu *et al*. 2022)**. The experiments were performed on tryptone broth, MR-VP medium, and Simon citrate agar, respectively. UTIs caused by *E. coli* are the most prevalent forms of infections **(Lee *et al*., 2019).**

Antimicrobial resistance (AMR) is a multifaceted health issue that affects the entire world. The complexity is defined as the intersection of AMR across different hosts and interspecies interactions within microorganisms. Resistance refers to the alteration in the ability of bacteria to respond to antibiotics, leading to the ineffectiveness of these drugs. This phenomenon can occur soon after the administration of antibiotics **(WHO, 2020).**

2.2.2.2. *Klebsiella pneumonia*

Klebsiella pneumoniae(*Kp*) belongs to the *Enterobacteriaceae* family **(Rønning *et al* ., 2019)** and is described as a gram-negative, encapsulate, facultative anaerobic and non-motile bacterium **(Ashurst and Dawson , 2023).** *Kp* is an opportunistic pathogen that mostly causes healthcare-associated infections, particularly in those with weakened immune systems or concurrent bacterial illnesses **(Arato *et al*., 2021).**

Klebsiella pneumoniae (*KP*) is the predominant pathogen in the *Klebsiella* genus and is responsible for a wide range of infections in hospitals, long-term care facilities, and communities worldwide. These infections include lung, urinary tract, abdominal cavity, surgical site, soft tissue infections, and even bloodstream infections. This encapsulated Gram-negative bacterium is commonly present in the natural microbial communities of the mouth, skin, and intestine. Additionally, it ranks as the third most commonly identified microbe in blood cultures obtained from patients with sepsis **(Cristea *et al*., 2017).**

The prevalence of urinary tract infections (UTIs) caused by *Klebsiella pneumoniae* has shown a rising trajectory and has become a significant burden for numerous public health systems, particularly in hospital environments **(Miftode *et al*., 2021).**

2.2.2.3. *Enterobacter aerogenes*

Enterobacter aerogenes formerly known as *Klebsiella aerogenes* , belongs to the family *Enterobacteria* and is a facultative Gram-negative anaerobe. It is widely distributed in the environment and is found in the human gastrointestinal tract, also being a common opportunistic pathogen in hospitals**(Gu *et al* ., 2022).**

Enterobacter aerogenes was recently renamed *Klebsiella aerogenes* on the basis of whole-genome sequence (WGS)-based comparative bacterial phylogenetics demonstrated that *Enterobacter aerogenes* is more closely related to *Klebsiella pneumoniae* than to the *Enterobacter* species **(Wesevich *et al* ., 2020).**

Enterobacter is a group of bacteria that are gram-negative, rod-shaped, and can survive with or without oxygen. They belong to the *Enterobacteriaceae* family. It is additionally characterized as a bacterium that does not produce spores, contains flagella, tests positive for urease, and ferments lactose. The pathogenicity of this bacterium is contingent

upon a multitude of variables. Similar to other gram-negative enteric bacilli, the bacteria utilize adhesins to attach to host cells. The existence of a lipopolysaccharide (LPS) capsule can assist the bacteria in evading opsonophagocytosis. The LPS capsule has the ability to trigger a series of inflammatory reactions in the host cell, potentially resulting in sepsis. The main cause of antibiotic resistance in *Enterobacter* spp. is the existence of beta-lactamases. Beta lactamases possess the ability to catalyze the hydrolysis of the beta-lactam ring, which is present in penicillin and cephalosporins. The existence of this enzyme has led to a rise in the quantity of *Enterobacter* infections that are resistant to treatment **(Ramirez and Giron, 2024).**

Klebsiella aerogenes, a bacterium commonly acquired in healthcare settings, is becoming more frequently linked to high levels of resistance to several drugs and increased virulence characteristics. *Klebsiella aerogenes* is a member of the ESKAPE group of pathogens, which have a substantial influence on public health. *Klebsiella aerogenes* is widely distributed, commonly found in the human gastrointestinal tract, and is a significant opportunistic pathogen that is more frequently associated with nosocomial infections rather than community-acquired illnesses. It has the potential to induce urinary tract infections (UTIs), infections of the skin and soft tissues, lung infections, and bloodstream infections in those with impaired immune systems or those with damaged intestinal mucosa. *Klebsiella aerogenes* has been linked to elevated mortality rates in patients in intensive care units. There is a wealth of information available on the high occurrence of antibiotic-resistant *Escherichia coli* and *Klebsiella pneumoniae* UTIs. Nevertheless, there is a scarcity of information regarding *Klebsiella aerogenes* **(Mazumder *et al* ., 2023).**

2.2.3. Fungal Infection

Candida species cause urinary tract infection by either the hematogenous or ascending routes. Most kidney infection occurs by hematogenous seeding during an episode of candidemia, but this event is usually asymptomatic with regard to urinary tract symptoms**(Carol and Kauffman , 2014).** Fungal urinary tract infection is unusual. UTI arises when there are temporary or chronic weaknesses in the local or systemic immune system of the lower urinary tract, similar to bacterial UTI. Funguria can occur as a result of primary infections in the lower urinary tract or as a later consequence of the release of fungal components into the urine in individuals with systemic diseases**(Behzadi *et al* ., 2019).**

The most often recognized species is *Candida albicans*, followed by *Candida glabrata and Candida tropicalis*. Occasionally, other widely distributed fungi such as *Aspergillus* spp, *Blastomycosis* spp, and *Cryptococcus* spp may also cause primary fungal UTIs **(Olin and Bartges, 2015).**

2.3. Immune Responses to UTIs

2.3.1. Immune System

The lymphatic system consists of primary lymphoid organs: The organs in question are the bone marrow and the thymus. Lymphocytes, which are specialized immune system cells, are produced by them. Secondary lymphoid organs encompass the lymph nodes, spleen, tonsils, and specific tissue found in different mucous membrane layers throughout the body, such as in the intestine. The immune system cells carry out their primary function of combating pathogens and foreign substances within these organs **(IQWiG, 2023).** The resistance to infection is mainly accomplished by the versatility of the immune system in the urinary tract, with both innate and adaptive immune responses **(Ortega , 2020).**

The Immune response is the body's ability to stay safe by affording protection against harmful agents and involves lines of defense against most microbes as well as specialized and highly specific response to a particular offender. There are two subsystems within the immune system, known as the innate (non-specific) immune system and the adaptive (specific) immune system. Both of these subsystems are closely linked and work together whenever a germ or harmful substance triggers an immune response **(Justiz and Qurie, 2023).**

2.3.1.1. Innate Immune System

The innate immune system serves as the initial barrier against microbial infections and has a crucial role in preserving overall well-being **(Acosta and Alonzo, 2023).**

When the natural immune system is weakened or disrupted, noticeable symptoms of ongoing inflammation and infection become evident in a clinical setting **(Becknell *et al*., 2015).** The innate immune system consists of various components, including pattern recognition receptors like Toll-like receptors (TLR), plasma proteins, chemokines, cytokines, cellular components such as epithelial cells, bone marrow-derived phagocytes, dendritic cells, and natural killer cells, toxic molecules like reactive oxygen and reactive nitrogen intermediates, and antimicrobial peptides (AMPs) **(Riera Romo *et al* ., 2016).**

Macrophages restrict bacterial infection partly by stimulating phagocytosis and partly by stimulating release of cytokines and complement components **(Jiang *et al* ., 2022).**

The connection between bacterial metabolism and innate immunity is supported by the capacity of immune cells to recognize and react to metabolic products produced by bacteria, some of which possess immunomodulatory properties **(Traven and Naderer, 2019).** Short-chain fatty acids (SCFAs) produced during bacterial fermentation serve as

immunomodulators in various types of immune cells, including gut-resident macrophages **(Schulthess *et al.*, 2019).** Unlike the adaptive immune response, the innate immune system produces a quicker reaction to microbial assault **(Ching *et al* ., 2020).** Despite the innate immune response, bacteria still can persist in the urinary tract. Therefore, a more specific adaptive immune response ensues that protects the urinary tract **(Spencer *et al* ., 2014).**

2.3.1.2. Adaptive Immune System

The adaptive immune system, also known as the acquired immune system, is a part of the immune system that comprises of specialized, systemic cells and processes that kill infections by inhibiting their proliferation **(Khalid *et al* ., 2020).**

The adaptive immune system respond to bacterial antigens to orchestrate persisting protective immune responses and generate immunological memory**(Shepherd and Mclaren , 2020).** The adaptive immune responses are limited, particularly when only the lower urinary tract is infected. Whereas the wide-ranging innate immune responses of the urinary tract are highly responsive to infections, the adaptive immune responses, particularly in the bladder, tend to be limited **(Abraham and Miao , 2015).**

2.3.2. Immunological Biomarker

2.3.2.1. Interleukins

Interleukins (IL) are a class of cytokines first believed to be exclusively expressed by leukocytes, but further research has revealed their production by various other cells in the body **(Justiz Vaillant and Qurie, 2023),** including immunological cells **(Ferreira *et al* ., 2018).**

Cytokines are a class of proteins that are produced in response to infections and other antigens. They play a crucial role in regulating and

facilitating inflammatory and immunological responses **(Zhu *et al* ., 2017).**

They have a crucial role in various essential cellular activities, such as proliferation, maturation, migration, and adhesion. Additionally, they are involved in the activation and differentiation of immune system cells **(Ferreira *et al*., 2018).** There are three distinct groups. The initial and most extensive category comprises inflammatory cytokines, encompassing a total of 22 molecules, namely IL-1, IL-4, IL-5, IL-6, IL-8, IL-9, IL-13, IL-14, and IL-15. The second category comprises anti-inflammatory chemicals, specifically 14 interleukins, namely IL-7, IL-10, IL-30, and IL-37. The final category comprises interleukins that possess a dual capacity, being able to serve as both inflammatory and anti-inflammatory molecules. These interleukins include IL-2, IL-3, IL-11, and IL-12 **(Lissoni *et al*., 2020).** Cytokines and interleukins share three distinct mechanisms of action on other cells: autocrine, paracrine, and endocrine. Autocrine refers to the substance affecting the cell that produces it, paracrine refers to the substance affecting nearby tissues, and endocrine refers to the substance being produced by the cell and entering the bloodstream to reach distant organs **(Corwin, 2000).**

Traditional indicators for urinary tract infections (UTIs) exhibit limited specificity. Urinary interleukins have the potential to enhance the accuracy and precision of laboratory detection of urinary tract infections (UTIs) **(Horváth *et al*., 2020).** UTIs are accompanied by inflammation, which involves several cytokines such as TNF-α, interleukin (IL)-1β, IL-6, and IL-8 **(Sundac *et al*., 2020).**

2.3.2.1.1. Interleukin-1

Interleukin-1, a cytokine that causes inflammation, is known to have several physiological roles and pathological implications, and it plays a

crucial role in both maintaining good health and contributing to diseases **(Kaneko *et al*., 2019).**

IL-1 acts as a key controller of inflammation by regulating many innate immune processes**.** IL-1 is secreted by macrophages, large granular lymphocytes, B cells, endothelium, fibroblasts, and astrocytes. The primary targets include T cells, B cells, macrophages, endothelium, and tissue cells **(Justiz Vaillant and Qurie , 2023).**

IL-1 is a superfamily of eleven structurally similar proteins, all involved in inflammation or its control, which mainly act through binding to specific receptors on the plasma membrane of target cells**(Boraschi , 2022).** Some with inflammatory activity and some with anti-inflammatory functions **(Dinarello , 2018).** Including 7 pro-inflammatory agonists (IL-1α, IL-1β, IL-18, IL-33, IL-36α, IL-36β, IL-36γ) and 4 defined or putative antagonists (IL-1R antagonist (IL-1Ra), IL-36Ra, IL-37, and IL-38) exerting anti-inflammatory activities**(Palomo *et al* ., 2015).**

UTIs are accompanied by inflammation, which involves several cytokines such as TNF-α, interleukin (IL)-1β, IL-6, and IL-8 **(Flores-Mireles *et al*., 2019).** The origins of interleukin-1 (IL-1) can be traced back to the 1940s when researchers first identified the fever-inducing properties of "soluble factors" produced by leukocytes stimulated by endotoxins **(Dinarello, 2018).** IL-1 consists of two agonists, IL-1α and IL-1β, that initiate signals by binding to IL-1 receptor 1 (IL-1R1) and enlisting an additional peptide chain for assistance **(Fields *et al*., 2019).**

Despite the relatively low homology (27%) in terms of amino acid sequences, IL-1α and IL-1β exhibit structural similarities and perform similar functions. They both interact with the IL-1 type 1 receptor (IL-1R1) and possess a core β-barrel structure with adjacent loops **(Kaneko *et al* ., 2019).**The reason for having two IL-1 agonists may lie in the

difference in robustness or specific functions between them **(Dinarello *et al* ., 2019).**

Interleukin-1 beta (IL-1β) is a pro-inflammatory cytokine, meaning it plays a role in promoting inflammation as part of the immune response. It is produced by various cells, including immune cells (such as macrophages and monocytes) and non-immune cells (such as epithelial cells). IL-1β is one of the most potent pro-inflammatory cytokines and it has been linked to dysregulated inflammation and to the severity of the UTI **(Masajtis-Zagajewska and Nowicki , 2017).**

IL-1β is induced by inflammatory signals in a broad number of immune cell types **(Bent *et al* ., 2018).** Monocytes and macrophages are the main sources of IL-1β secretion. It causes harm to the tissue and the entry of neutrophils into it. In order to prevent unregulated inflammation, the release of the active form of IL-1β is carefully controlled and influenced by a molecular complex known as the inflammasome **(Flores-Mireles *et al*., 2019).** IL-1β is synthesized as a 269-amino acid precursor protein and undergoes processing by caspase-1, also known as IL-1β-converting enzyme (ICE), which is activated in inflammasomes. This processing results in the production of mature IL-1β, consisting of the C-terminal 153 amino acids **(Lachman *et al*., 2023).** During the interaction between the host cell and the pathogen, there is a sudden release of cytokines. This release is aimed at attracting the cells of the innate immune system and strengthening the body's defense against pathogens. Cytokines in urinary tract infections (UTIs) are mostly generated within the uroepithelial cell lining of the bladder and released into the urine **(Sundvall *et al*., 2014).**

IL-1β shows potential as a useful indicator for distinguishing between upper and lower urinary tract infections (UTIs) **(Nanda and Juthani-Mehta 2019).** Interleukin-1 beta (IL-1β), a substance commonly

seen in the blood of children with urinary tract infections (UTIs), has been utilized as an indicator for acute pyelonephritis **(Sheu et al., 2017).**

2.3.2.1.2 Interleukin-8

Interleukin-8 is a pro-inflammatory CXC chemokine with a primary function in attracting and activating neutrophils, but also implicated in a variety of other cellular processes **(Vilotić *et al* ., 2022).** IL-8 is a key regulator of the acute inflammatory response and it recruits, migration and activates monocytes and neutrophils to the site of inflammation **(Marta Gomarasca et al ., 2020),** and leading to pyuria in patients with UTI **(Gokce *et al* ., 2010).**

IL-8 is rapidly expressed upon encountering microorganisms. IL-8 has the ability to both attract immune cells and trigger a series of gene reactions that result in the production of antimicrobial peptides **(Ching *et al* ., 2018).** Because of its significant function, it can serve as an indicator for urinary tract infections (UTIs) and a distinguishing characteristic **(Horváth *et al*., 2020).** IL-8 plays a pivotal function in all inflammatory processes. While its levels are higher in urinary tract infections (UTIs) and can indicate the likelihood of acute pyelonephritis, it has a low level of specificity. It occurs in all types of congenital urinary anomalies, except for prenatal renal pelvic dilatation. Therefore, IL-8 is not appropriate for the diagnosis of UTIs in the presence of an anatomical issue **(Bitsori *et al*., 2011).** IL-8 is synthesized as a result of bacterial infections and serves as significant agents in the process of inflammation **(Tramma *et al*., 2012).** Several studies have indicated that levels of IL-8 in urine and blood are increased in cases of urinary tract infection (UTI**) (Krzemień *et al*., 2019).**

Research has shown that urine IL-8 has a strong ability to accurately predict the absence of UTIs. As a result, it could be valuable as a tool for initial screening. The level of IL-8 was elevated in 92% of urinary tract

infections (UTIs), regardless of the specific germs responsible, with an average concentration of 627 pg/mL. IL-8 was found to be a more effective indicator of urinary tract infection (UTI) compared to IL-6. This is because the levels of IL-8 increased on the same day as the illness was diagnosed **(Oregioni *et al* ., 2015).**

2.3.3 Lipopolysaccharide Binding Protein (LBP)

Lipopolysaccharide (LPS)-binding protein (LBP) is mostly synthesized in hepatocytes and serves as a secretory acute-phase protein of class I **(Jappe *et al*., 2019).**

It has a crucial function in the natural immunological response. The process begins with the binding of LPS to LBP, forming the LPS-LBP complex. As a result, signal transduction pathways are activated, leading to the production of cytokines and other pro-inflammatory mediators. Lipopolysaccharide (LPS)-binding protein (LBP) is essential in the innate immune response and contributes significantly to the development of inflammatory and infectious-related disorders **(Meng *et al*., 2021).**

Lipopolysaccharide, often known as endotoxin, is a primary constituent of the outer membrane of gram-negative (GN) bacteria **(Gnauck *et al* ., 2016).** The LPS divides into three parts: Lipid A anchors the molecule to the outer membrane, the core oligosaccharide that is integral to imparting and maintaining membrane integrity, and the O-antigen polysaccharide that is connected to the core oligosaccharide as is in direct contact with the external environment **(Sperandeo *et al* ., 2019).** LPS are often used as markers for bacterial translocation. Elevated levels of LPS in the bloodstream can indicate increased permeability of the intestinal barrier, allowing bacteria or their components to enter systemic circulation. This phenomenon is associated with various health conditions and can trigger inflammatory responses **(Adda-Rezig *et al* ., 2021).**

(LBP) is an important mediator of the inflammatory reaction **(Brănescu *et al* ., 2012).**

LBP, a 50-kDa polypeptide mainly synthesized in the liver and released into the bloodstream after glycosylation, is the first protein to bind with LPS, which indicates that it might be a reliable biomarker that predicts the activation of innate immune responses **(Lepper *et al* ., 2020).**

According to a study conducted on children, the sensitivity of LBP was found to be 96%, meaning it accurately identified 96% of the cases. Additionally, the specificity of LBP was 100%, indicating that it correctly ruled out the presence of LBP in all cases where it was absent **(Horváth *et al*., 2020).** The serum LBP concentration constitutes a reliable biologic marker for the diagnosis of UTI in children **(Tsalkidou *et al* ., 2013).**

2.3.4 Mannose Receptor

Mannose is a sugar monomer of the aldohexose series of carbohydrates. It is a C-2 epimer of glucose. Mannose is important in human metabolism, especially in the glycosylation of certain proteins. Several congenital disorders of glycosylation are associated with mutations in enzymes involved in mannose metabolism **(Cummings , 2022).** Mannose is a vital component in human metabolism since it plays a crucial role in the process of glycosylating specific proteins. In addition, Mannose has been documented to alleviate abdominal cystic pain and to address bacterial urinary tract infections. Mannose demonstrates efficacy in treating lipopolysaccharide-induced acute lung damage in rats. Recent research have shown that Mannose is a potent inhibitor of autoimmune and inflammatory disorders. It successfully reduces a range of conditions, such as Type I diabetes, asthma, colitis, obesity, osteoarthritis, chronic graft-versus-host disease, and lupus. The immune regulating properties of Mannose have also been uncovered **(Dhanalakshmi *et al*., 2023).**

The mannose receptor (MR), also known as Cluster of Differentiation 206 (CD206), belongs to the C-type lectin (CLEC) family. The individuals in this family possess C-type lectin domains (CTLDs), which have a crucial role in recognizing ligands. Mannose receptor (MR) is capable of binding and internalizing a diverse range of ligands that are either naturally occurring or associated with pathogens. It is commonly located on the outer surface of antigen-presenting cells, including dendritic cells and macrophages. Recent evidence has demonstrated that the mannose receptor has a direct impact on the activation of different types of immune cells **(Van der Zande *et al.*, 2021).** Increased levels of soluble MR in the serum have been detected in individuals with various inflammatory disorders, indicating an association between soluble MR and inflammation **(Rødgaard-Hansen *et al*., 2014).**

Studies have shown that sMR concentrations are associated with the severity of the disease, portal hypertension, gut permeability, bacterial translocation, and even mortality **(Støy *et al* ., 2021).** Non-survivors tend to have higher levels of sMR. Therefore, the soluble mannose receptor (sMR) has been suggested as a new biomarker for inflammation **(Fan *et al* ., 2019).**

The mannose receptor can recognize multiple pathogens, including bacteria, e.g., *Mycobacterium tuberculosis* **(Lugo-Villarino *et al* ., 2021)** and *pneumococcus Streptococcus pneumoniae* **(Subramanian *et al* ., 2019).** The mannose receptor is important as it has major roles in diverse biological processes, including regulation of circulating levels of reproductive hormones, homeostasis, innate immunity and infections **(Cumming , 2022).**

2.4 Diagnosis of UTI

A urinary tract infection (UTI) is diagnosed based on the patient's clinical history and the results of a urinalysis, which is further confirmed

by a urine culture. Accurate urine sample collection is crucial for thorough assessment and culture analysis **(Aggarwal and Lotfollahzadeh , 2022).** The laboratory assessment for urinary tract infections (UTIs) comprises three primary examinations: dipstick urinalysis, microscopic urinalysis, and urine culture. The most common type of dipstick urinalysis permits analysis of multiple urine components, the most important being leukocyte esterase (LE), nitrite, and red blood cells. LE is expressed in white blood cells (WBCs), which are elevated in urine during infection Urine testing typically commences with dipstick urinalysis, a readily accessible procedure that may be performed in the office and takes only a few minutes to interpret **(Chu and Lowder, 2018).**

Macroscopic examination focuses on parameters such as color, clarity, odor, and specific gravity. Urine test strips are used to measure chemical properties like pH, glucose concentration, and protein levels. Microscopy is conducted to identify elements such as cells, urinary casts, crystals, and organisms **(Mcpheron and Pincus, 2017).**

Light microscopy is used to perform microscopic urinalysis. A UTI can be diagnosed in part by looking for leukocytes (pyuria, defined as >5–10 leukocytes/hpf) or bacteria (bacteriuria, defined as 15 bacteria/hpf) in the urine. Hematuria occasionally indicates a urinary tract infection (UTI) when combined with bacteriuria or pyuria **(Chaudhari *et al*., 2016).** The presence of pyuria was required for the diagnosis of UTI **(European Medicines Agency , 2022).**

The typical biochemical properties of urine consist of a pH level of 5.8, a hue ranging from pale yellow to deep amber, and the absence of bilirubin, red blood cells, protein, and pus cells. Changes in the biochemical properties of urine, such as alterations in pee frequency or kidney inflammation, can suggest problems with the ureter, urethra,

urinary bladder, and genital organs. The most probable reason for the described symptoms is urinary tract infections (UTIs) caused by various bacteria **(Chandra *et al*., 2020).**

The gold standard for diagnosing urinary tract infections (UTIs) is urine culture, which is also the best suitable screening test for asymptomatic bacteriuria. The determination of whether urine culture findings are positive or negative is based on the quantification of colony-forming units that develop on the culture media. A urine culture is considered positive if it reveals a bacterial colony count of 103 or more colony-forming units (CFUs) per milliliter of a common urinary tract organism. These cultures can also be used to determine antibiotic susceptibility, which is helpful in determining the appropriate antibiotic treatment. Nevertheless, women who have negative cultures may still experience improvement through antibiotic treatment **(Nicolle, 2018).**

A diagnosis of symptomatic urinary tract infection (UTI) in older persons typically necessitates the existence of localized genitourinary symptoms, the presence of pus in the urine (pyuria), and a urine culture that identifies a specific urinary pathogen **(Rowe and Juthani-Mehta, 2019).**

The diagnosis of UTIs is typically made by evaluating clinical symptoms and findings, such as the presence of pus cells (pyuria) or bacteria in the urine (bacteriuria). However, the most reliable method for diagnosis is urine culture, however it can take 24-48 hours to obtain results. Recently, there has been an increase in studies utilizing automated approaches like VITEK 2, which are demonstrating encouraging outcomes. Although there is increasing evidence to support this claim, the American Society for Microbiology (ASM), the British Society for Antimicrobial Chemotherapy (BSAC), and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) remain doubtful about

its application due to the lack of standardized inoculum and its reduced sensitivity in detecting all bacteria in a given sample. Conversely, direct testing offers clinicians prompt microbiological data, enabling customized antibiotic treatment and reducing antimicrobial-related negative effects **(Torres-Sangiao et al., 2022).**

2.5 Treatments of UTIs

Urinary tract infections (UTI) are common in emergency departments (ED), and at least 15% of them are bacteremic **(Lalueza *et al* ., 2018).** Urinary tract infections (UTIs) are highly prevalent worldwide, characterized by a diverse range of symptoms and varying degrees of illness severity, which might pose challenges in their management **(Marantidis and Sussman, 2023)**.The treatment approach that takes into account the specific culture and sensitivity of the patient **(Gupta *et al*., 2017)**.

The selection of an antibiotic is based on several key factors, including the patient's individual risk and prior antibiotic treatment, the range of pathogens and their sensitivity to the antibiotic, the effectiveness of the antimicrobial agent, the impact on the patient's resistance situation and potential ecological effects, and the undesired side effects of the drug **(Wagenlehner *et al* ., 2020).** Asymptomatic bacteriuria does not necessarily require treatment; however, therapy is advisable for pregnant women, renal transplant recipients, and patients undergoing urological surgery **(Zalmanovici Trestioreanu *et al* ., 2015).**

Chapter Three Subjects, Materials and Methods

Chapter Three: Subjects, Materials and Methods

3.1. Subjects

A case-control study was conducted at the College of Applied Medical Sciences/ University of Kerbala. A total of seventy patients with UTI were included in this study. They were diagnosed with UTI based on the signs and symptoms observed by urologists at Al-Imam Al-Husaien Hospital/Karbala Health Directorate.

The study was conducted between October 2023 to February 2024.The patient group has been separated into two subgroups: one subgroup is referred to as the UTI with culture positive growth bacterial group, while the other group is referred to as the UTI with culture negative growth bacterial group. The patients included in the study are adults of both sexes, aged 18 years or older. The control group consisted of 70 individuals who were apparently healthy and had no previous record of UTI disease. The selection criteria for matching patients and controls included sex, age and Body Mass Index. Therefore, the Male/Female ratio and the age range were identical in both the patient and control groups. Case and control subjects were chosen using a random selection process based on certain criteria for inclusion and exclusion. The questionnaire in Appendix (1).

Both UTI patients and volunteers who were healthy provided blood and urine samples for investigative purposes.

3.1.1 Criteria for Inclusion and Exclusion

3.1.1.1 Inclusion Criteria: The present study strictly followed the following criteria for including patients and control groups:

1. Patients diagnosed with UTI based on clinical assessment by physicians.
2. Both sexes male and female.
3. The patients age are restricted to people who are 18 years or older.
4. Healthy individuals without a prior history of UTI, who are of the same age, sex and BMI as the patient group.

3.1.1.2 Exclusion Criteria:

The exclusion criteria were as follows:

1. Individuals under the age of 18.
2. Individuals diagnosed with an autoimmune disorder.
3. Pregnant woman.
4. People with a catheter.
5. Patients suffering from chronic conditions such as hypertension, diabetes mellitus, and cardiovascular disease.
6. Men experiencing prostate issues.

3.1.2 Questionnaires

Data was obtained from both the patients and control groups, including details such as Information required includes: name, sex, age, family history, BMI, symptoms of UTI, and duration of UTI and other relevant inquiries, as indicated in Appendix (1).

3.1.3 Ethical Considerations

The research received approval from the College of Applied Medical Science/University of Kerbala Ethical Committee and the Ethical Committee at Al- Al-Imam Al-Hussein Hospital. Prior to collecting the samples, all participants in this study were informed and verbally consented to participate.

3.1.4 Study design

A case control study design was implemented, as depicted in Figure (3.1).

Figure (3-1): Study design

3.2 Materials

3.2.1 Kits

The kits utilized in the present study were displayed in Table (3.1)

Table 3.1: Study Kits

No	Kits	Company	Origin
1.	Human IL1- β (Interleukin 1-Beta) ELISA Kit	ELK Biotechnology	USA
2.	Human IL-8(Interleukin 8) ELISA Kit	ELK Biotechnology	USA
3.	Human LBP (Lipopolysaccharide Binding Protein) ELISA Kit	ELK Biotechnology	USA
4.	Human Mannose Receptor(MR) ELISA Kit	SUNLONG	China

3.2.2 Devices, Equipment, and Apparatus

Displays the instruments and apparatuses utilized in this study show in Table (3.2).

Table 3.2: Presents the equipment and apparatuses used in the study.

No	Devices , Equipment's and Apparatuses	Company	Origin
3.	Autoclave	Labtech	Korea
12.	Benson Burner	GEL	Germany
13.	Biological Cabinet	Thermo scientific	Germany
1.	Centrifuge	ROTOFIX 32 A (Hettich)	Germmany
14.	Deep freezer	GEL	Germany
17.	ELISA automated washer	Biotek	USA
18.	ELISA Printer	Biotek	USA
2.	ELISA reader Hs	Human	Germany
11.	Hematology Analyzer	Human	Germany
4.	Incubator	Gallenkamp	England
16.	Micro titer plate reader– spectrophotometer	Human	Germany
10.	Oven	Memmert	Germany
5.	Refrigerator	LG	Korea
9.	Sensitive balance	Kern	Germany
6.	VITIC2-compact	BIONMERIEUX	France
7.	Vortex	Scientific Industries	Korea
15.	Water bath	Memmert	Germany
8.	Water Distling	GEL	Germany

3.2.3 Instruments

Table (3.3) detailed the instruments utilized in this investigation.

Table 3.3 : The instruments used in the research.

No	Tools	Company	Origin
16.	Cohol	TKMD	Germany
20.	Conical flask	AFCO	Jorden
15.	Cotton	TKMD	Germany
1.	Disposable syringe 5 ml	AL-Shaghaf	China
21.	Distillwator (Water distiller)	GFL	Germany
3.	EDTA tube	ALS Laboratory supplies	China
2.	Eppendorf tube	TRUST LAB	China
4.	Gel tube	TRUST LAB	China
13.	Glass wear	AFCO	Jorden
5.	Gloves	KINGFA/MEDICAL	China
6.	Mask	TKMD	Germany
7.	Micro plate	Mybiosource	USA
12.	Micropipettes	Micropipette	Germany
14.	Microscope	Olympus	Japan
8.	Multi-channel pipette	CappAero 96	Germany
18.	Petridish	CITOTEST	China
9.	Pipette Tips	CITOTEST	China
19.	Plane tube	CITOTEST	China
17.	Plaster	TKMD	Germany
10.	Single-channel Micropipette	Dragon Laboratory	China
11.	Tourniquet	Voltaren	China
22.	Urine cup	AL-Shaghaf	China

3.3 Methods

3.3.1 Collection of the samples

The sample collected from positive UTI patients was diagnosed following a general urine examination (G.U.E.) by urologist and control**.**

3.3.1.1 Collecting the Blood Sample

Each participant provided a 5 ml sample of venous blood using a disposable syringe. A volume of 1.5 ml of blood was collected in the EDTA tube for CBC detection, while 3.5 ml of blood was drawn in a gel tube and allowed to rest at room temperature for 15 minutes. The serum samples were concentrated using a centrifuge at an approximate speed of 3000 revolutions per minute (rpm) for a duration of 10 minutes. An measurement of CRP was derived from the serum sample.

The remaining serum was carefully transferred into two eppendorf tubes and stored at -20°C to prevent any potential damage from repeated freezing-thawing cycles, to be used to measure ILs , MR and LBP.

3.3.1.2 Collection Urine Sample

A disposable sterile plastic container was used , About 5 ml "mid-stream" of urine was collected from each patient and control subjects. Used urine in G.U.E and for inoculated on standard culture media urine, including Mac Conkey and Blood agar. The samples were then incubated aerobic conditions at 37 °C for a period of 24-48 hours.

3.3.2 The calculation of Body Mass Index (BMI)

The BMI index is currently utilized to identify and categorize adult anthropometric height/weight characteristics according to the World

Health Organization, as demonstrated in Table (3.4) by**(Nuttall, 2015)** . A formula was utilized to compute BMI, which involves dividing weight in kilograms by height in meters

Body Mass Index =Weight (kg) / Height (m), **(Dang *et al* ., 2022).**

Table 3.4: The ranges of Body Mass Index (BMI)

Weight Status	**BMI range (kg/m)**
Underweight	15-19.9
Normal weight	20-24.9
Overweight	25-29.9
Class I obesity	30-34.9
Class II obesity	35-39.9
Class III obesity	≥40

3.3.3 Preparation of Culture Media

3.3.3.1 Blood Agar

A suspension of 40 g of blood agar was made in 1Lof distilled water (DW). The mixture was heated until it completely dissolved. Next, the sterilization process involves subjecting the material to a temperature of 121°C for a duration of 15 minutes. The agar was cooled to a temperature of 45 - 50°C and then 7% of sterilized defibrinated blood was added. The media was utilized for culturing and activating bacteria that had been collected from various samples. The bacteria that was collected from samples was activated **(Yeh *et al* ., 2009).**

3.3.3.2 MacConkey Agar

MacConkey Agar is a type of agar used in laboratory settings. It is commonly used to differentiate between different types of bacteria based on their ability to ferment lactose. The agar contains specific indicators

that change color depending on whether lactose fermentation has occurred. This allows researchers to analyze and identify different bacterial species. To prepare this medium, dissolve 40gm of agar in 1000 ml of D.W and sterilize it in an autoclave at 121C° for 20 minutes. Once cooled, the mixture was carefully poured onto the plates. These plates were specifically designed to selectively culture gram-negative bacteria **(MacFadden, 2000).**

3.3.3.3 Muller Hinton Agar

The steps of weighing 38 g of media, dissolving it in 1L of D.W, and autoclaving it for 15 minutes was carried out in accordance with the instructions provided by the company **(Murray and Zeitinger, 1983).**

3.3.4 Preparation of Solution and Reagent

Solutions for Gram staining have been prepared in accordance with the necessary microbiological procedures. The solutions included crystal violet, iodine, pure alcohol, and safranin.**(Leboffe and Pierce, 2012).**

3.3.5 Isolation and Identification of Microorganisms

A loopful of sample was taken from well-mixed urine cup and inoculated on MacConkey agar and blood agar. The samples were incubated overnight at 37°C in bacteriological incubators under aerobic conditions. The identification of bacteria was determined by:

A. **Morphological characteristics**

The characteristics of the colonies were thoroughly examined, including their shape, borders, size, color, and texture.

B. **Microscopic Characteristics**

The bacteria were examined using a light microscope after being stained with the Gram stain. The process entailed extracting a small sample from a bacterial colony and dispersing it onto a pristine slide using a droplet of regular saline solution. The slide was subsequently secured by momentarily subjecting it to a flame and coated with crystal violet. Subsequently, it underwent treatment with Iodine, followed by decolorization using alcohol, and finally counterstaining using safranine. Ultimately, the slide was scrutinized using oil immersion**(Tille, 2017).**

C. **Identification through the use of automated methods The VITEK2 system:**

Automated methods are highly efficient and accurate when it comes to identifying bacteria. The VITEK2 system is composed of plastic reagent cards that contain small amounts of various biochemical test media in 30 wells. These wells provide a biochemical profile that is used to diagnose organisms. The inoculum is transferred from cultured samples into the card, and a photometer periodically measures the color changes in the card resulting from the microbe's metabolic activity. The data was thoroughly analyzed and efficiently stored in a computerized database. A variety of cards, such as those for Gram-negative identification (GN) and Gram-positive identification (GP), are available **(Maina and Kagotho , 2014).**

3.3.6 Antibiotics Susceptibility Determination

Antibiotic susceptibility testing involves assessing the susceptibility of a bacterial isolate to a specific range of antibiotics. After been inoculated, the cards were put into the Vitek 2 autoatic reader-incubator. The following manufacturer's instructions were followed for the inoculation and interpretation of the susceptibility and identification

cards. The researchers utilized colony counts to ensure the accuracy of the number and density of microorganisms that were introduced into the Vitek cards **(Bazzi *et al* ., 2017).**

3.3.7 Hematological Parameter Estimation

Assessment of Complete Blood Count (CBC) Blum meticulously followed the procedure using the swelab device.

1. The samples were initially at the natural temperature.
2. The thing was repeatedly reversed by hand until it was suspended.
3. If the samples have barcodes, they were treated in the same manner as conventional patient samples (Caps lock was turned off).
4. Once the sample was placed on the analyzer, the operator hit the RUN button.
5. After a comprehensive evaluation of all the samples, the results were printed with great attention to detail.
6. The data was printed by using the "Stored Data" option.
7. The output button was triggered.
8. Press the "Mark" button, followed by "All Clear," and then "Cancel" to remove all marks**(Arief *et al* ., 2021).**

3.3.8 Measurement of Immunological parameters

3.3.8.1 C-Reactive Protein (CRP)

3.3.8.1.1 The basic concept or principle.

Centrifugation is used to separate the erythrocytes from the serum or plasma in a capillary or venous blood sample. Next, the serum or plasma sample is diluted using HEPES buffer and then passed into a reaction chamber, where it is combined with CRP antibody latex reagent. The C-reactive protein (CRP) present in the diluted plasma forms a complex with the CRP antibody located on the latex particle. The CRP

concentration is determined by calculating the absorbance shift at 525 nm and 625 nm, which is directly proportional to the degree of agglutination.

3.3.8.1.2. The substances used in the experiment

The contents of one test are as follows:

- HEPES buffer: 1.79 mg
- Anti-human CRP antibody (goat) Latex conjugate: 41.84 µg

3.3.9 Assay for Immunological and Biomarkers Profile Using ELISA Technique :

The levels of Interleukin 1-β, Interleukin 8, Lipopolysaccharide Binding Protein and Mannose Receptor were measured using Sandwich enzyme linked immunosorbent assay ELISA research kits.

3.3.9.1 Estimating the level of Human Interlukin-1β and Human Interlukin-8

Principle of IL-1β: The test principle utilized in this kit is the Sandwich enzyme immunoassay. The microtiter plate included in this kit comes pre-coated with an antibody that targets Interleukin 1 Beta (IL-1β). Standards or samples are added to the appropriate microtiter plate wells, followed by the addition of a biotin-conjugated antibody that specifically targets IL-1β.Then, Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated, just like a scientist carefully conducting an experiment. When the TMB substrate solution is added, the wells that have IL-1β, biotin-conjugated antibody, and enzyme-conjugated Avidin will be the ones that show a color change. Termination of the enzyme-substrate reaction involves the addition of a sulphuric acid solution, followed by the measurement of the resulting color change using spectrophotometry at an approximately 450 nm ± 10

nm in wavelength. The concentration of IL-1β in the samples is determined by comparing OD of the samples to the standard curve(32).

Principle of IL-8: The test principle utilized in this kit is the Sandwich enzyme immunoassay. The microtiter plate included in this kit comes pre-coated with an antibody that specifically targets Interleukin 8 (IL-8). Standards or samples are carefully added to the appropriate microtiter plate wells, followed by the addition of a biotin-conjugated antibody that specifically targets IL-8. After that, Avidin conjugated to Horseradish Peroxidase (HRP) is introduced into each microplate well and allowed to incubate. Following the addition of the TMB substrate solution, a change in color will only be observed in the wells that contain IL-8, biotin-conjugated antibody, and enzyme-conjugated Avidin. The enzyme-substrate reaction is concluded by introducing a solution of sulphuric acid, and the resulting change in color is quantitatively assessed using a spectrophotometer at a specific wavelength of 450nm ± 10nm. The concentration of IL-8 in the samples is determined by comparing the OD of the samples to the standard curve. Figure (3-3).

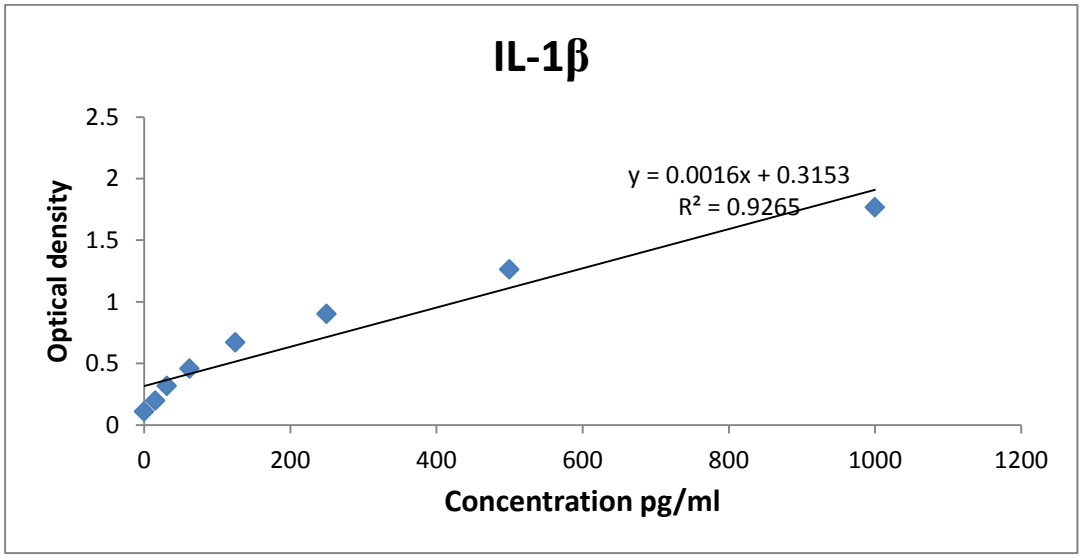


Figure (3-2): The standard curve of IL-1β concentration (pg/ml) and trend linear equation that display on chart Y.

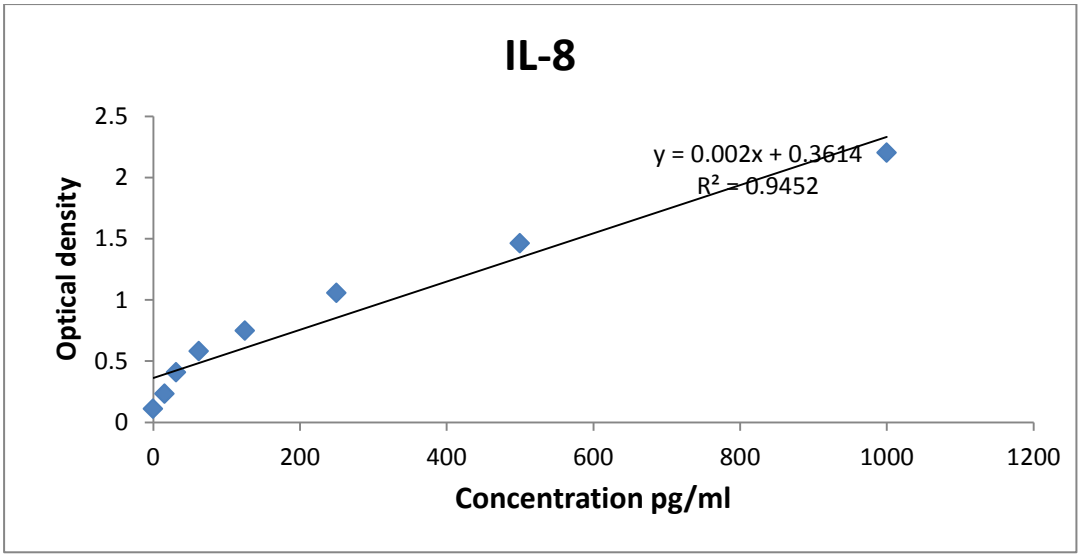


Figure (3-3): The standard curve of IL-8 concentration (pg/ml) and trend linear equation that display on chart Y.

KIT Components and Storage : The components and storage information for the IL-1β ELISA Kit were provided in Table (3.5).

Table 3.5: Components and Storage of the IL-1β ELISA Kit

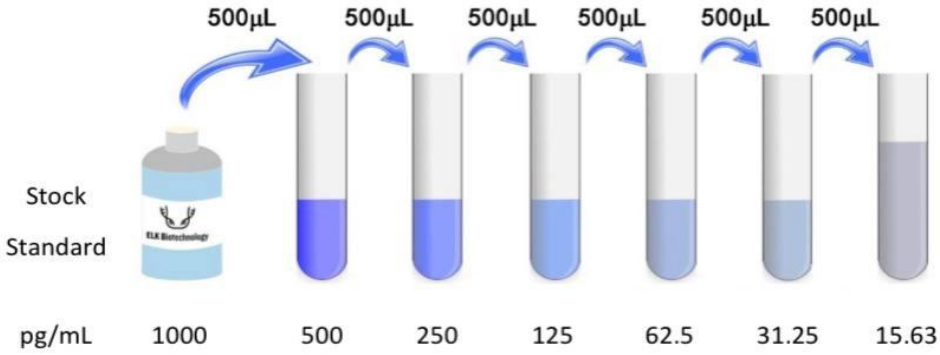
Reagents	Quantity		Storage Condition
	48 T	96 T	
Pre-Coated Microplate	6 strips x 8 wells	12 strips x 8 wells	-20ºC (6 months)
Standard (Lyophilized)	1 vial	2 vials	-20°C (6 months)
Biotinylated Antibody (100X)	60 uL	120 uL	-20°C (6 months)
Streptavidin-HRP (100X)	60 uL	120 uL	-20°C (6 months)
Standard/Sample Diluent Buffer	10 mL	20 mL	4°C
Biotinylated Antibody Diluent	6 mL	12 mL	4°C
HRP Diluent	6 mL	12 mL	4°C
Wash Buffer (25X)	10 mL	20 mL	4°C
TMB Substrate Solution	6 mL	10 mL	4°C(store in dark)
Stop Reagent	3 mL	6 mL	4°C
Plate Covers	1 Piece	2 Pieces	4°C

Preparing the reagents

1. The kit components and samples were brought to room temperature (18-25°C) before being used.
2. Mix the 25×Wash Buffer with double-distilled Water to create a 1×Wash Buffer.
3. Follow the standard working solution protocol by centrifuging the standard at 1000 × g for 1 minute. Prepare the Standard by adding 1.0 mL of Standard Diluent Buffer and allowing it to sit at room temperature for 10 minutes. Gently shake the mixture to avoid foaming. The concentration of the standard in the stock solution is 1000 pg/mL. There are seven tubes containing 0.5 mL of Standard Diluent Buffer. These tubes are utilized for the purpose of generating a double dilution series, as depicted in the picture provided below. Make sure to properly mix each tube before moving on to the next transfer by repeatedly pipetting the solution up and down.

Arrange 7 points of Diluted Standard with varying concentrations, including 1000 pg/mL, 500 pg/mL, 250 pg/mL, 125 pg/mL, 62.5 pg/mL, 31.25 pg/mL, and 15.63 pg/mL. The last EP tubes containing Standard Diluent serve as the Blank with a concentration of 0 pg/mL. To ensure the validity of the experimental results, it is essential to use the new Standard Solution for each experiment. When diluting the Standard from high concentration to low concentration, it is important to replace the pipette tip for each dilution.

Important: The final tube should be treated as a blank and no solution should be transferred into it from the previous tube.



4. Before used, it is recommended to briefly spin or centrifuge the stock Biotinylated Antibody and Streptavidin-HRP. Prepare a 100-fold dilution of the antibodies using Biotinylated Antibody Diluent and HRP Diluent.
5. The required amount of TMB Substrate Solution was carefully aspirated using sterilized tips, and the remaining solution was not discarded into the vial.

Preparing Samples

1. Ensure that all materials and prepared reagents are at room temperature before use. Thoroughly mix all reagents, ensuring that no foam is created within the vials.
2. It is important to determine the total number of samples used in the entire test.
3. Anticipate the concentration prior to conducting the assay. Whether the values fall within or outside the range of the Standard curve is being considered.

Procedure for conducting the assay.

1. All reagents of the kit and samples was transported to room temperature and was prepared as prescribed by the manufacture before use.

2. Test Preparation

a- Remove the solution and rinse each well with 200 µL of 1×Wash Solution. Allow it to sit for 1-2 minutes. Ensure that all remaining liquid is thoroughly removed from each well by firmly attaching the plate to absorbent paper. Wash three times in total. Following the final wash, ensure that all remaining Wash Buffer is removed by either aspirating or decanting. Turn the plate upside down and press it onto absorbent paper.

b- Standard: The Reference Standard vial was diluted with 1 ml of Reference Standard & Sample Diluent and allowed to rest for 1-2 minutes. After the standard had been completely dissolved, it was mixed thoroughly with a vortex meter, and the tube was labeled as working solution. The standard curve's concentration values were:1000, 500, 250, 125, 62.5, 31.25, 15.63, 0 pg/mL

c- The standard sample dilution method: seven clean tubes were taken and labeled with their predicted concentrations of 1000, 500, 250, 125, 62.5, 31.25, 15.63, 0 picogram per microliter. Five hundred microliters of Reference Standard & Sample Diluent were added to each tube. Five hundred microliters were pipetted from the 1000pg/mL working solution to the first tube and was mixed to produce a 500pg/mL working solution. Five hundred microliters of diluent were pipetted out from the 250pg/mL tube and added to the 125pg/mL, and it was mixed well. These steps were repeated until the 62.5 pg/mL standard was reached. the last tube is regarded as a blank served as the negative control.

3- Steps:

a- After the wells for blank, diluted standard and sample were determined, 100 µL of each diluted standard, blank and sample were

added into the appropriate wells and the plate was covered with the sealer and then immediately it was incubated for 80 min at 37℃.

b- One hundred microliters of the Biotinylated Ab working solution was added to each well. The microplate then was closed with sealer and incubated for 50 min at 37°C.

c- The solution in microplate was removed and then each well was filled with of wash buffer and its was immersed for 30 second, then the solution was discarded and then the microplate was dried with filter paper. This wash step was replicated 3 times.

d- One hundred microliters of streptavidin HRP Conjugate working solution was applied to each well. the microplate was closed with a clean sealer and incubated for 50 minutes at 37°C.

e- The microplate was washed as described in step 4 but the wash step was repeated 5 times.

f- Ninety μL of Substrate Reagent was added to each well. The plate was sealed with a new sealer and incubated for about 15 min at 37°C.

g- Fifty μL of Stop Solution was added to each well.

h- Micro-plate reader was used to determine the optical density (OD value) for each well at 450 nm.

3.3.9.2 Estimation the level of Human Lipopolysaccharide Binding Protein

Principle:

The test principle utilized in this kit is the Sandwich enzyme immunoassay. The microtiter plate included in this kit comes pre-coated with an antibody that specifically targets Lipopolysaccharide Binding Protein (LBP). Standards or samples are carefully added to the designated

microtiter plate wells, followed by the addition of a biotin-conjugated antibody that specifically targets LBP. After that, Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated. When the TMB substrate solution is added, the color change will only occur in the wells that have LBP, biotin-conjugated antibody, and enzyme-conjugated Avidin. The enzyme-substrate reaction is concluded by introducing a solution of sulphuric acid, and the resulting change in color is quantitatively assessed using a spectrophotometer at a specific wavelength of 450nm ± 10nm. The concentration of LBP in the samples is determined by comparing the OD of the samples to the standard curve. Figure (3-4).

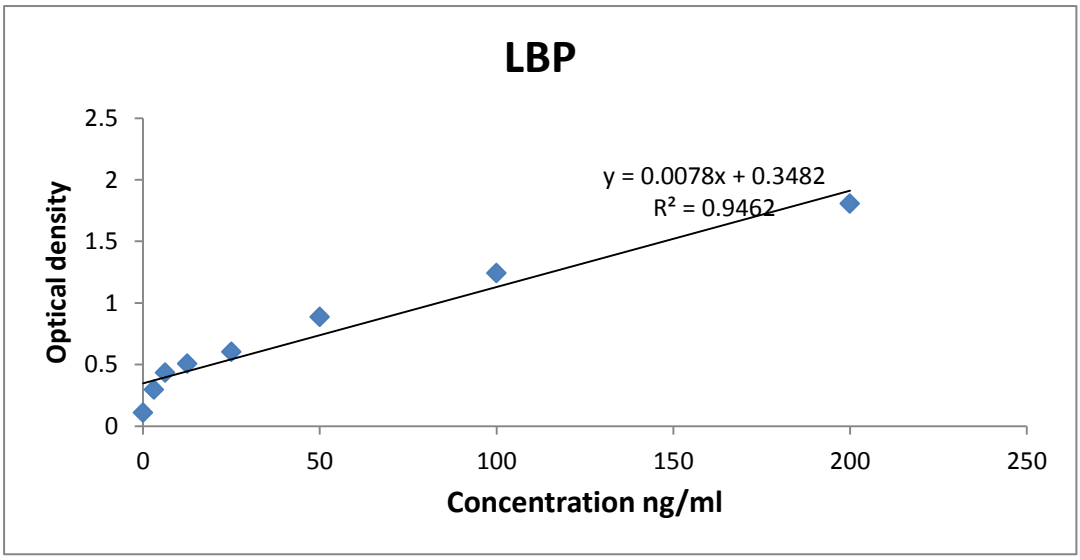


Figure (3-4): The standard curve of LBP concentration (ng/L) and trend linear equation that display on chart Y.

KIT Components and Storage

The components and storage information of the LBP ELISA Kit were presented in Table (3.7).

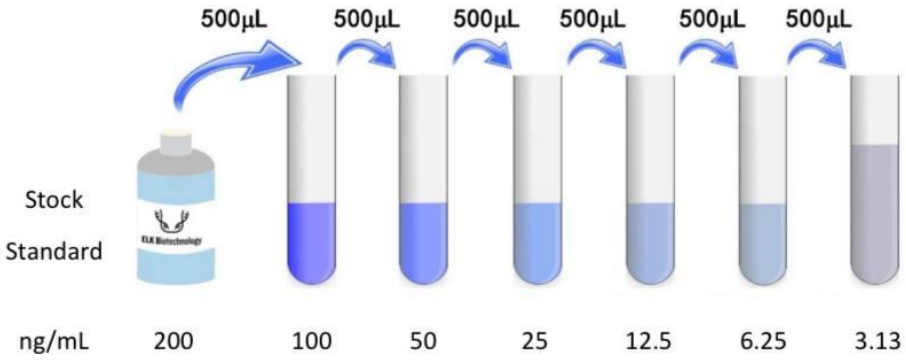
Table 3.6: LBP ELISA Kit Components and Storage

Reagents	Quantity		Storage Condition
	48 T	96 T	
Pre-Coated Microplate	6 strips x 8 wells	12 strips x 8 wells	-20ºC (6 months)
Standard (Lyophilized)	1 vial	2 vials	-20°C (6 months)
Biotinylated Antibody (100X)	60 uL	120 uL	-20°C (6 months)
Streptavidin-HRP (100X)	60 uL	120 uL	-20°C (6 months)
Standard/Sample Diluent Buffer	10 mL	20 mL	4°C
Biotinylated Antibody Diluent	6 mL	12 mL	4°C
HRP Diluent	6 mL	12 mL	4°C
Wash Buffer (25X)	10 mL	20 mL	4°C
TMB Substrate Solution	6 mL	10 mL	4°C(store in dark)
Stop Reagent	3 mL	6 mL	4°C
Plate Covers	1 Piece	2 Pieces	4°C

Preparing the Reagents

1. Ensure that all kit components and samples are at room temperature (18-25°C) before use.
2. Mix the 25×Wash Buffer with double-distilled Water to create a 1×Wash Buffer.
3. Follow the standard working solution procedure by centrifuging the standard at 1000 × g for 1 minute. Prepare the Standard by adding 1.0 mL of Standard Diluent Buffer. Allow it to sit at room temperature for 10 minutes, then gently shake it without causing foaming. The concentration of the standard in the stock solution is 200 ng/mL. There are seven tubes containing 0.5 mL of Standard Diluent Buffer, which are used for creating a double dilution series as depicted in the

picture below. For optimal results, it is important to ensure that each tube is mixed thoroughly before proceeding to the next transfer. To achieve this, gently pipette the solution up and down multiple times. Arrange 7 points of Diluted Standard with varying concentrations, including 200 ng/mL, 100 ng/mL, 50 ng/mL, 25 ng/mL, 12.5 ng/mL, 6.25 ng/mL, and 3.13 ng/mL. The final EP tube containing Standard Diluent serves as the Blank with a concentration of 0 ng/mL. To ensure the accuracy of the experimental results, it is important to use the new Standard Solution for each experiment. It is important to replace the pipette tip for each dilution when transitioning from a high concentration to a low concentration of the Standard. Please note that the final tube should be considered as a blank and no solution should be pipetted into it from the previous tube.



4. Before using the stock Biotinylated Antibody and Streptavidin-HRP, it is recommended to briefly spin or centrifuge them. Prepare a 100-fold dilution of the working concentration using Biotinylated Antibody Diluent and HRP Diluent.
5. TMB Substrate Solution - Carefully remove the required amount of solution using sterilized tips and avoid returning any leftover solution to the vial.

Preparing Samples

1. Ensure that all materials and prepared reagents are brought to room temperature before use. Thoroughly mix all reagents, being mindful to avoid creating any foam within the vials.
2. It is important to determine the total number of samples used in the entire test.
3. Anticipate the concentration prior to conducting the assay. Whether the values fall within or outside the range of the Standard curve is being considered.

Procedure for conducting the assay.

1. All reagents of the kit and samples was transported to room temperature and was prepared as prescribed by the manufacture before use.

2. Test Preparation

a- Remove the solution and rinse each well with 200 µL of 1×Wash Solution. Allow it to sit for 1-2 minutes. Ensure that all remaining liquid is thoroughly removed from each well by firmly attaching the plate to absorbent paper. Wash three times in total. Following the final wash, ensure that all remaining Wash Buffer is removed by either aspirating or decanting. Turn the plate upside down and press it onto absorbent paper.

b- Standard: The Reference Standard vial was diluted with 1 ml of Reference Standard & Sample Diluent and allowed to rest for 1-2 minutes. After the standard had been completely dissolved, it was mixed thoroughly with a vortex meter, and the tube was labeled as working solution. The standard curve's concentration values were:200, 100, 50, 25, 12.5, 6.25, 3.13, 0 ng/mL

c- The standard sample dilution method: seven clean tubes were taken and labeled with their predicted concentrations:200, 100, 50, 25, 12.5, 6.25, 3.13, 0 ng/mL picogram per microliter. Five hundred microliters of Reference Standard & Sample Diluent were added to each tube. Five hundred microliters were pipetted from the 200ng/mL working solution to the first tube and was mixed to produce a 100ng/mL working solution. Five hundred microliters of diluent were pipetted out from the 50ng/mL tube and added to the 25ng/mL, and it was mixed well. These steps were repeated until the 12.5ng/mL standard was reached. the last tube is regarded as a blank served as the negative control.

3- Steps:

a- After the wells for blank, diluted standard and sample were determined, 100 µL of each diluted standard, blank and sample were added into the appropriate wells and the plate was covered with the sealer and then immediately it was incubated for 80 min at 37℃.

b- One hundred microliters of the Biotinylated Ab working solution was added to each well. The microplate then was closed with sealer and incubated for 50 min at 37°C.

c- The solution in microplate was removed and then each well was filled with of wash buffer and its was immersed for 30 second, then the solution was discarded and then the microplate was dried with filter paper. This wash step was replicated 3 times.

d- One hundred microliters of streptavidin HRP Conjugate working solution was applied to each well. the microplate was closed with a clean sealer and incubated for 50 minutes at 37°C.

e- The microplate was washed as described in step 4 but the wash step was repeated 5 times.

f- Ninety μL of Substrate Reagent was added to each well. The plate was sealed with a new sealer and incubated for about 15 min at 37°C.

g- Fifty μL of Stop Solution was added to each well.

h- Micro-plate reader was used to determine the optical density (OD value) for each well at 450 nm.

3.3.9.3 Estimation the level of Human Mannose Receptor

Principle:

The method used for this ELISA kit is Sandwich-ELISA. The Microelisa stripplate included in this kit comes pre-coated with an antibody that targets MR. Standards or samples are carefully added to the appropriate Microelisa stripplate wells and mixed with the specific antibody. Next, a Horseradish Peroxidase (HRP)-conjugated antibody that targets MR is introduced into each well of the Microelisa stripplate and allowed to incubate. Components that are provided at no cost are removed. The TMB substrate solution is applied to every well. Wells that have MR and HRP conjugated MR antibody will display a blue color, which will later change to yellow upon the addition of the stop solution. The optical density (OD) is measured using spectrophotometry at a wavelength of 450 nm. The OD value varies directly with the concentration of MR. By comparing the OD of the samples to the standard curve, you can determine the concentration of MR in the samples. Figure (3-5).

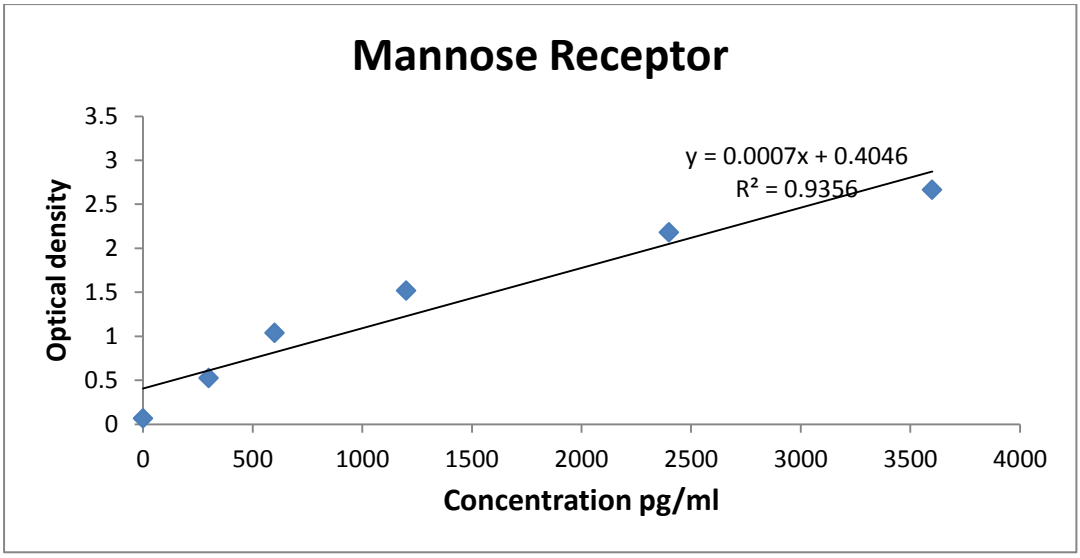


Figure (3-5): The standard curve of Mannose receptor concentration (ng/L) and trend linear equation that display on chart Y.

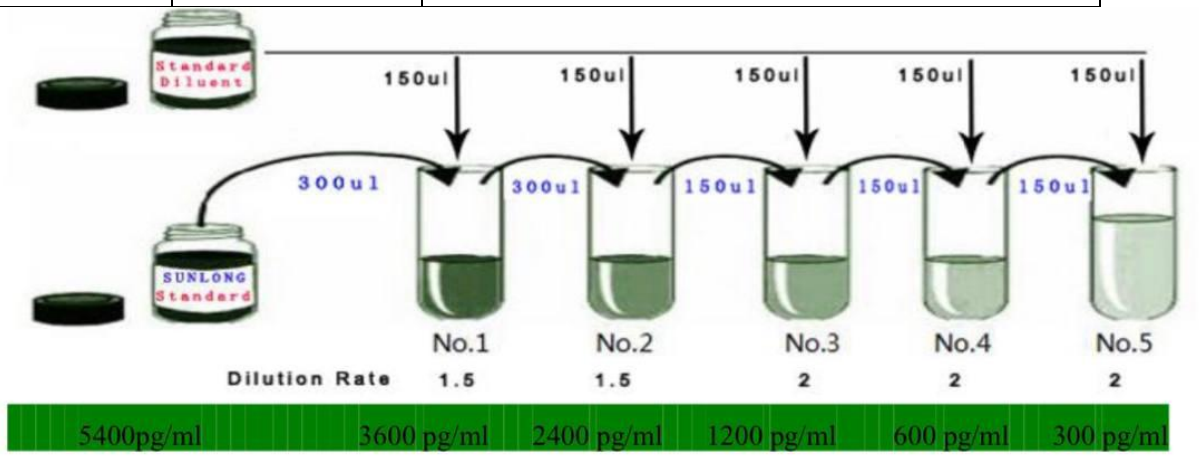
Sample preparation

Preparation of serum Once the whole blood has been collected, it is important to let it clot undisturbed at room temperature. Typically, this process requires 10-20 minutes. Separate the clot by using centrifugation at a speed of 2,000-3,000 rpm for a duration of 20 minutes. If precipitates are observed during the reservation process, it is recommended to centrifuge the sample once more.

Procedure

1. Standard Dilution begin by diluting the standard using small tubes. Next, carefully pipette 50ul from each tube into separate wells on the microplate. Remember to use two wells for each tube, for a total of ten wells.

3600pg/ml	Standard No. 1	300ul Original Standard + 150ul Standard diluents
2400pg/ml	Standard No.2	300ul Standard No. 1 + 150ul Standard diluents
1200pg/ml	Standard No.3	150ul Standard No.2 + 150ul Standard diluent
600pg/ml	Standard No.4	150ul Standard No.3 + 150ul Standard diluent
300pg/ml	Standard No	150ul Standard No.4 + 150ul Standard diluent



2. In the Microelisa stripplate, it is important to leave one well empty as a blank control. For the sample wells, a total of 40µl of sample dilution buffer and 10µl of sample are added, resulting in a dilution factor of 5. It is important to load the samples onto the bottom of the well without making contact with the well wall. Ensure thorough mixing by gently shaking.
3. During the incubation process, the sample should be sealed with the Closure plate membrane and kept at a temperature of 37℃ for a duration of 30 minutes.
4. Dilution: The concentrated washing buffer should be diluted with distilled water. For 96T, dilute it 30 times, and for 48T, dilute it 20 times.
5. Washing: Peel off the Closure plate membrane with caution, remove the solution, and then refill with the wash solution. Dispose of the

wash solution after allowing it to rest for 30 seconds. Perform the washing procedure five times consecutively.

6. 50 µl of the HRP-Conjugate reagent was added to each well, excluding the blank control well.
7. Incubation as outline in Step 3.
8. Washing as outlined in Step 5.
9. For coloring, 50 µl of Chromogen Solution A and 50 µl of Chromogen Solution B were added to each well. The mixture was gently shaken and incubated at 37℃ for 15 minutes. It is recommended to refrain from exposing the coloring to light.
10. Termination: To halt the reaction, 50 µl of stop solution were added to each well. It is important to note that the color in the well should transition from blue to yellow.
11. Measure the absorbance at 450nm using a Microtiter Plate Reader. The OD value of the blank control well is considered as zero. It is important to conduct the assay within 15 minutes after adding the stop solution.

3.4 Statistical Analysis

The Statistical Package for the Social Sciences (SPSS), version 22 software (IBM Corp., NY, and USA), was used to analyze data. Descriptive statistics were used to determine frequencies, the mean, standard error, median, range, and cross-tabulation. Bivariate correlations were analyzed to determine significant positive and negative correlations between variables if they were present. An independent sample T-test and the Analysis of Variance (ANOVA) test were used to compare means. The Least Significant Difference (LSD) was also determined.

The categorical variables were tested by the chi-square test. The statistical significance level was established at $P \leq 0.05$.

Chapter Four
Results and Discussion

Chapter Four: Results and Discussion

4.1. Demographic and Some Clinical Characteristics

The current study included two subject group are case and control. The group of patients are divided to subgroups as follows: **The first subgroup** of patients with urinary tract infection who showed positive results for bacterial growth in urine culture their number was 35 patients. **The second subgroup**, which is the group of patients with urinary tract infection whose results were negative for bacterial growth in urine culture their number 35. The group of control it was individuals apparently healthy their number 70.

Through statistical comparison of the results in Table 4-1, it was found that the two groups do not differ significantly ($P>0.05$) in average age, as the P value was 0.949, which indicates the homogeneity of the sample selected in this study in terms of age for the two groups.

Each of the subject groups for the current study was divided into three age groups, distributed as follows:18-37, 38-57 and 58-77. Through the results of the statistical analysis of these age groups in terms of their number, are significant difference ($P<0.05$) was observed between the age groups of positive growth and control separately, as the P values were (0.00024 and 0.00925) for the categories of each of the groups. As in Table 4-1.

The results of the distribution based on sex in Table 4-1 indicate that the percentage of females is 80% and the percentage of males is 20% for each of the three groups. Based on the results of statistical analysis, the number of females for each group is significantly greater than the number of males, as the P value was (0.00039 , 0.00039 and 0.00001) for each of the three groups, respectively.

Based on the height and weight of each person in this study, extracting the body mass index(BMI) (kg/m^2) and comparing the three groups, it was found that the BMI ranged between 18.82 - 39.15, with an average of 27.46 kg/m^2 for the group of patients with urinary tract infection positive for bacterial growth, and The BMI ranged between 18.02 - 39.85, at a rate of 27.77 kg/m^2, for the group of patients with bacterial growth-negative urinary tract infections. As for the healthy group, the BMI ranged between 18.90 - 35.37, at a rate of 27.83 kg/m^2. The results of the statistical analysis also indicated that there was no significant difference ($P > 0.05$) showed the average BMI in the three groups, as the *P* value reached 0.9129, as in Table (4-1)

Table (4-1): Demographic Data of Urinary Tract Infection Patients and Controls

Criteria	UTI Patients		Control (Total N=70)
	Positive Bacterial Growth (N=35)	Negative Bacterial Growth (N=35)	
Age in years			
Median(Range)	41 (18 – 77)	40 (20 – 75)	44 (20 – 71)
Mean ±SE	43.25 ± 3.04	43.77 ± 2.76	42.71 ± 1.78
Age groups N (%)			
18 – 37 years	16 (45.7 %)	15 (42.9 %)	31 (44.3 %)
38 – 57 years	14 (40.0 %)	12 (34.3 %)	26 (37.1 %)
58 – 77 years	5 (14.3 %)	8 (22.8 %)	13 (18.6 %)
Sex N (%)			
Female	28 (80.0 %)	28 (80.0 %)	56 (80.0 %)
Male	7 (20.0 %)	7 (20.0 %)	14 (20.0 %)
BMI kg/m^2			
Median(Range)	27.63(18.82–39.15)	27.54(18.02-39.85)	27.85(18.90-35.37)
Mean ±SE	27.46 ± 0.82	27.77 ± 0.90	27.83 ± 0.38

* means significant difference NS: no significant

4.2. Distribution of bacteria in patient group with bacterial growth

The results in Figure (4-1) showed that the percentage of Gram-positive bacteria in this study was 52%, while the percentage of Gram-negative bacteria was 48%.

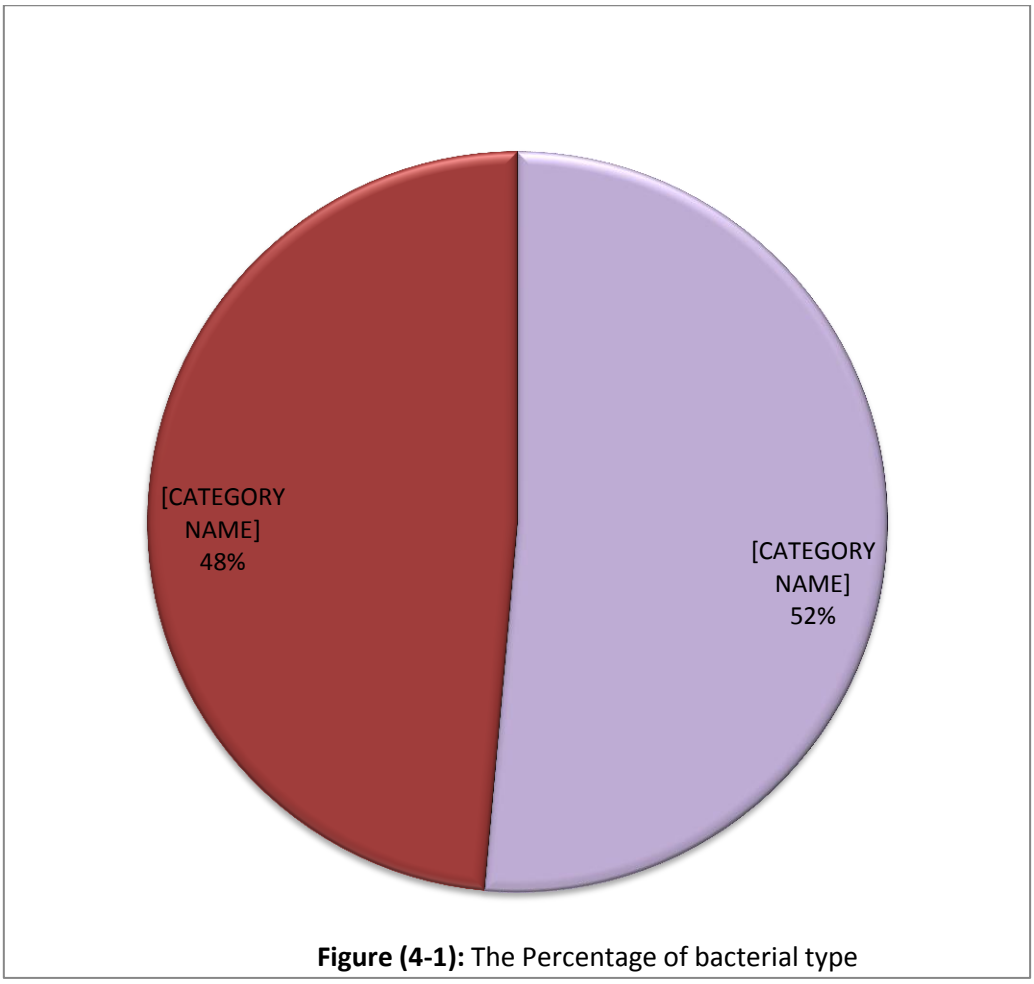


Figure (4-1): The Percentage of bacterial type

Gram-negative bacteria (GNB) are among the world's most significant public health problems especially with UTI due to their high resistance to antibiotics **(Oliveira J and Reygaert WC , 2024).**

UTI are caused by Enterococcus species, with *E. faecalis* and *E. faecium* being the most common. These bacteria possess many mechanisms that enhance their ability to cause disease. These

mechanisms encompass the processes of biofilm formation and the presence of virulence agents **(Dunny and Weaver., 2023).**

Gram positive bacterial such as *Staph. Saprophyticus* It is frequently responsible for simple UTIs, especially in young sexually active females. Additionally, it can lead to less frequent but nonetheless significant consequences such as acute pyelonephritis, urethritis, epididymitis, and prostatitis **(Argemi *et al*., 2019).**

E. coli strains have been extensively studied and categorized, leading to a wide range of diseases that can be caused by this bacterium. These diseases can vary from minor cases of gastroenteritis that resolve on their own, to more severe conditions such as renal failure and septic shock. The virulence of *E. coli* allows it to avoid the host's immune system and acquire resistance to commonly used antibiotics **(Mueller and Tainter , 2023).**

The cell surface of many *E. coli* strains is enveloped in a gelatinous layer composed of tightly packed strands of long-chain polysaccharides called capsular polysaccharide or capsule **(Sande *et al* ., 2020).**

The prevalence of urinary tract infections (UTIs) caused by *Klebsiella pneumoniae* has shown a rising trajectory and has become a significant burden for numerous public health systems, particularly in hospital environments **(Miftode *et al*., 2021).**

The results of bacterial isolation in the group of patients with bacterial growth showed that the most common bacterial species that appeared in this study were *E. coli* at a percentage 33%, followed by *Staphylococcus saprophyticus*, at a percentage 26%, while *Enterococcus faecalis* and *Enterococcus faecium* were the least, at a percentage 3% to each one. As shown in Figure (4-2).

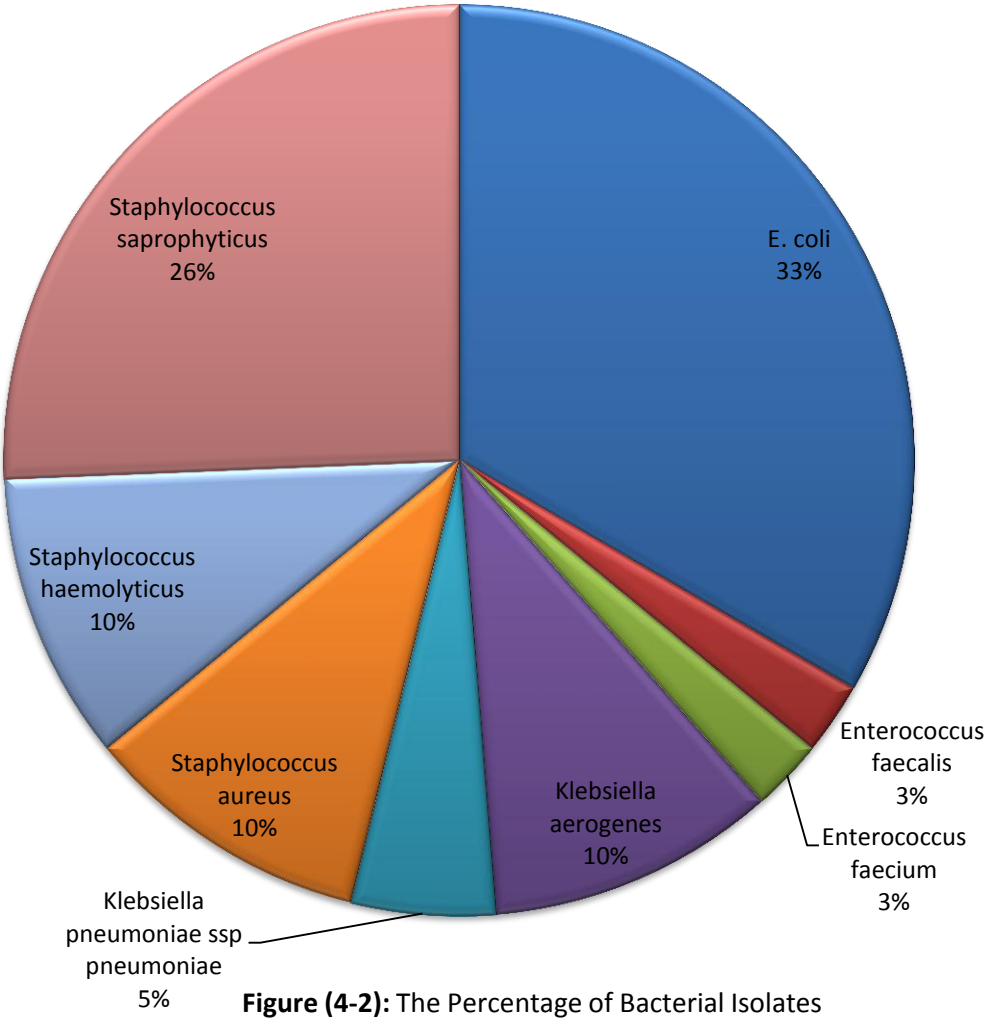


Figure (4-2): The Percentage of Bacterial Isolates

In study of **(Bono MJ *et al* ., 2024)** showed *Escherichia coli* causes the vast majority of UTIs, followed by *staphylococcus* , but other organisms of importance include *Klebsiella* and *Enterococcus.*

4.3. Heamatological Parameters

4.3.1. Distribution of WBC among studied groups

The results in Table (4-2) indicate that there are no significant differences ($P > 0.05$) in the concentration of white blood cells between the studied groups.

Table (4-2): The mean of WBC (10^9/L) **in studied groups.**

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	8.80 ± 0.90	0.416	NS
	No Bacterial Growth	7.94 ± 0.34		
Control		8.60 ± 0.01		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

Elevated white blood cell (WBC) count is a nonspecific marker of inflammation associated with immune system response to both acute and chronic infection, body mass index increased slightly across deciles of WBC count **(Kabat *et al* ., 2017).**

A study was made by **(Mahende *et al* ., 2017)** reported there was weak association between the WBC levels and positive cultures. Additionally, The study founded patients with confirmed urinary tract infections, both WBC and ANC demonstrated poor performance as diagnostic indicators of bacterial infection. Oure results agreement with Mahende *et al*,.

The study conducted in Iran revealed that the sick group exhibited a greater white blood cell (WBC) count compared to the control group**(Mahyar *et al*., 2013).** Our results disagreement with Mahyar *et al*., but agree with result of Han *et al*., observed that the level of WBC was not significant between patient and control group with bacterial infection **(Han *et al*., 2016).** Based on a study by De Jager *et al*., the number of leukocytes of 4.0 × 10^9/L or 12.0 × 10^9/L was used as the definition of systemic inflammatory syndrome response**(De Jager *et al* ., 2010)**.

The results in Table (4-3) indicate that there are significant differences ($P < 0.05$) in mean of WBC between males and females in the two groups of patients. There was also a significant difference ($P < 0.05$)

in mean of WBC in the two groups of patients compared to control group for the age group 38 - 57.

Table(4-3): Mean of WBC among studied groups according to sex, age and BMI.

Criteria	Class	N	Mean ± SE of WBC in studied Groups			P value	LSD
			Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	112	8.55±0.20 (56)	7.95± 0.87 (28)	7.50±0.25 (28)	**0.2213**	**NS**
	Male (N)	28	8.86±0.60 (14)	12.70±2.63 (7)	10.13±0.1.2 (7)	**0.1536**	**NS**
P value		**0.00001***	**0.5526**	**0.0365***	**0.0028***		
Age (years)	18 – 37 (N)	62	8.59 ± 0.01 (31)	8.7 ± 0.99 (16)	8.62 ± 0.49 (15)	**0.9874**	**NS**
	38 – 57 (N)	52	4.16 ± 0.01 (26)	8.97± 0.04 (14)	7.52 ± 0.44 (12)	**0.0000***	**2.541**
	58 – 77 (N)	26	8.59 ± 0.01 (13)	8.6 ± 0.52 (5)	7.57 ± 0.96 (8)	**0.8170**	**NS**
P value		**0.00091***	**0.0000***	**0.9869**	**0.3281**		
LSD			**3.871**	**NS**	**NS**		
BMI (kg/m^2)	Normal < 25	28	8.68±0.41 (14)	10.30±3.93 (3)	8.01± 0.55 (11)	**0.3843**	**NS**
	Overweight 25 – 29.9	88	8.71±0.28 (44)	9.46±1.00 (29)	8.36±2.07 (15)	**0.5618**	**NS**
	Obese ≥ 30	24	8.83±0.62 (12)	6.20±1.14 (3)	7.62±0.04 (9)	**0.0515**	**NS**
P value		**0.00001***	**0.9766**	**0.5719**	**0.7407**		
LSD			**NS**	**NS**	**NS**		

* means significant difference NS: no significant

A case-control research conducted in China revealed that adults with bacterial growth had a significantly greater white blood cell (WBC)

count compared to those without bacterial growth (P=0.002) **(Yang *et al.*, 2016**. In contrast, a study conducted by Moon et al. yielded contradictory findings, indicating that there was no statistically significant difference (P=0.213) in white blood cell count (WBC) between those with bacterial growth and no growth**(Moon *et al.*, 2020).**

On the other hand the results was approved that there was significant difference in WBC level according to the types of bacterial isolates. So, the WBC mean in patients whom *Klebsiella aerogenes* bacteria were isolated was the highest, as show in table (4-4).

Table (4-4): The mean of WBC in patient group with bacterial growth according to type of bacteria

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	8.01	1.05	0.0347*	10.245
Enterococcus faecalis	1	8.5	0.0		
Enterococcus faecium	1	6.5	0.0		
Klebsiella aerogenes	3	18.5	4.38		
Klebsiella pneumoniae ssp	2	6.0	1.39		
Staphylococcus aureus	4	6.32	1.01		
Staphylococcus haemolyticus	3	9.15	1.38		
Staphylococcus saprophyticus	8	7.6	1.87		

* means significant difference NS: no significant

The study conducted by Falup *et al*. revealed no significant variations in white blood cell (WBC) count among patients with urinary tract infections (UTIs) caused by *E. coli, Klebsiella spp., or Enterococcus spp*. **(Falup-Pecurariu *et al.*, 2020**). Furthermore, it has been noted by others that there was no statistically significant difference in the total white blood cell (WBC) count (P=0.637) and neutrophil count (P=0.525) between the gram-positive and gram-negative groups **(Akya *et al*., 2019).**

The current study agreement with the results of Akaya *et al* because our results showed that not significant between WBC count and type of bacterial in UTI patients.

The level of WBC increased because the role of macrophage and neutrophil in fight the pathogen during infection these lade to stimulation and release of WBC.

4.3.2. Distribution of Neutrophils among studied groups

The results in Table (4-5) indicate that there are no significant differences ($P > 0.05$) in the concentration of neutrophils (10^9/L) between the studied groups.

Table (4-5): The mean of Neutrophils (10^9/L) in study groups.

Groups		**Mean ± SE**	***P value***	**LSD**
Case	**Bacterial Growth**	6.74 ± 2.08	0.068	NS
	No Bacterial Growth	3.65 ± 0.11		
Control		4.16 ± 0.007		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

Based on a study by De Jager *et al*., the number of neutrophil used as the definition of systemic inflammatory syndrome response. This is due to the phenomenon that neutrophilia often occurred during an inflammatory reaction **(De Jager *et al* ., 2010).** Neutrophil count ratio (NCR) is a laboratory parameter that can predict bacterial infection in patients **(Sumardi *et al* ., 2021)**.

The results in Table (4-6) confirmed that there was a significant increase ($P < 0.05$) in the number of neutrophils in male patients in the PG group compared with control males. It is worth noting that the

number of neutrophils decreased significantly (P < 0.05) in both groups of patients compared to control in the age group 58-77.

Table (4-6): Mean of Neutrophils (10^9/L) among studied groups according to sex, age and BMI.

Criteria	Class	Mean ± SE of NEU in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	4.11±0.21 (56)	3.95±0.30 (28)	3.82±0.13 (28)	0.6686	NS
	Male (N)	4.00±0.41 (14)	19.47±10.12 (7)	3.25±0.13 (7)	0.0377*	14.12
P value		0.8170	0.0031*	0.0466*		
Age (years)	18 – 37 (N)	4.16 ± 0.01 (31)	9.66 ± 4.68 (16)	3.75 ± 0.14 (15)	0.1291	NS
	38 – 57 (N)	4.16 ± 0.01 (26)	5.22 ± 1.06 (14)	3.76 ± 0.20 (12)	0.1714	NS
	58 – 77 (N)	4.16 ± 0.02 (13)	3.23 ± 0.34 (5)	3.31 ± 0.24 (8)	0.0009*	0.389
P value LSD		0.9999 NS	0.5194 NS	0.2395 NS		
BMI (kg/m^2)	Normal < 25	4.18±0.38 (14)	6.02±2.95 (3)	3.85±0.24 (11)	0.2142	NS
	Overweight 25 – 29.9	4.13±0.23 (44)	9.58±3.46 (29)	3.41±0.15 (15)	0.0866	NS
	Obese ≥ 30	4.26±0.42 (12)	3.38±0.53 (3)	3.98±0.18 (9)	0.4947	NS
P value LSD		0.9658 NS	0.8111 NS	0.0946 NS		

* means significant difference NS: no significant

On the other hand the results was approved that there was non-significant difference in Neutrophils concentration according to the types of bacterial isolates as show in table (4-7).

Table (4-7): The mean of NEU in patient group with bacterial growth according to type of bacteria.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	10.35	5.74	0.9342	NS
Enterococcus faecalis	1	3.3	0.0		
Enterococcus faecium	1	3.9	0.0		
Klebsiella aerogenes	3	9.85	4.50		
Klebsiella pneumoniae ssp	2	3.35	0.54		
Staphylococcus aureus	4	3.32	0.36		
Staphylococcus haemolyticus	3	6.55	1.67		
Staphylococcus saprophyticus	8	3.55	0.35		

* means significant difference NS: no significant

Jonathan *et al*. reported that NCR was significantly higher in gram-positive bacteria than in gram-negative bacteria ($p < 0.05$) **(Jonathan PE and Zulfariansyah, 2019)**. Another report by Nurdani *et al*. showed that the ratio of neutrophil–lymphocytes in gram-positive bacteria was higher compared to gram-negative bacteria **(Nurdani et al ., 2019)**. Also same results in study of **(Hessle *et al* ., 2000)**. The results of current study disagreement with these studies.

4.3.3. Distribution of Lymphocytes among studied groups

The results in Table (4-8) indicate that there are no significant differences ($P > 0.05$) in the concentration of lymphocytes (10^9/L) among the studied groups.

Table (4-8): The mean of Lymphocytes (10^9/L) in study groups.

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	2.62 ± 1.80	0.8255	NS
	No Bacterial Growth	2.48 ± 0.63		
Control		2.54 ± 0.11		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

Inversely of our results Elemam *et al*. reported were show high significant in the mean of LYM (p <0.05) when compared between patients and control group with bacterial infection **(Elemam *et al*., 2021).** Lymphocyte count ratio (LCR) is a laboratory parameter that can predict bacterial infection in patients **(Sumardi *et al* ., 2021)**.

It is noted from the table (4-9) that the number of lymphocytes increases significantly (P < 0.05) in male of both patient groups compared to females. There was a significant increase (P < 0.05) in the number of lymphocytes in PNG patients in the Overweight and Obese groups compared to the Normal group.

Table(4-9):Mean of Lymphocytes(10^9/L) among studied groups according to sex, age and BMI.

Criteria	Class	Mean ± SE of LYM in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	2.64±0.08 (56)	2.39±0.13 (28)	2.71±0.08 (28)	0.1081	NS
	Male (N)	2.46±0.24 (14)	4.70±2.05 (7)	4.92± 1.17 (7)	0.1609	NS
P value		0.3772	0.0301*	0.0006*		
Age (years)	18 – 37 (N)	2.55 ± 0.01 (31)	2.80 ± 0.69 (16)	2.64 ± 0.13 (15)	0.8486	NS
	38 – 57 (N)	2.54 ± 0.01 (26)	2.51 ± 0.15 (14)	2.40 ± 0.20 (12)	0.6786	NS
	58 – 77 (N)	2.53 ± 0.01 (13)	2.46 ± 0.31 (5)	2.36 ± 0.25 (8)	0.7492	NS
P value LSD		0.8502 NS	0.8989 NS	0.4919 NS		
BMI (kg/m^2)	Normal < 25	2.59±0.27 (14)	2.23±0.45 (3)	2.15±0.27 (11)	0.5162	NS
	Overweight 25 – 29.9	2.64±0.16 (44)	3.25±0.59 (29)	2.90±0.02 (15)	0.4503	NS
	Obese ≥ 30	2.51±0.37 (12)	2.53±0.46 (3)	2.80±0.09 (9)	0.7897	NS
P value LSD		0.9376 NS	0.8093 NS	0.0025* 0.432		

* means significant difference NS: no significant

In the study conducted by **(Buonacera *et al* .,2022)** reported the LYM concentration elevated significantly in female than meal, also the rate was highly significant in age 22-33. These results corresponding with our study.

The results was approved that there was non-significant difference in lymphocytes concentration according to the types of bacterial isolates as show in table (4-10).

Table (4-10): The mean of LYM in patient group with bacterial growth according to type of bacteria.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	3.23	2.93	0.8895	NS
Enterococcus faecalis	1	1.0	0.0		
Enterococcus faecium	1	2.1	0.0		
Klebsiella aerogenes	3	1.95	0.88		
Klebsiella pneumoniae ssp	2	2.85	0.21		
Staphylococcus aureus	4	2.45	0.97		
Staphylococcus haemolyticus	3	2.35	0.4		
Staphylococcus saprophyticus	8	2.45	0.6		

* means significant difference NS: no significant

Patients with bacterial infections had an increase in the B-lymphocytes of peripheral venous blood, whereas patients with viral infections had an increase in T-lymphocytes as compared to controls **(Thorley *et al* ., 1977)**. Lymphocyte count ratio (LCR) is a laboratory parameter that can predict bacterial infection in sepsis patients **(Sumardi *et al* ., 2021)**.

4.4. Immunological Parameters

4.4.1. Distribution of CRP among studied groups

This study was conducted for CRP titer for all 140 participant subjects 70 of them cases with symptomatic UTI (35 were bacterial growth positive and 35 were bacterial growth negative) , and the other 70 were control group, this study was found that there were a highly

significant difference in CRP level among studied groups the highly increase level was in bacterial growth positive group . As show in table (4-11).

Table (4-11): The mean of CRP level among studied groups.

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	1.43 ± 0.26	0.0000**	0.62
	No Bacterial Growth	1.17 ± 0.33		
Control		0.25 ± 0.15		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

A study revealed that individuals with urinary tract infections (UTIs) caused by bacterial growth had higher levels of C-reactive protein (CRP) in their blood. The mean CRP level in these patients was 84.1±62.1 mg/l, while those without bacterial growth had a mean CRP level of 36.7±25.8 mg/l **(Lee *et al* ., 2015).** Similar findings were observed in other investigations, which demonstrated that CRP served as a reliable indicator for the existence of UTIs. The same result was shown in other studies where they found that CRP was a good predictive marker for the presence of UTIs **(Mithaq *et al*., 2011; Sim *et al*., 2015, Moon *et al*., 2020).**

Other investigators have observed similar findings, indicating a significant correlation between CRP levels and bacterial isolation in urinary tract infections **(AL- Khikani and Ayit, 2019**). The results of current study agreement with these studies.

In addition the study was presented that there was a highly significant difference in CRP mean level between patients and control

groups according to sex , age and BMI, the higher level was in male, age 58-77 in years and overweight in growth positive group in comparison to the other groups as show in table (4-12).

Table(4-12):Mean of CRP level among studied groups according to sex, age and BMI

Criteria	Class	Mean ± SE of CRP in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	0.24± 0.02 (56)	1.71 ± 0.47 (28)	1.11 ± 0.34 (28)	0.0002*	0.851
	Male (N)	0.25±0.02 (14)	5.48 ± 0.82 (7)	1.38 ± 0.31 (7)	0.0000*	3.791
P value		0.8445	0.0105 *	0.7528		
Age (years)	18 – 37 (N)	0.22 ± 0.01 (31)	1.31 ± 0.25 (16)	0.93 ± 0.24 (15)	0.0033*	0.813
	38 – 57 (N)	0.25 ± 0.02 (26)	1.39 ± 0.27 (14)	1.62 ± 0.38 (12)	0.0197*	0.621
	58 – 77 (N)	0.30 ± 0.01 (13)	1.85 ± 0.31 (5)	0.77 ± 0.13 (8)	0.0139*	1.475
P value LSD		0.3362 NS	0.8052 NS	0.5468 NS		
BMI (kg/m^2)	Normal < 25	0.20±0.01 (14)	1.57 ±0.28 (3)	1.60± 0.31 (11)	0.8449	NS
	Overweight 25 – 29.9	0.26±0.01 (44)	1.85 ±0.32 (29)	1.31 ±0.43 (15)	0.0031*	0.815
	Obese ≥ 30	0.25±0.01 (12)	0.67 ±0.05 (3)	0.41 ±0.05 (9)	0.1672	NS
P value LSD		0.4833 NS	0.5665 NS	0.3962 NS		

* means significant difference NS: no significant

CRP consider a good diagnostic tool and can be considered an economically feasible, indirect, and non-invasive method to detect UTIs

even in peripheral setups to differentiate upper UTIs from lower UTIs for specific therapy and prevent morbidities. A significant increase in the CRP levels in upper UTI can help determine the anatomical location and can help in targeting effective management of the infection by anti-microbial therapy (**Narayan Swamy *et al* ., 2022).**

A study conducted by (**Narayan Swamy *et al* ., 2022)** releveled association of CRP levels with age (p=0.03) and sex (p=0.013) of UTI patients was significant. A study was made by (**Al-Khikani *et al* ,. 2019)** reported a significant association between CRP levels and sex (p=0.000) but not age (p=1.38) of UTI patients.

On the other hand the results was approved that there was non-significant difference in CRP level according to the types of bacterial isolates as show in table (4-13)

Table (4-13): The mean of CRP in patient group with bacterial growth according to type of bacterial isolates.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	1.59	0.40	0.3552	NS
Enterococcus faecalis	1	0.10	0.0		
Enterococcus faecium	1	0.3	0.0		
Klebsiella aerogenes	3	3.0	1.20		
Klebsiella pneumoniae ssp	2	0.35	0.24		
Staphylococcus aureus	4	0.77	0.23		
Staphylococcus haemolyticus	3	1.95	1.16		
Staphylococcus saprophyticus	8	1.12	0.38		

* means significant difference NS: no significant

In the current research weren't agreement with **(Mushi *et al* ., 2019)** , Because C-reactive protein was significantly positive among children with UTI due to gram-negative bacteria and those with fever. In

children with age ≤ 2 years, positive CRP indicates UTI due to gram-negative enteric bacteria.

In a study conducted by Gao *et al.*, it was found that the levels of CRP were significantly higher in the group of patients with gramnegative bacterial infections compared to the group with Gram positive infections. **(Gao *et al.*, 2017),** This finding contradicts a study conducted in Basra, which showed no correlation between high-sensitivity C-reactive Protein (hs-CRP) levels and the type of bacteria in patients with urinary tract infections (UTIs), even though some patients were infected with *E. coli* had a significantly higher amount of CRP compared to other reported bacterial types **(Alhamedy and Shani, 2020).**

4.4.2. Distribution of IL-1β among studied groups

The results in Table (4-14) showed that there was a highly significant increase ($P < 0.05$) in the concentration of IL-1β (pg/ml) in two groups of patients compared with control group.

Table (4-14): The mean of IL-1β (pg/ml) in study groups.

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	165.66 ± 10.31	0.0000 **	31.145
	No Bacterial Growth	229.79 ± 10.94		
Control		127.24 ± 5.54		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

IL-1β is a pivotal proinflammatory cytokine involved in the regulation of the hosts' innate immune response. Intrinsically IL-1β-mediated inflammation has evolved to combat microbes and aid in tissue repair mechanisms, The extracellular recognition of a disturbance in

homeostasis sets the stage for IL-1β processing and its ability to execute inflammatory activities**(Dinarello CA , 2018).**

The results of current study not similar with results of Alfadul *et al*. Founded there is not relationship between UTI and elevation of levels of IL-1β **(Alfadul *et al* ., 2022).** IL-1β could be a promising marker for differentiation between upper and lower UTIs **(Horváth *et al* ., 2020).**

Butler *et al*. who suggested IL-1β release to be important for the progression of urinary tract infection (UTI**) (Butler *et al* ., 2022).**

The current study agreed with a study of **(Wasnaa *et al* ., 2017)** which showed highly significant relationship between the level of IL-1β (pg/ml) in patient group and would not agree highly significant relationship between the level of IL-1β (pg/ml) in control ($P < 0.01$).

Inversely , found that IL-1β level were higher in patient with growth bacterial compared with no growth bacterial **(Kim *et al* ., 2017)**.

IL-1β is a proinflammatory cytokine, and its increased presence suggests activation of the immune system in response to various stimuli, such as infection or tissue damage. IL-1β play a role in infection lead to increase nonspecific resistance to infection and development of the immune response to foreign antigens.

The results showed that there was a highly significant increase ($P < 0.05$) in the concentration of IL-1β (pg/ml) in two patient groups (female and male) compared to control group. The current study founded that the concentration of IL-1β increases significantly ($P<0.05$) in the two patient groups compared to the control group in all groups. Based on the BMI criterion, a significant increase ($P<0.05$) was observed in the concentration of IL-1β for all BMI categories, whether Normal,

Overweight, or Obese, in two patient groups compared to Control, as show in the table (4-15).

Table (4-15): Mean of IL-1β (pg/ml) among studied groups according to sex, age and BMI.

Criteria	Class	Mean ± SE of IL-1β in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	132.7±6.12 (56)	164.2±12.07 (28)	231.2±13.20 (28)	0.0000*	27.53
	Male (N)	136.1±9.96 (14)	171.9±18.63 (7)	212.8±24.83 (7)	0.0076*	52.78
P value		0.7981	0.7689	0.5333		
Age (years)	18 – 37 (N)	130.53±8.15 (31)	188.2±14.87 (16)	234.9±12.23 (15)	0.0000*	32.736
	38 – 57 (N)	141.18±8.80 (26)	144.9±15.02 (14)	205.8±22.02 (12)	0.0053*	15.769
	58 – 77 (N)	92.32±9.73 (13)	164.1±29.82 (5)	263.3±20.04 (8)	0.0000*	46.792
P value LSD		0.0056* 14.628	0.1506 NS	0.1278 NS		
BMI (kg/m^2)	Normal < 25	135.8±11.59 (14)	160.7±23.90 (3)	207.9±16.22 (11)	0.0037*	50.11
	Overweight 25 – 29.9	147.7±5.96 (44)	165.8±11.40 (29)	239.7±11.87 (15)	0.0000*	21.89
	Obese ≥ 30	94.7±10.21 (12)	170.7±46.70 (3)	235.9±32.23 (9)	0.0006*	83.07
P value LSD		0.0006* 15.63	0.9805 NS	0.4391 NS		

* means significant difference NS: no significant

Maculewicz *et al*. were observed relationship between BMI and IL-1β, in patients with infection and BMI ≥ 30 they have high significant , obesity is a major factor that leads to increase IL-1β with infections **(Maculewicz *et al*., 2022).**

The similar study reported by **(Kato *et al*., 2013)** founding the level of IL-1β increase with age , when age ≥ 18 observed highly significant (P<0.05) in IL-1β.

The results was approved that there was non-significant difference in IL-1β concentration according to the types of bacterial isolates as show in table (4-16).

Table (4-16): The mean of IL-1β in patient group with bacterial growth according to type of bacteria

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	173.2	15.03	0.5193	NS
Enterococcus faecalis	1	268.0	0.0		
Enterococcus faecium	1	203.6	0.0		
Klebsiella aerogenes	3	151.9	27.42		
Klebsiella pneumoniae ssp	2	99.2	12.44		
Staphylococcus aureus	4	168.8	42.2		
Staphylococcus haemolyticus	3	145.7	25.46		
Staphylococcus saprophyticus	8	167.2	25.80		

* means significant difference NS: no significant

The results of current study disagreement with **(Demirel *et al* ., 2020)** they founded that the release of IL- 1β was linked with *E. coli* infections.

4.4.3. Distribution of IL-8 among studied groups

The results in Table (4-17) indicate that there are no significant differences (P > 0.05) in the concentration of IL-8 (pg/ml) between the studied groups.

Table (4-17): The mean of IL-8 (pg/ml) in studied groups.

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	205.47 ± 10.50	0.0639	NS
	No Bacterial Growth	180.97 ± 25.85		
Control		158.41 ± 9.77		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

Many studies have reported elevated levels of IL-8 in the serum of patients with urinary tract infection, including study by Al Rushood *et al*, who reported that the levels of IL-8 elevated in UTI patient **(Al Rushood *et al* ., 2020).**

These results is similar to a study by *Abbas et al*. who founded that levels of IL-8 in serum were elevated in patients with UTI **(Abbas *et al* ., 2022).**

IL-8 are expressed rapidly after getting into contact with pathogens **(Ching *et al* ., 2018)** This result was agreement with current study.

Depending on age, the results in Table (4-18) appeared that the concentration of IL-8 in the patients growth group (in age 18 – 37) only increased significantly (P < 0.05) over control group. In addition, that the concentration of IL-8 in the patients growth group (Obese) only increased significantly (P < 0.05) over control group.

Table(4-18): Mean of IL-8 (pg/ml) among studied groups according to sex, age and BMI

Criteria	Class	Mean ± SE of IL-8 in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	165.1±12.25 (56)	198.0±10.56 (28)	191.2±33.10 (28)	0.3745	NS
	Male (N)	136.2±7.82 (14)	239.2±40.85 (7)	157.9±60.5 (7)	0.0711	NS
P value		0.2560	0.1219	0.6505		
Age (years)	18 – 37 (N)	155.2±18.12 (31)	217.5±15.57 (16)	186.6±12.31 (15)	0.0500*	52.349
	38 – 57 (N)	169.5±14.53 (26)	197.9±17.85 (14)	196.0±68.50 (12)	0.7440	NS
	58 – 77 (N)	144.8± 7.04 (13)	194.5±24.50 (5)	145.3±19.97 (8)	0.0881	NS
P value LSD		0.6455 NS	0.6312 NS	0.7305 NS		
BMI (kg/m^2)	Normal < 25	159.8±114.9 (14)	190.5±49.7 (3)	226.0±263.6 (11)	0.6829	NS
	Overweight 25 – 29.9	168.4±77.4 (44)	209.6±78.5 (29)	183.8±50.4 (15)	0.0724	NS
	Obese ≥ 30	142.7±25.3 (12)	215.6±47.9 (3)	136.4±49.9 (9)	0.0161*	12.61
P value LSD		0.6170 NS	0.8948 NS	0.4377 NS		

* means significant difference NS: no significant

The current study indicated that there was a higher level of IL-8 in males compared to females. However, this difference was not statistically significant in the analysed groups. These findings are in line with those

reported in earlier studies **(Alirezaei *et al*., 2019 ; Nasiri *et al*., 2022),** The current study agreement to study present by **(Gonzalez-Aparicio and, Alfaro, 2020)** found that IL-8 concentration higher significant in patients age ≥ 18. Also, showed the BMI effected on the level of IL-8 significantly.

In the current study, no significant differences could be observed in the levels of IL-8 between the deferent groups of patients (complicated versus uncomplicated UTI; culture positive versus culture negative UTI). The appearance of interleukin-8 (IL-8) in blood serum usually indicates an inflammatory response in the body.

The results was approved that there was non-significant difference in IL-8 concentration according to the types of bacterial isolates as show in table (4-19).

Table (4-19): The mean of IL-8 in patient group with bacterial growth according to type of bacteria.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	210.0	18.97	0.7149	NS
Enterococcus faecalis	1	168.9	0.0		
Enterococcus faecium	1	320.3	0.0		
Klebsiella aerogenes	3	206.7	33.89		
Klebsiella pneumoniae ssp	2	179.0	4.55		
Staphylococcus aureus	4	202.1	32.9		
Staphylococcus haemolyticus	3	218.8	34.64		
Staphylococcus saprophyticus	8	192.4	22.87		

* means significant difference NS: no significant

The results of the current research disagreements with results done by studies of **(Hosny *et al* ., 2021)** reported increase in the inflammatory IL8 in gram-positive bacterial infections than that in gram-negative

bacterial infections or in the mixed bacterial infections was observed and **(De Bont *et al* ., 2017)** reported that IL-8 was significantly higher in patients with gram-negative bacteria than patients with gram-positive bacteria.

4.4.4. Distribution of LBP among studied groups

The results in Table (4-20) showed that there was a highly significant increase ($P < 0.05$) in the concentration of LBP (ng/ml) in two groups of patients compared with control group.

Table (4-20): The mean of LBP (ng/ml) in studied groups.

Groups		**Mean ± SE**	***P value***	**LSD**
Case	**Bacterial Growth**	176.32 ± 16.45	0.0000 **	58.59
	No Bacterial Growth	34.41 ± 4.08		
Control		22.73 ± 2.11		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

In the study was made by **(Horváth *et al* ., 2020)** reported Lipopolysaccharide Binding Protein (LBP) study are promising, but confirming data are lacking. The measurable components of the innate immune system and local host cell response could be appropriate biomarkers, but their significance is currently unknown. LBP is an acute phase protein. In a single, observational study among children, LBP had a sensitivity of 96%, and a specificity of 100% **(Tsalkidou *et al* ., 2018).**

The current study disagreements with a study of **(Lo Basso *et al* ., 2021)** they founded no significant statistical changes were observed in UTI recurrence in level of LBP among their study groups.

The results of Table (4-21) indicated that the concentration of LBP receptor (ng/ml) in both females and males in the patient growth group increases significantly ($P < 0.05$). One of the important results in this table is that the concentration of LBP receptor (ng/ml) increased significantly ($P<0.05$) in all three age groups in the patient growth group compared to the control group and the patient no growth group. It is also evident from the results of Table (4-21) that the concentration of LBP receptor (ng/ml) increased significantly ($P<0.05$) in the three BMI categories (Normal, Overweight, and Obese) in the patient growth group compared to the control group and the patient no growth group.

Table (4-21): Mean of LBP (ng/ml) among studied groups according to sex, age and BMI.

Criteria	Class	Mean ± SE of LBP in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	47.38±2.61 (56)	175.4±19.33 (28)	35.7±5.00 (28)	0.0000*	16.684
	Male (N)	45.45±3.24 (14)	180.1±28.91 (7)	38.3±9.18 (7)	0.0000*	22.158
P value		0.7262	0.9104	0.8152		
Age (years)	18 – 37 (N)	45.31 ± 3.61 (31)	180.4±24.07 (16)	33.48 ± 3.53 (15)	0.0000*	37.089
	38 – 57 (N)	51.79±3.21 (26)	186.1±26.35 (14)	36.31±9.32 (12)	0.0000*	62.347
	58 – 77 (N)	40.51±2.94 (13)	137.6±46.51 (5)	32.59±8.40 (8)	0.0009*	29.091
P value LSD		0.1378 NS	0.6283 NS	0.9302 NS		
BMI (kg/m^2)	Normal < 25	42.28±5.90 (14)	160.4±49.65 (3)	42.38±11.25 (11)	0.0001*	17.104
	Overweight 25 – 29.9	53.78±2.41 (44)	207.0±19.47 (29)	36.22±3.18 (15)	0.0000*	34.560
	Obese ≥ 30	40.19±3.18 (12)	149.0±53.86 (3)	28.68±5.08 (9)	0.0000*	15.514
P value LSD		0.0125* 12.591	0.5295 NS	0.4455 NS		

* means significant difference NS: no significant

Study done by **(Kim KE *et al* ., 2016)** they reached LBP levels were significantly increased in overweight/obese participants compared with those in normal-weight participants (7.8±1.9 µg/mL vs. 6.0±1.6

µg/mL, P<0.001). LBP levels were significantly and positively associated with BMI. The results of this study are agreement with our study.

During infection caused by Gram-negative bacteria carrying lipopolysaccharide (LPS), LPS binding protein (LBP) secreted by hepatocytes form a complex with LPS. LBP recruits this complex to the cell surface receptor (CD14) present over monocyte to trigger the signalling pathway resulting in an inflammatory response.

The results was approved that there was non-significant difference in LBP concentration according to the types of bacterial isolates as show in table (4-22).

Table (4-22): The mean of LBP in patient group with bacterial growth according to type of bacteria.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	171.5	27.18	0.4393	NS
Enterococcus faecalis	1	167.0	0.0		
Enterococcus faecium	1	89.6	0.0		
Klebsiella aerogenes	3	138.1	29.38		
Klebsiella pneumoniae ssp	2	312.8	1.08		
Staphylococcus aureus	4	129.6	65		
Staphylococcus haemolyticus	3	218.3	37.35		
Staphylococcus saprophyticus	8	182	38.39		

* means significant difference NS: no significant

4.4.5. Distribution of MR among studied groups

The results in Table (4-23) showed that there was a highly significant increase (P < 0.05) in the concentration of MR (pg/ml) in patient group with bacterial growth compared with control group.

Table (4-23): The mean of MR (pg/ml) in study groups.

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	793.67 ± 44.18	0.0005 **	109.01
	No Bacterial Growth	492.64 ± 32.89		
Control		500.50 ± 61.33		

NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*

A study conducted by **(van der Zande *et al* ., 2021)** mannose receptor have been reported to be increased in patients suffering from a variety of inflammatory diseases and to correlate with severity of disease. A study of **(Loonen AJ *et al* ., 2019)** Increased serum MR levels were also observed in patients with a wide variety of inflammatory diseases, such as UTIs.Table (4-24) shows the results of Mannose receptor concentration (pg/ml) in the study groups according to sex, age and BMI. It is clear from the results in this table that the concentration of MR increases significantly ($P < 0.05$) of patient groups with bacterial growth (female and male) (824.9 pg/ml) compared to its concentration in control group. Also, showed that there are significant differences ($P<0.05$) in two age groups (38-57 and 58 – 77) years.

Evidence strongly suggests that mannose receptors play a role in the clearance of pathogens. The mannose receptor is known to bind to mannose- and fucose-containing microorganisms by carbohydrate recognition domains. Numerous reports have detailed mannose receptor recognition of bacteria.

Referring to Table (4-24), presents that the concentration of MR in the Overweight group in two patient groups (with bacterial growth and without bacterial growth) is significantly higher ($P < 0.05$) than the

control group. Also, in the obese group only in patient groups with bacterial growth is significantly higher ($P < 0.05$) than the control group.

Table(4-24):Mean of MR(pg/ml) among studied groups according to sex, age and BMI.

Criteria	Class	Mean ± SE of MR in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	561.5±77.7 (56)	824.9±46.8 (28)	518.8±34.18 (28)	0.0166*	62.471
	Male (N)	340.0±16.0 (14)	650.6±110.7 (7)	469.2±71.13 (7)	0.0031*	227.62
P value		0.1617	0.1177	0.5240		
Age (years)	18 – 37 (N)	641.6±128.4 (31)	760.1±6.25 (16)	510.1±52.38 (15)	0.4142	NS
	38 – 57 (N)	390.7±35.9 (26)	749.5±59.59 (14)	451.4±54.5 (12)	0.0000*	71.871
	58 – 77 (N)	364.3±45.04 (13)	1008.3±144 (5)	536.2±69.6 (8)	0.0000*	245.09
P value LSD		0.1007 NS	0.0258* 56.628	0.6076 NS		
BMI (kg/m^2)	Normal < 25	797.8±218.4 (14)	818.0±223.8 (3)	490.9±43.65 (11)	0.4287	NS
	Overweight 25 – 29.9	376.7±26.94 (44)	798.6±37.97 (29)	561.4±51.09 (15)	0.0000*	125.97
	Obese ≥ 30	375.0±47.57 (12)	759.8±99.07 (3)	463.2±74.76 (9)	0.0177*	301.82
P value LSD		0.0028* 38.781	0.9437 NS	0.4303 NS		

* means significant difference NS: no significant

The important function of recognizes a range of carbohydrates present on the surface and cell walls of micro-organisms. The MR is primarily expressed on macrophages and dendritic cells and is involved in MR-mediated endocytosis and phagocytosis.

The results was approved that there was non-significant difference in MR concentration according to the types of bacterial isolates as show in table (4-25).

Table (4-25): The mean of MR in patient group with bacterial growth according to type of bacteria.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	833.7	89.3	0.5846	NS
Enterococcus faecalis	1	354.8	0.0		
Enterococcus faecium	1	869.8	0.0		
Klebsiella aerogenes	3	607.8	189.9		
Klebsiella pneumoniae ssp	2	848	83.15		
Staphylococcus aureus	4	820.7	81.0		
Staphylococcus haemolyticus	3	753.4	161.08		
Staphylococcus saprophyticus	8	846.5	63.63		

* means significant difference NS: no significant

4.5. Estimation of Pus cells among studied groups

The results in Table (4-26) showed that there was a highly significant increase ($P < 0.05$) in the concentration of pus cells (HPF) in two groups of patients compared with control group.

Table (4-26): The mean of Pus cells (HPF) in studied groups.

Groups		Mean ± SE	*P value*	LSD
Case	**Bacterial Growth**	34.70 ± 4.59	0.0000 **	7.229
	No Bacterial Growth	35.79 ± 2.43		
Control		2.50 ± 0.13		
NS: Non significant *P value* * : Significant *P value* ** : Highly Significant *P value*				

The presence of urinary pus cells ≥ 5 per HPF in the diagnosis of UTI**(Prah *et al* ., 2019).** In a previous study, conducted by Baral and Nepal, the number of pus cells in patients with culture negative was higher than the number of pus cells in patients with culture positive.

Table (4-27) show there is a significant increase ($P < 0.05$) in pus cells of the two patient groups (with bacterial growth and those without bacterial growth) compared to the control group in all criteria studied (sex, age and BMI).

Table (4-27): Mean of Pus cells(HPF) among studied groups according to sex, age and BMI.

Criteria	Class	Mean ± SE of Pus cells in studied Groups			P value	LSD
		Control (70)	Patients Growth(35)	Patients No Growth(35)		
Sex	Female (N)	2.52±0.15 (56)	32.38±4.69 (28)	35.18±2.69 (28)	0.0000 *	3.868
	Male (N)	2.38±0.31 (14)	46.66±14.21 (7)	38.14±5.89 (7)	0.0001*	10.275
P value		**0.6828**	**0.2294**	**0.6339**		
Age (years)	18 – 37 (N)	2.56 ± 0.21 (31)	30.81±7.50 (16)	39.92±4.33 (15)	**0.0000***	**14.231**
	38 – 57 (N)	2.32 ± 0.22 (26)	37.88±7.20 (14)	32.15±3.56 (12)	**0.0000***	**15.587**
	58 – 77 (N)	2.69 ± 0.28 (13)	38.16±6.37 (5)	35.0±4.69 (8)	**0.0000***	**13.431**
P value		**0.5810**	**0.7442**	**0.3902**		
LSD						
BMI (kg/m^2)	Normal < 25	2.38±0.31 (14)	36.75±17.42 (3)	35.18±3.52 (11)	0.0000*	19.385
	Overweight 25 – 29.9	2.48±0.16 (44)	33.57±5.69 (29)	37.78±4.07 (15)	0.0000*	8.032
	Obese ≥ 30	2.66±0.35 (12)	33.90±11.94 (3)	33.44±5.45 (9)	0.0000*	15.274
P value		**0.8225**	**0.9849**	**0.7735**		
LSD						

* means significant difference NS: no significant

The results was approved that there was non-significant difference in pus cells according to the types of bacterial isolates as show in table (4-28).

Pyuria is a useful marker for assessing urinary tract infection (UTI) in the general population. The presence of pyuria is, in general, highly

suggestive of UTI, especially in symptomatic patients. The term "pyuria" literally means "pus in the urine" but, in common usage, the focus is not on the presence of pus but on the number of white blood cells (WBCs) or amount of leukocyte esterase (LE) that exceeds a threshold and suggests a UTI.

Table (4-28): The mean of Pus cells (HPF) in patient group with bacterial growth according to type of bacteria.

Type of bacteria	N	Mean	SE	*P value*	LSD
E. coli	13	34.46	8.33	0.0916	NS
Enterococcus faecalis	1	55.00	0.00		
Enterococcus faecium	1	120.00	0.00		
Klebsiella aerogenes	3	22.00	9.67		
Klebsiella pneumoniae ssp	2	23.50	16.49		
Staphylococcus aureus	4	34.14	7.08		
Staphylococcus haemolyticus	3	38.50	12.15		
Staphylococcus saprophyticus	8	31.80	7.25		

* means significant difference NS: no significant

In addition, the number of pus cells in the patient with gram negative bacteria is higher than in gram positive **(Baral and Nepal, 2017).**

4.6. Correlation between markers in studied groups

4.6.1. Correlation between markers in control group

When studying the correlation between the study markers in the control group, it was revealed that there is a positive correlation between neutrophils and CRP, and between IL-1β on the one hand and both IL-8 and LBP on the other hand, and there is also a positive correlation between IL-8 and LBP, as show in table (4-29).

Table (4-29): The correlation (r) between markers in control group.

Markers	CRP	WBC	Neutrophils	Lymphocytes	IL-1β	IL-8	LBP	MR
CRP	-	- 0.024 (*P=0.843*)	0.292* (*P=0.014*)	- 0.141 (*P=0.245*)	- 0.014 (*P=0.910*)	- 0.006 (*P=0.962*)	- 0.006 (*P=0.962*)	- 0.022 (*P=0.854*)
WBC		-	0.057 (*P=0.642*)	0.000 (*P=1.000*)	- 0.088 (*P=0.495*)	- 0.046 (*P=0.707*)	- 0.046 (*P=0.707*)	- 0.172 (*P=0.154*)
Neutrophils			-	0.124 (*P=0.307*)	0.192 (*P=0.112*)	- 0.092 (*P=0.450*)	- 0.092 (*P=0.450*)	- 0.194 (*P=0.108*)
Lymphocytes				-	- 0.033 (*P=0.789*)	- 0.224 (*P=0.062*)	- 0.224 (*P=0.062*)	- 0.128 (*P=0.291*)
IL-1β					-	0.326** (*P=0.006*)	0.326** (*P=0.006*)	0.108 (*P=0.372*)
IL-8						-	0.760** (*P=0.000*)	- 0.012 (*0.923*)
LBP							-	0.025 (*P=0.840*)
MR								-

**. Correlation is significant at the 0.01 level (2-tailed) *. Correlation is significant at the 0.05 level (2-tailed).

The results of Mousavi-Nasab *et al*. showed that Neutrophils was positively correlated with CRP levels (R=0.23) and also showed Neutrophils was negatively correlated with WBC (R=-0.38) **(Mousavi-Nasab SD *et al* .,2020)**. Similar results of the study done by **(Trifunović *et al*., 2019)** showed a significant correlation between Neutrophils and CRP. Also, **(Parantainen *et al* .,2022;Gassid *et al* .,2012;Ahmed and Zgair .,2021)**

Min *et al*.. found positive correlations between IL-1b levels and IL-8**(Min *et al*.,2020).** Previous investigations have identified a notable positive correlation between LBP and (IL1b)**(Shi *et al* .,2020; Martín-Sánchez et al.,2016).** Result of correlation in current study agreement with results of these studies. Other study reported by **(Ferrà *et al*., 2007)**

have negatively corrlation between the level of IL-1b and IL-8 , disagreement with Ferrà *et al*

4.6.2.Correlation between markers in patient group with bacterial growth

The results in Table (4-30) for detecting correlations between markers in the group of patients with bacterial growth indicate that there is a positive correlation between (CRP and WBC), (neutrophils and WBC), (lymphocytes and neutrophils), (IL-8 and neutrophils). The correlation relationship was negative between (WBC and MR) and (LBP and IL-1β).

Table(4-30):The correlation(r)between markers in patient group with bacterial growth

Markers	CRP	WBC	Neutrophils	Lymphocytes	IL-1β	IL-8	LBP	MR
CRP	-	0.456** (*P=0.004*)	0.094 (*P=0.571*)	- 0.120 (*P=0466*)	0.058 (*P=0.726*)	- 0.132 (*P=0.424*)	- 0.178 (*P=0.279*)	- 0.292 (*P=0.071*)
WBC		-	0.332* (*P=0.039*)	0.035 (*P=0.834*)	- 0.063 (*P=0.701*)	0.144 (*P=0.382*)	- 0.151 (*P=0.359*)	- 0.443** (*P=0.005*)
Neutrophils			-	0.870** (*P=0.000*)	0.088 (*P=0.593*)	0.337* (*P=0.036*)	- 0.206 (*P=0.209*)	- 0.164 (*P=0.317*)
Lymphocytes				-	0.029 (*P=0.859*)	0.263 (*P=0.106*)	- 0.123 (*P=0.456*)	- 0.033 (*P=0.841*)
IL-1β					-	0.297 (*P=0.067*)	- 0.427** (*P=0.007*)	- 0.019 (*P=0.909*)
IL-8						-	- 0.07 (*P=0.634*)	0.141 (*P=0.393*)
LBP							-	0.244 (*P=0.134*)
MR								-

**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

Previous investigations have identified a notable positive correlation between LBP and IL1b **(Shi *et al* .,2020; Martín-Sánchez et al.,2016).** Result of correlation in current study disagreement with results of these studies. A same finding has been recorded in a previous investigation, in which the author reported the CRP and WBC count were significantly higher positive correlation ($P<0.001$) in patients with bacterial infection**(Gans *et al* .,2020).**

Higher positively correlation were showed in result of **(Kabak and Hocanlı, 2021)** between the rates of neutrophil and lymphocyte and these result disagreement with results of current study.

Disagreement with previous investigations done by **(Shi *et al* .,2020; Martín-Sánchez et al.,2016)** have identified a notable positive correlation between LBP and (IL-1β)**.** Iskandar *et al*. were observed a positive correlation between IL-8 ($r = 0.58$; $p < 0.05$), NUL ($r = 0.45$, $p < 0.05$) as similarly to our results finding **(Iskandar *et al* .,2023).**

The current study detecting negative correlations between MR and WBC in the group of patients with bacterial growth this results corresponds with **(Ishimine *et al* ., 2019).**

4.6.3. Correlation between markers in patient group without bacterial growth

The results in Table (4-31) for detecting correlations between markers in the group of patients without bacterial growth indicate that there is a positive correlation only between (LBP and IL-8).

Table (4-31): The correlation (r) between markers in patient group without bacterial growth.

Markers	CRP	WBC	Neutrophils	Lymphocytes	IL-1β	IL-8	LBP	MR
CRP	-	- 0.261 (*P=0.130*)	- 0.248 (*P=0.150*)	0.095 (*P=0.588*)	- 0.319 (*P=0.062*)	- 0.124 (*P=0.478*)	0.042 (*P=0.811*)	- 0.133 (*P=0.447*)
WBC		-	0.159 (*P=0.363*)	- 0.268 (*P=0.120*)	0.175 (*P=0.316*)	0.307 (*P=0.073*)	0.203 (*P=0.242*)	0.159 (*P=0.362*)
Neutrophils			-	- 0.161 (*P=0.357*)	- 0.021 (*P=0.904*)	0.097 (*P=0.580*)	0.166 (*P=0.341*)	- 0.059 (*P=0.736*)
Lymphocytes				-	- 0.021 (*P=0.907*)	- 0.232 (*P=0.179*)	- 0.203 (*P=0.243*)	0.071 (*P=0.685*)
IL-1β					-	0.018 (*P=0.917*)	- 0.202 (*P=0.245*)	0.203 (*P=0.242*)
IL-8						-	0.780** (*P=0.000*)	- 0.005 (*P=0.977*)
LBP							-	0.224 (*P=0.196*)
MR								-

**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

Inversely of current study results , the study investigation by **(Gonzalez-Aparicio and Alfaro, 2020)** recorded negative correlation between the rates of LBP and IL-8 in infection without bacterial growth. Also, the study coeducated by Peng *et al*. Finding same results of **Gonzalez-Aparicio and Alfaro**, **(Peng *et al* .,2018).**

Conclusions and Recommendations

Conclusions

The current study concludes the following :

1. The current study observed that frequency of UTI in adult were more caused by *E.coli* , *Staph. saprophyticus*.
2. The percentage of females suffering from urinary tract infections is four times higher than that of males.
3. The majority of age groups with urinary tract infections were from 18 to 37 years.
4. Increase the parameters (CRP, IL-1β and pus cells) in patients with urinary tract infections.
5. Increase the concentration of both LBP and MR in the UTI patients with positive bacterial growth.
6. There is a positive correlation in patients with bacterial growth between: (WBC and CRP), (WBC and neutrophils), (Neutrophils and lymphocytes), and (Neutrophils and IL-8).
7. There is a negative correlation in patients with bacterial growth between (WBC and MR) and (LBP and IL-1β).

Recommendations

The current study recommends the following :

1. Design a cohort study with follow-up of UTI patients aiming to determine immune response at different periods of disease to show the extent to which immunological biomarkers level are effected by disease duration and treatment.
2. Study the evaluation of mannose receptor in patients has suffering from sepsis.
3. Conducting study measure the concentration of LBP in urine to classify UTI to upper and lower infections.
4. Study the genetic predisposing factors associated with UTI.
5. Study the effect of bacterial translocation in induced immune response with UTI patients.

References

References

Abbas, S., Mahdi, N., & Ahmed, K. (2022). Blood Groups, IL-6, IL-8 and HS-CRP Levels in NonPregnant Women With Urinary Tract Infection Caused by *Escherichia coli.* INTERNATIONAL JOURNAL OF MEDICAL SCIENCES, 5(2), 33-43.

Abou Heidar NF, Degheili JA, Yacoubian AA, Khauli RB. (2019). Management of urinary tract infection in women: A practical approach for everyday practice. Urol Ann, 11(4) ,339-346.

Abraham SN, Miao Y.(2015). The nature of immune responses to urinary tract infections. Nat Rev Immunol ,15(10) ,655-63.

Acosta IC, Alonzo Iii F. (2023). The intersection between bacterial metabolism and innate immunity. J Innate Immun, 26(2), 91-98.

Adamus-Białek W, Baraniak A, Wawszczak M, Głuszek S, Gad B, Wróbel K, Bator P, Majchrzak M, Parniewski P. (2018). The genetic background of antibiotic resistance among clinical uropathogenic Escherichia coli strains. Mol Biol Rep, 45(5),1055–1065.

Adda-Rezig H, Carron C, Pais de Barros JP, Choubley H, Charron É, Rérole AL, Laheurte C, Louvat P, Gaiffe É, Simula-Faivre D, Deckert V, Lagrost L, Saas P, Ducloux D, Bamoulid J. (2021). New Insights on End-Stage Renal Disease and Healthy Individual Gut Bacterial Translocation: Different Carbon Composition of Lipopolysaccharides and Different Impact on Monocyte Inflammatory Response. Front Immunol. 7;12:658404.

Aggarwal N, Lotfollahzadeh S.(2022). StatPearls Publishing; Treasure Island (FL):. Recurrent Urinary Tract Infections, 7(33), 17-22.

Ahmadi M, Ranjbar R, Behzadi P, Mohammadian T. (2022). Virulence factors, antibiotic resistance patterns, and molecular types of clinical isolates of Klebsiella Pneumoniae. Expert Rev Anti Infect Ther, 20(1), 463–72.

Al Rushood, M., Al-Eisa, A., & AL-Attiyah, R. (2020). Serum and urine interleukin-6 and interleukin-8 levels do not differentiate acute pyelonephritis from lower urinary tract infections in children. Journal of Inflammation Research, 789-797.

Al-Achi A (2016). An introduction to botanical medicines : history, science, uses, and dangers. Westport, Conn.: Praeger Publishers. p. 126. ISBN 978-0-313-35009-2.

Alfadul, H., Sabico, S., & Al-Daghri, N. M. (2022). The role of interleukin-1β in type 2 diabetes mellitus: A systematic review and meta-analysis. Frontiers in Endocrinology, 13, 901616.

Alidjanov JF, Naber KG, Pilatz A, Radzhabov A, Zamuddinov M, Magyar A, Tenke P, Wagenlehner FM. (2020). Additional assessment of Acute Cystitis Symptom Score questionnaire for patient-reported outcome measure in female patients with acute uncomplicated cystitis: part II. World J Urol. Aug;38(8):1977–1988.

AL-Khikani FH, Auda Ga, Ayit AS. (2019). Correlation study between urinary tract bacterial infection and some acute inflammatory responses. Biomed Biotechnol , 11(3), 236–239.

Ambite I, Rydstrom G, Schwaderer AL, Hains DS. (2019). The Genetics of Urinary Tract Infections and the Innate Defense of the Kidney and Urinary tract. J Pediatr Genet, 5(1) , 25-32.

Ambite, I. et al.(2016). Molecular Basis of Acute Cystitis Reveals Susceptibility Genes and Immunotherapeutic Targets. PLoS Pathog 12, e1005848.

Amenyogbe, E. et al.(2020). A review on sex steroid hormone estrogen receptors in human Int. J. Endocrinol, 5386193 .

Anger J, Lee U, Ackerman AL, et al.(2019). Recurrent uncomplicated urinary tract infections in women: AUA/CUA/SUFU guideline. J Urol, 202(2),282–289.

Arato V, Raso MM, Gasperini G, Berlanda Scorza F, Micoli F. (2021). Prophylaxis and Treatment against Klebsiella pneumoniae: Current Insights on This Emerging Anti-Microbial Resistant Global Threat. Int J Mol Sci, 14;22(8):4042.

Argemi X, Hansmann Y, Prola K, Prévost G. (2019). Coagulase-Negative Staphylococci Pathogenomics. Int J Mol Sci, 11;20(5).

Arientová S, Beran O, Štefan M, Čurdová M, Holub M. (2018). Bacteremia due to Staphylococcus aureus - the importance of appropriate management. Epidemiol Mikrobiol Imunol, 67(2):88-91.

ARIF, Z. N., ALHIDARY, A. Q. and AL-DAAMY, A. A. A.-H. (2021). Evaluation the Heart Failure Test in Heart Failure patients with Bacterial Infection. Scientific Journal of Medical Reaserch, 21,2520-5234.

Ashurst JV, Dawson A. (2023). Klebsiella Pneumonia. Jan-. Available from, Klebsiella Pneumonia. Urology of human infection with urinary tract;5(23),152-161.

Badiger ,A.S, K.R. Maruthi, S.N. Bajpe, R. Ramu, K. (2021). Jayadev Urinary tract infection – a review on its prevalence and recent advances J Pharm Res Int, 582-592.

Bai AD, Bonares MJ, Thrall S, Bell CM, Morris AM. (2020). Presence of urinary symptoms in bacteremic urinary tract infection: a retrospective cohort study of Escherichia coli bacteremia. BMC Infect Dis. 20(1),781-786.

Banik A, Bhat SH, Kumar A, Palit A, Snehaa K. (2018). Bloodstream infections and trends of antimicrobial sensitivity patterns at Port Blair. J Lab Physicians, 10(3),332-337.

Baral, R., & Nepal, S. (2017). Rapid nitrite dip stick vs urine culture for diagnosis of urinary tract infections (UTI): Laboratory prospective. Int J Biomed Res, 8(4), 204-209.

Bartoletti R, Cai T, Wagenlehner FM, Naber K, Bjerklund Johansen TE.(2016). Treatment of urinary tract infections and antibiotic stewardship. Eur Urol Suppl., 15(4),81–87.

Bartoletti R, Wagenlehner FME, Bjerklund Johansen TE, Köves B, Cai T, Tandogdu Z, Bonkat G. (2019). Management of Urethritis: Is It Still the Time for Empirical Antibiotic Treatments? Eur Urol Focus., 5(1):29-35.

BAZZI, A. M., RABAAN, A. A., FAWARAH, M. M., AL-TAWFIQ, J. A. J. J. O. I. & HEALTH, P. (2017). Direct identification and susceptibility testing of positive blood cultures using high speed cold centrifugation and Vitek II system. 10, 299-307.

Becker K, Heilmann C, Peters G.(2014). Coagulase-negative staphylococci. Clin Microbiol Rev. 27(4),870-926.

Becknell N, Kang Y, Chen C, Resasco J, Kornienko N, Guo J, Markovic NM, Somorjai GA, Stamenkovic VR, Yang P. (2015). Atomic Structure of Pt3Ni Nanoframe Electrocatalysts by in Situ X-ray Absorption Spectroscopy. J Am Chem Soc. 23;137(50):15817-24.

Behzadi P, Behzadi E, Ranjbar R. (2019). Urinary tract infections and Candida albicans. Cent European J Urol;68(1):96-101.

Behzadi P, Sameer AS, Nissar S, Banday MZ, Gajdács M, García-Perdomo HA, Akhtar K, Pinheiro M, Magnusson P, Sarshar M, Ambrosi C. (2022). The Interleukin-1 (IL-1) Superfamily Cytokines and Their Single Nucleotide Polymorphisms (SNPs). J Immunol Res. Mar 26;2022:2054431.

Belyayeva M, Jeong JM. (2023). Acute Pyelonephritis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 ,3(24), 27-31.

Bent R, Moll L, Grabbe S, Bros M. (2018). Interleukin-1 Beta-A Friend or Foe in Malignancies? Int J Mol Sci. Jul 24;19(8):21-55.

Bitsori M, Karatzi M, Dimitriou H, Christakou E, Savvidou A, Galanakis E. (2011). Urine IL-8 concentrations in infectious and non-infectious urinary tract conditions. Pediatr Nephrol, 26(11),190-202.

Bonkat G, Bartoletti R, Bruyère F, et al. (2020). EAU guidelines on urological infections European as sociation of Urologym7(56),1-8.

Bono MJ, Leslie SW, Reygaert WC. (2023). Urinary Tract Infection. [Updated 2022 Nov 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan, 1(33), 176-182.

Boraschi D. (2022). What Is IL-1 for? The Functions of Interleukin-1 Across Evolution. Front Immunol. 6(13), 872155.

Brănescu C, Şerban D, Şavlovschi C, Dascălu AM, Kraft A. (2012). Lipopolysaccharide binding protein (L.B.P.)--an inflammatory marker of prognosis in the acute appendicitis. J Med Life, 15;5(3),342-347.

Butler, D., Ambite, I., Wan, M. L. Y., Tran, T. H., Wullt, B., & Svanborg, C. (2022). Immunomodulation therapy offers new molecular strategies to treat UTI. Nature Reviews Urology, 19(7), 419-437.

Carol A. ,Kauffman D. (2014). Diagnosis and Management of Fungal Urinary Tract Infection,Infectious Disease Clinics of North America,Volume 28(1),61-74.

Keywords: Candida; Fungal urinary tract infection; Fungus ball; Cystitis; Pyelonephritis; Fluconazole; Amphotericin B; Flucytosine

Cavanagh JP, Pain M, Askarian F, Bruun JA, Urbarova I, Wai SN, Schmidt F, Johannessen M. (2019). Comparative exoproteome profiling of an invasive and a commensal Staphylococcus haemolyticus isolate. J proteomics, 197(1),06-114.

Chandra, H, C. Singh, P. Kumari, et al. (2020). Promising roles of alternative medicine and plant-based nanotechnology as remedies for urinary tract infections Molecules, 25(23).

Chaudhari, P. P., Monuteaux, M. C., & Bachur, R. G. (2016). Urine concentration and pyuria for identifying UTI in infants. Pediatrics, 138(5).

Ching C, Schwartz L, Spencer JD, Becknell B. (2020). Innate immunity and urinary tract infection. Pediatr Nephrol,35(7),1183-1192.

Ching CB, Gupta S, Li B, Cortado H, Mayne N, Jackson AR, McHugh KM, Becknell B.(2018). Interleukin-6/Stat3 signaling has an essential role in the host antimicrobial response to urinary tract infection. Kidney Int ,93(6),1320–1329.

Chu, C. M., & Lowder, J. L. (2018). Diagnosis and treatment of urinary tract infections across age groups. American journal of obstetrics and gynecology, 219(1), 40-51.

Confederat LG, Condurache MI, Alexa RE, Dragostin OM. (2023). Particularities of Urinary Tract Infections in Diabetic Patients: A Concise Review. Medicina (Kaunas), 29;59(10):1747.

Corwin E.J. (2000). Understanding Cytokines Part I: Physiology and Mechanism of Action. Biol, 2(16), 30–40.

Cristea OM, Avrămescu CS, Bălăşoiu M, Popescu FD, Popescu F, Amzoiu MO. (2017). Urinary tract infection with Klebsiella pneumoniae in Patients with Chronic Kidney Disease. Curr Health Sci J. 43(2), 137-148.

Cummings RD. (2022). The mannose receptor ligands and the macrophage glycome. Curr Opin Struct Biol, 75:102394.

Curtiss N, Meththananda I, Duckett J.(2017). Urinary tract infection in obstetrics and gynaecology. Obstet Ginecol Reprod Med ,27(5) 261-265.

Deltourbe, L., Lacerda Mariano, L., Hreha, T.N. et al.(2022). The impact of biological sex on diseases of the urinary tract. Mucosal Immunol 15(6), 857–866.

Demirel, I., Persson, A., Brauner, A., Särndahl, E., Kruse, R., & Persson, K. (2020). Activation of NLRP3 by uropathogenic Escherichia coli is associated with IL-1β release and regulation of antimicrobial properties in human neutrophils. Sci Rep, 10(1), 21837.

Den Bont S, Şahbudak Bal Z, Karadaş Özdemir N, Şen S, Yılmaz Karapınar D, Azarsız E, Aydemir Ş, Vardar F.(2017). Diagnostic Accuracy of Interleukin-6, Interleukin-8, and Interleukin-10 for Predicting Bacteremia in Children with Febrile Neutropenia , 34(3):254-257.

Dhanalakshmi M, Sruthi D, Jinuraj KR, Das K, Dave S, Andal NM, Das J. (2023). Mannose: a potential saccharide candidate in disease management. Med Chem Res, 32(3):391-408.

Dinarello A., Dinarello C. A., Molgora M., Garlanda C. (2019). Interleukin-1 and related cytokines in the regulation of inflammation and immunity. Immunity , 50(11),778–795

Dinarello C. A. (2010). IL-1: discoveries, controversies and future directions. European Journal of Immunology , 40(6) ,599–606.

Dinarello CA. (2018). Immunological and inflammatory functions of the interleukin-1 family. Annu Rev Immunol, 27(13),519–550.

Dinarello CA. (2018). The IL-1 Cytokine and Receptor Family. Immunol Rev 281. Oxford, UK: John Wiley & Sons Ltd. 247 p.

Drekonja DM, Rector TS, Cutting A, Johnson JR. (2013). Urinary tract infection in male veterans: treatment patterns and outcomes. JAMA Intern Med, 173(1),62–8.

Dunkelberger JR, Song WC. (2010). Complement and its role in innate and adaptive immune responses. Cell Res, 20(1),34–50.

Dunny DB, Weaver KE. (2023). Sex pheromones and plasmid transfer in Enterococcus faecalis. Plasmid;21(3):175–184.

Ehlers S, Merrill SA. Staphylococcus saprophyticus Infection. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

Eltwisy HO, Abdel-Fattah M, Elsisi AM, Omar MM, Abdelmoteleb AA, El-Mokhtar MA. (2020). Pathogenesis of Staphylococcus haemolyticus on primary human skin fibroblast cells. Virulence.,11(1),1142-1157.

Eltwisy HO, Twisy HO, Hafez MH, Sayed IM, El-Mokhtar MA.(2022). Clinical Infections, Antibiotic Resistance, and Pathogenesis of Staphylococcus haemolyticus. Microorganisms ,31,10(6):1130-1137.

European Medicines Agency . (2023). Evaluation of medicinal products indicated for treatment of bacterial infections.. Accessed 25 February. 77(12),621-630.

Fan W, Yang X, Huang F, Tong X, Zhu L, Wang S. (2019). Identification of CD206 as a Potential Biomarker of Cancer Stem-Like Cells and Therapeutic Agent in Liver Cancer. Oncol Lett 18:3218–26.

Farhana A, Khan YS. (2020). Biochemistry, Lipopolysaccharide. Treasure Island, (FL:StatPearls.

Feng, X., Xu, X., Shi, Y., Liu, X., Liu, H., Hou, H., Ji, L., Li, Y., Wang, W., (2019). Obesity with immune disease correlated and causes inflammation. 4(53),62-66.

Ferreira V.L., Borba H.H.L., Bonetti A.D.F., Leonart L.P., Pontarolo R.(2018). Cytokines and Interferons: Types and Functions. IntechOpen; London, UK,37(22),421-436.

Fields J. K., Günther S., Sundberg E. J. (2019). Structural basis of IL-1 family cytokine signaling. Frontiers in Immunology 10(34), p. 1412.

Fiore E, Van Tyne D, Gilmore MS. (2019). Pathogenicity of Enterococci. Microbiol Spectr.;7(4) ,271-278.

Flores-Mireles A.L., Walker J.N., Caparon M., Hultgren S.J.(2019). Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. Nat. Rev. Microbiol. ;13:269–284.

Foxman B. (2014). Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am ,28(1),1–13. This paper presents the most recent information about UTIs and their socioeconomic impact.

Fukui, H. (2016). Endotoxin and other microbial translocation markers in the blood: A clue to understand leaky gut syndrome. Cell Mol Med, 2(3).

Fünfstück R, Nicolle LE, Hanefeld M, Naber KG. (2022). Urinary tract infection in patients with diabetes mellitus. Clin Nephrol ,77(1), 40-8.

García-Solache M, Rice LB. (2019). The Enterococcus: a Model of Adaptability to Its Environment. Clin Microbiol Rev.30;32(2):e00058-18.

GBD 2020 risk factors collaborators. global burden of 87 risk factors in 204 countries and territories: a systematic analysis for the global burden of disease study 2020 . Lancet(396:1223–49. 10.1016/S0140-6736(20)30752-2 .

Geletu US, Usmael MA, Ibrahim AM. (2022). Isolation, Identification, and Susceptibility Profile of E. coli, Salmonella, and S. aureus in Dairy Farm and Their Public Health Implication in Central Ethiopia. Vet Med Int 14;2022:1887977.

Ghosh AK (2018) Sphene and Zircon Fission Track Analysis of Syenite Rocks of the Sushina Hills, Purulia-Bankura Shear Zone (TPSZ). International Journal of Geography and Geology, 7(4): 73-79.

Ghosh AK, Kishore B, Shaikh I, Satyavrat V, Kumar A, Shah T, Pote P, Shinde S, Berde Y, Low YL, Tan VMH, Huynh DTT. (2018). Effect of oral nutritional supplementation on growth and recurrent upper respiratory tract infections in picky eating children at nutritional risk: a randomized, controlled trial. J Int Med Res.46(6):2186-2201.

Givler DN, Givler A. (2021). Asymptomatic Bacteriuria. StatPearls [Internet] Treasure Island (FL): StatPearls Publishing; Jul 25, Asymptomatic Bacteriuria; 7(22),15-20.

Gnauck A, Lentle RG, Kruger MC. (2016). The Characteristics and Function of Bacterial Lipopolysaccharides and Their Endotoxic Potential in Humans. Int Rev Immunol ,35(3) ,189–218.

Godaly G, Ambite I, Puthia M, Nadeem A, Ho J, Nagy K, Huang Y, Rydström G, Svanborg C. (2016). Urinary Tract Infection Molecular Mechanisms and Clinical Translation. Pathogens. 24;5(1), 24-37.

Godaly G, Ambite I, Svanborg C.(2015). Innate immunity and genetic determinants of urinary tract infection susceptibility. Curr Opin Infect Dis. 28(1):88-96.

Gokce, I., Alpay, H., Biyikli, N., Unluguzel, G., Dede, F., & Topuzoglu, A. (2010). Urinary levels of interleukin-6 and interleukin-8 in patients with vesicoureteral reflux and renal parenchymal scar. Pediatric Nephrology, 25, 905-912.

Goldman JD, Julian K. (2019). Urinary tract infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. Sep, 33(9):e13507.

González de Llano, D., Moreno-Arribas, M. V., & Bartolomé, B. (2020). Cranberry polyphenols

Gould CV, Umscheid CA, Agarwal RK, Kuntz G, Pegues DA. Healthcare Infection Control Practices Advisory Committee. Guideline for prevention of catheter-associated urinary tract infections. Infect Control Hosp Epidemiol , 31(4) ,319-26.

Grit E. Leg¡¥rd, Bente K.(2019). Pedersen,Chapter 13 - Muscle as an Endocrine Organ,Editor(s): Jerzy A. Zoladz,Muscle and Exercise Physiology,Academic Press,2019,Pages 285-307.

Gu, J., Liu, S., Ni, W. *et al.* (2022). Modulating electric field distribution by alkali cations for CO_2 electroreduction in strongly acidic medium. *Nat Catal* **5**, 268–276.

Guha M, Mackman N. (2001). LPS Induction of Gene Expression in Human Monocytes. Cell Signal, 13(2), 85–94.

Gupta K, Grigoryan L, Trautner B.(2017). Urinary tract infection. Ann Intern Med, 167:ITC49–64.

Gupta K, Hooton TM, Naber KG, et al.(2011). International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;52(5):e103-20.

Ha, E.K., Kim, J.H., Yon, D.K. et al. (2021). Association of serum lipopolysaccharide-binding protein level with sensitization to food allergens in children. Sci Rep 11, 2143

Habak PJ, Griggs, Jr RP. (2023). Urinary Tract Infection in Pregnancy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan ,22(1),481-485.

Horváth J, Wullt B, Naber KG, Köves B.(2020). Biomarkers in urinary tract infections - which ones are suitable for diagnostics and follow-up? GMS Infect Dis, 26(8).

Hosny AES, El-Bazza ZE, Ramadan MA, Shafik MA, Shafeek MA, Khattab RA.(2021). Expression levels of pro-inflammatory interleukin-8 and certain antimicrobial peptides in concurrent with bacterial conjunctivitis. Int J Ophthalmol. 18;14(5):666-675.

Hu Z, Wang Y, Cheng C, He Y. (2019). Structural basis of the pH-dependent conformational change of the N-terminal region of human mannose receptor/CD206. J Struct Biol. Dec 1;208(3):107384. doi: 10.1016/j.jsb.2019.09.001. Epub Sep 3. PMID: 31491467.

InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. How does the immune system work? [Updated 2023 Apr 23].

Jappe U, Schwager C, Schromm AB, Roldan NG, Stein K, Heine H, et al. (2019). Lipophilic Allergens, Different Modes of Allergen-Lipid Interaction and Their Impact on Asthma and Allergy. Front Immunol , 10:122.. 10.3389/fimmu.

Jiang M, Chen ZG, Li H, Zhang TT, Yang MJ, Peng XX, Peng B. (2022). Succinate and inosine coordinate innate immune response to bacterial infection. PLoS Pathog, 26;18(8):e1010796.

Jindal J, Meelu A, Kaur S, Chahal HS, Makkar V, Garg V. (2022). Clinical Profile and Outcome in Patients of Complicated Urinary Tract Infections: A Single-Center Prospective Observational Study. Int J Appl Basic Med Res ,12(3),167-170.

Johansen TE, Botto H, Cek M, Grabe M, Tenke P, Wagenlehner FM, Naber KG. (2022). Critical review of current definitions of urinary tract infections and proposal of an EAU/ESIU classification system. Int J Antimicrob Agents ,38 Suppl:64-70.

Justiz Vaillant AA, Qurie A. (2023). Interleukin. In: journal of molecular sciences, 24(4), 3277.

Kabat GC, Kim MY, Manson JE, Lessin L, Lin J, Wassertheil-Smoller S, Rohan TE.(2017). White Blood Cell Count and Total and Cause-Specific Mortality in the Women's Health Initiative. Am J Epidemiol.186(1), 63-72.

Kaneko N, Kurata M, Yamamoto T, Morikawa S, Masumoto J. (2019). The role of interleukin-1 in general pathology. Inflamm Regen.Jun 6;39:12.

Kaneko, N., Kurata, M., Yamamoto, T. et al.(2019). The role of interleukin-1 in general pathology. Inflamm Regener 39, 12-20.

Kato, A., Gabay, C., & Okaya, T. (2023). Mechanisms of dysregulated production of interleukin-1 beta in rheumatoid arthritis. Arthritis Research & Therapy, 15(3), 1-11.

Khalid, S., Saeed, S., Kausar, H., & Siddiqui, M. F. (2020). Immune system and types of Immune responses. Pakistan Journal of Health Sciences, 1(01).

Kim JK, Lee YG, Han K, Han JH. (2021). Obesity, metabolic health, and urological disorders in adults: a nationwide population-based study. Sci Rep, 22;11(1):8687.

Kim KE, Cho YS, Baek KS, Li L, Baek KH, Kim JH, Kim HS, Sheen YH.(2016). Lipopolysaccharide-binding protein plasma levels as a biomarker of obesity-related insulin resistance in adolescents. Korean J Pediatr , (5) ,231-8.

Kim, H. J., Lee, J. P., Kim, H. K., Kim, S. G., Oh, J. E., & Kim, Y. S. (2017). Association between cytokine levels and arteriovenous fistula dysfunction in hemodialysis patients. Kidney Research and Clinical Practice, 36(2), 177- 184.

Klein, R.D., Hultgren, S.J. (2020). Urinary tract infections: microbial pathogenesis, host–pathogen interactions and new treatment strategies. Nat Rev Microbiol 18, 211–226.

Kline KA, Lewis AL. (2016). Gram-Positive Uropathogens, Polymicrobial Urinary Tract Infection, and the Emerging Microbiota of the Urinary Tract. Microbiol Spectr. Apr;4(2):103-111.

Kontiokari T, Nuutinen M, Uhari M. (2023). Dietary factors affecting susceptibility to urinary tract infection. Pediatr Nephrol. 2023;19(4):378-83.

Kostakioti M, Hultgren SJ, Hadjifrangiskou M. (2023). Molecular blueprint of uropathogenic Escherichia coli virulence provides clues toward the development of anti-virulence therapeutics. Virulence, 3(1),592–594.

Kotagiri P., Chembolli D., Ryan J., Hughes P.D., Toussaint N.D.(2020). Urinary Tract Infections in the First Year Post–Kidney Transplantation: Potential Benefits of Treating Asymptomatic Bacteriuria. Transplant. Proc,49(3),2070–2075.

Kramer, N.E., Cosgrove, V.E., Dunlap, K., Subramaniapillai, M., McIntyre, R.S. and Suppes, T., 2019. A clinical model for identifying an inflammatory phenotype in mood disorders. Journal of psychiatric research, 113, pp.148-158.

Krzemień G, Szmigielska A, Turczyn A, Pańczyk-Tomaszewska M. (2019). Urine interleukin-6, interleukin-8 and transforming growth factor β1 in infants with urinary tract infection and asymptomatic bacteriuria. Cent Eur J Immunol, 41(3):260–267.

Lachman LB, Hacker MP, Handschumacher RE. (2023). Partial purification of human lymphocyte-activating factor (LAF) by ultrafiltration and electrophoretic techniques. J Immunol, 119(3),461-468.

Lacour, A. G., Gervaix, A., Zamora, S. A., Vadas, L., Lombard, P. R., Dayer, J.-M.& Suter, S. 2001. Procalcitonin, IL-6, IL-8, IL-1 receptor antagonist and C-reactive protein as identificators of serious bacterial infections in children with fever without localising signs. European journal of pediatrics, 160, 95-100.

Lalueza A, Sanz-Trepiana L, Bermejo N, Yaiza B, Morales-Cartagena A, Espinosa M, García-Jiménez R, Jiménez-Rodríguez O, Ponce B, Lora D, Orellana MÁ, Fernández-Ruiz M, Bermejo S, Aguado JM.(2018). Risk factors for bacteremia in urinary tract infections attended in the emergency department. Intern Emerg Med. Jan;13(1):41-50.

Leboffe, M. J., & Pierce, B. E. (2012). A photographic atlas for the microbiology laboratory. Morton Publishing Company

Lee DS, Lee SJ, Choe HS.(2019). Community-Acquired Urinary Tract Infection by Escherichia coli in the Era of Antibiotic Resistance. Biomed Res Int. 26;e7656752.

Lee UJ(2019). Urinary tract infection in women United Kingdom: BMJbest practice, 2(11),33-51.

Lepper PM, Kleber ME, Grammer TB, Hoffmann K, Dietz S, Winkelmann BR, et al. (2020). Lipopolysaccharide-binding protein (LBP) is associated with total and cardiovascular mortality in individuals with or without stable coronary artery disease–results from the Ludwigshafen Risk and Cardiovascular Health Study (LURIC). Atherosclerosis, 219:291-7.

Li R, Leslie SW. (2023). StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL):. Cystitis,5(2),11-14.

Lissoni P., Messina G., Pelizzoni F., Rovelli F., Brivio F., Monzon A., Crivelli N., Lissoni A., Tassoni S., Sassola A., et al. (2020). The Fascination of Cytokine Immunological Science. J. Infect, 3(12),18–28.

Liu F, Li L, Lan M, Zou T, Kong Z, Cai T, Wu XY, Cai Y. (2021). Key Factor Regulating Inflammatory Microenvironment, Metastasis, and Resistance in Breast Cancer: Interleukin-1 Signaling. Mediators Inflamm. Sep 23;2021:7785890.

Lo Basso F, Pilzer A, Ferrero G, Fiz F, Fabbro E, Oliva D, Cazzarolli C, Turrina A.(2021). Manual treatment for kidney mobility and symptoms in women with nonspecific low back pain and urinary infections. J Osteopath Med, 121(5):489-497.

Lo E, et al. (2019). Strategies to prevent catheter-associated urinary tract infections in acute care hospitals: update. Infect Control Hosp Epidemiol, 35:464–479.

Loonen AJ, Leijtens S, Serin O, Hilbink M, Wever PC, van den Brule AJ, et al.(2019). Soluble Mannose Receptor Levels in Blood Correlate to Disease Severity in Patients With Community-Acquired Infections . Immunol Lett , (206),28–32.

Luciani LG, Mattevi D. (2022). Urinary Tract Infections: Virus. Encyclopedia of Infection and Immunity.1(5),32–43.

Lugo-Villarino G, Hudrisier D, Tanne A. & Neyrolles O. (2021). C-type lectins with a sweet spot for Mycobacterium tuberculosis. Eur J Microbiol Immunol (Bp) 1, 25–40 .

MacFaddin, J. F.(2000). Biochemical tests for identification of medical bacteria, Baltimore (Md.) : Williams and Wilkins.

Maculewicz, E.; Dzitkowska-Zabielska, M.; Antkowiak, B.; Antkowiak, O.; Mastalerz, A.; Garbacz, A.; Massidda, M.; Bojarczuk, A.; Dziuda, Ł.; Cięszczyk, P. (2022). Association of Interleukin Genes IL1, IL10 and IL10RB with Parameters of Overweight in Military Students. Genes, 13, 291.

Mączyńska B, Frej-Mądrzak M, Sarowska J, Woronowicz K, Choroszy-Król I, Jama-Kmiecik A. (2023). Evolution of Antibiotic Resistance in Escherichia coli and Klebsiella pneumoniae Clinical Isolates in a Multi-Profile Hospital over 5 Years (2017-2021). J Clin Med. 2023 Mar 21;12(6):2414.

Magill S., O'Leary S. Janelle D., et al. (2019). Changes in Prevalence of Health Care Associated Infection in the U.S. Hospitals. New England Journal of Medicine. 2019 ;379: 1732-1744.

Mahapatra S, Heffner AC. (2023). Septic Shock. In: StatPearls . Treasure Island (FL): StatPearls Publishing; ;Jan ,16(41),71-88.

Maina, D., & Kagotho, E. (2014). Suitability of Vitek 2 System in Identification and Susceptibility Testing of Gram Negative Bacteremias by Direct Inoculation. East African medical journal, 91(4), 115-118 .

Maisto, M., Iannuzzo, F., Novellino, E., Schiano, E., Piccolo, V., & Tenore, G. C. (2023). Natural admistation urinary tract infection. health human tin medicine ;2(16),37-45

Mamatha, G., Gandhi, M.V.V. and Phanindra, M.2020. Role of Biomarker levels in Differentiating Upper Urinary Tract Infection and Lower Urinary Tract Infection in Adults. Journal of medical science and clinical research.

Mancuso G, Midiri A, Gerace E, Marra M, Zummo S, Biondo C. (2023). Urinary Tract Infections: The Current Scenario and Future Prospects. Pathogens. Apr 20(12),614-623.

Marantidis J, Sussman RD. (2023). Unmet Needs in Complicated Urinary Tract Infections: Challenges, Recommendations, and Emerging Treatment Pathways. Infect Drug Resist. 11(16)1391-1405.

Marta Gomarasca, ... Giovanni Lombardi,. (2020). in Advances in Clinical Chemistry,Myokines: The endocrine coupling of skeletal muscle and bone.

Marta Gomarasca, Giuseppe Banfi, Giovanni Lombardi, (2020). Chapter Four - Myokines: The endocrine coupling of skeletal muscle and bone, Editor(s): Gregory S. Makowski, Advances in Clinical Chemistry, Elsevier, Volume 94, 2020, Pages 155-218,

Masajtis-Zagajewska, A., & Nowicki, M. (2017). New markers of urinary tract infection. Clinica chimica acta, 471, 286-291.

Mayne S, Bowden A, Sundvall PD, Gunnarsson R. (2019). The scientificevidence for a potential link between confusion and urinary tractinfection in the elderly is still confusing–a systematic literaturereview.BMC Geriatr2019;19: 32.

Mazumder R, Hussain A, Bhadra B, Phelan J, Campino S, Clark TG, Mondal D.(2023). Case report: A successfully treated case of community-acquired urinary tract infection due to Klebsiella aerogenes in Bangladesh. Front Med (Lausanne). Jun 26;10:1206756.

McPherson, R.A.; Pincus, M.R. (2017). Henry's Clinical Diagnosis and Management by Laboratory Methods (23 ed.). Elsevier Health Sciences. ISBN 978-0-323-41315-2.

Medina M, Castillo-Pino E. (2019). An introduction to the epidemiology and burden of urinary tract infections. Ther Adv Urol. May 2;11:1756287219832172.

Meng L, Song Z, Liu A, Dahmen U, Yang X, Fang H. (2021). Effects of Lipopolysaccharide-Binding Protein (LBP) Single Nucleotide Polymorphism

(SNP) in Infections, Inflammatory Diseases, Metabolic Disorders and Cancers. Front Immunol. Jul 6;12:681810.

Michels R, Last K, Becker SL, Papan C. (2021). Update on Coagulase-Negative Staphylococci-What the Clinician Should Know. Microorganisms ,14;9(4):830.

Miftode IL, Nastase EV, Miftode RȘ, Miftode EG, Iancu LS, Luncă C, Anton Păduraru DT, Costache II, Stafie CS, Dorneanu OS. (2021). Insights into multidrug-resistant K. pneumoniae urinary tract infections: From susceptibility to mortality. Exp Ther Med;22(4):1086.

Miller WR, Murray BE, Rice LB, Arias CA. (2016). Vancomycin-Resistant Enterococci: Therapeutic Challenges in the 21st Century. Infect Dis Clin North Am, Jun;30(2):415-439.

Minasyan, H. (2019). Sepsis: mechanisms of bacterial injury to the patient. Scand J Trauma Resusc Emerg Med 27, 19.

Monteiro J.T., Lepenies B. (2017). Myeloid C-type lectin receptors in viral recognition and antiviral immunity. Viruses.;9:59. [PMC free article] [PubMed] [Google Scholar] [Ref list]

Mueller M, Tainter CR. (2023). Escherichia coli Infection. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; ,3(22),131-139.

MURRAY, P. & ZEITINGER, J. (1983). Evaluation of Mueller-Hinton agar for disk diffusion susceptibility tests. Journal of clinical microbiology, 18, 1269-1271.

Mushi MF, Alex VG, Seugendo M, Silago V, Mshana SE.(2019). C - reactive protein and urinary tract infection due to Gram-negative bacteria in a pediatric population at a tertiary hospital, Mwanza, Tanzania. Afr Health Sci,19(4),3217-3224

Nagamatsu, K. et al. (2021). Dysregulation of Escherichia coli alpha-hemolysin expression alters the course of acute and persistent urinarytract infection. Proc Natl Acad Sci USA 112, E871–880.

Nagpal, R., & Yadav, H. (2017). Bacterial translocation from the gut to the distant organs: an overview. Annals of Nutrition and Metabolism, 71(Suppl. 1), 11-16.

Nanda N, Juthani-Mehta M. (2019). Novel biomarkers for the diagnosis of urinary tract infection-a systematic review. Biomark Insights. Aug;4:111–121.

Narayan Swamy SN, Jakanur RK, Sangeetha SR. (2022). Significance of C-reactive Protein Levels in Categorizing Upper and Lower Urinary Tract Infection in Adult Patients. Cureus, 29, 14(6).

Nickel JC. (2019). Management of urinary tract infections: historical perspective and current strategies: Part 1--Before antibiotics. J UrolJan;173(1):21-6.

Nicolle L.E. (2016). The Paradigm Shift to Non-Treatment of Asymptomatic Bacteriuria. Pathogens.;5:38, 42-55.

Nicolle LE (2018). "Uncomplicated urinary tract infection in adults including uncomplicated pyelonephritis". The Urologic Clinics of North America. 35 (1): 1–12, v.

Nicolle LE, Gupta K, Bradley SF, Colgan R, DeMuri GP, Drekonja D, et al. (2019). Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America. Clin Infect Dis 2019; 68: e83– 110.

Nicolle LE. (2019). AMMI Canada Guidelines Committee*. Complicated urinary tract infection in adults. Can J Infect Dis Med Microbiol. Nov;16(6):349-360.

Nuttall, F. Q. (2015). Body mass index: Obesity, BMI, and health: A critical review. Nutrition Today, 50(3), 117-128.

Olin SJ, Bartges JW. (2015). Urinary tract infections: treatment/comparative therapeutics. Vet Clin North Am Small Anim Pract. 2015 Jul;45(4):721-46.

Oliveira J, Reygaert WC. (2024). Gram-Negative Bacteria. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan

Oniszczenko W, Stanisławiak E. (2019). Association between sex and body mass index as mediated by temperament in a nonclinical adult sample 24(9),291–298.

Oregioni O, Delaunay P, Bruna P, et al. (2015). urinary interleukin-8 is elevated in urinary tract infections independently of the causative germs. Cytokine.;31(6):415–418.

Ortega Martell JA. (2020). Immunology of urinary tract infections. GMS Infect Dis. May 12;8:Doc21.

Ozturk R, Murt A. (2020) . Epidemiology of urological infections: a global burden. World J Urol. 38:2669–79.

Palomo J, Dietrich D, Martin P, Palmer G, Gabay C. (2015). The interleukin (IL)-1 cytokine family--Balance between agonists and antagonists in inflammatory diseases. Cytokine. Nov;76(1):25-37.

Panuganti KK, Nguyen M, Kshirsagar RK. (2023). Obesity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan,12(5),46-53.

Polyphenols for Prevention and Treatment of Urinary Tract Infections. International Public Health Considerations Regarding Obesity. Tiwari A, Balasundaram P.362. Publishing; 2023 Jan 7(34),112-132.

Pormohammad A, Nasiri MJ, Azimi T. (2019). Prevalence of antibiotic resistance in *Escherichia coli* strains simultaneously isolated from humans, animals, food, and the environment: a systematic review and meta-analysis. Infect Drug Resist. 8;12:1181-1197.

Pugliese, G., Liccardi, A., Graziadio, C. et al. (2022). Obesity and infectious diseases: pathophysiology and epidemiology of a double pandemic condition. Int J Obes 46, 449–465 (2022).

Ragnarsdottir B., Jonsson K., Urbano A., Gronberg-Hernandez J., Lutay N., Tammi M., Gustafsson M., Lundstedt A.C., Leijonhufvud I., Karpman D., et al. (2015). Toll-like receptor 4 promoter polymorphisms: Common tlr4 variants may protect against severe urinary tract infection. PLoS ONE;5:24.

Ramirez D, Giron M.(2024). Enterobacter Infections. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. 67(1),1-4.

Razavi, M. R., Hossaini, K. E., Bayatani, N, Sepahi, M.A. & Arsang-Jang, 5.2021.The predictability of mean platelet volume as a biomarker of pyelonephritis among pediatrics with urinary tract infection. Journal of Nephropharmacology, 10.

Richey E.M., Waters P.W., Jovic M., Rakhman C. (2023). Treatment of Ampicillin-Resistant Enterococcus faecium Urinary Tract Infections. ;Fed. Pract. Health Care Prof. VA DoD PHS. 32:20–23.

Riera Romo, M., D. Pérez-Martínez, and C. Castillo Ferrer,(2016). Innate immunity in vertebrates: an overview.Immunology, 2016. 148(2): p. 125-39

Rødgaard-Hansen S, Rafique A, Christensen PA, Maniecki MB, Sandahl TD, Nexø E, et al. (2014). A Soluble Form of the Macrophage-Related Mannose Receptor (MR/CD206) Is Present in Human Serum and Elevated in Critical Illness. Clin Chem Lab Med 52:453–61.

Rodriguez-Mañas L. (2020). Urinary tract infections in the elderly: a review of disease characteristics and current treatment options. Drugs Context. Jul 8;9:2020-4-13.

Rogers J.(2020). Understanding the most commonly billed diagnoses in primary care. [Last accessed on 2020 Oct 28];Nurse Pract. 2020 45:35–40.

Rogers, SA. Kara M. (2024). "urinary tract infection". The Current Scenario and Future Prospects. Pathogens. Jan 44(16),326-335.

Rønning TG, Aas CG, Støen R, Bergh K, Afset JE, Holte MS, Radtke A. (2020). Investigation of an outbreak caused by antibiotic-susceptible Klebsiella oxytoca in a neonatal intensive care unit in Norway. Acta Paediatr. Jan;108(1):76-82.

Rossi CC, Santos-Gandelman JF, Barros EM, et al. (2016). Staphylococcus haemolyticus as a potential producer of biosurfactants with antimicrobial, anti-adhesive and synergistic properties. Lett Appl Microbiol. 2016;63(3):215–221.

Rowe TA, Juthani-Mehta M. (2019). Diagnosis and management of urinary tract infection in older adults. Infect Dis Clin North Am.;28(1):75–89.

Ryu JK, Kim SJ, Rah SH, Kang JI, Jung HE, Lee D, et al. (2019). Reconstruction of LPS Transfer Cascade Reveals Structural Determinants Within LBP, CD14, and TLR4-MD2 for Efficient Lps Recognition and Transfer. Immunity 46(1):38–50.

Sabih A, Leslie SW. (2024). Complicated Urinary Tract Infections. In: StatPearls Treasure Island (FL): StatPearls Publishing; Jan–.7(1)1-7. PMID: 28613784.

Said MS, Tirthani E, Lesho E. Enterococcus Infections.(2023). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-,32(7),271-280.

Salvatore S, Salvatore S, Cattoni E, Siesto G, Serati M, Sorice P, Torella M (2021). "Urinary tract infections in women". European Journal of Obstetrics, Gynecology, and Reproductive Biology. 156 (2): 131–136.

Samer le. (2023). "Correlation of inheritance in people with mane gens defect" ,12(7);34-51.

Sande C, Whitfield C, Slauch JM.(2021). Capsules and Extracellular Polysaccharides in Escherichia coli and Salmonella. EcoSal Plus 9:eESP-0033-3201

Santella B, Schettino MT, Franci G, De Franciscis P, Colacurci N, Schiattarella A, Galdiero M. (2022). Microbiota and HPV: The role of viral infection on vaginal microbiota. J Med Virol. Sep;94(9):4478-4484.

Schaeffer AJ, Nicolle LE. (2016). Urinary tract infections in older men. N Engl J Med. 2016;374(6):562-571.

Schappert SM, Rechtsteiner EA. (2011) Ambulatory medical care utilization estimates for Vital Health Stat.;13:1–38.

Schulthess, J., et al. (2019). The Short Chain Fatty Acid Butyrate Imprints an Antimicrobial Program in Macrophages. Immunity. 50(2): p. 432-445 e7.

Sell J, Nasir M, Courchesne C.(2022). Urethritis: Rapid Evidence Review. Am Fam Physician. May 1;103(9):553-558. Erratum in: Am Fam Physician. Jan 1;105(1):8.

Sharp, V.J.A.; Antes, L.M.; Sanders, M.L.; Lockwood, G.M. (2020). Urine Tests: A Case-Based Guide to Clinical Evaluation and Application. Springer. ISBN 978-3-030-29138-9.

Shepherd FR, McLaren JE. (2020). T Cell Immunity to Bacterial Pathogens: Mechanisms of Immune Control and Bacterial Evasion. Int J Mol Sci. Aug 26;21(17):6144.

Sheu, J. N. et al. (2017). Urine interleukin-1beta in children with acute pyelonephritis and renal scarring. Nephrology (Carlton) 12, 487–493.

Shields J, Maxwell AP. (2020). Acute pyelonephritis can have serious complications. Practitioner. Apr;254(11128):19, 21(7), 23-4 2.

Sims M., Mariyanovski V., McLeroth P., Akers W., Lee Y.C., Brown M.L., Du J., Pedley A., Kartsonis N.A., Paschke A.(2017). Prospective, randomized, double-blind, Phase 2 dose-ranging study comparing efficacy and safety of imipenem/cilastatin plus relebactam with imipenem/cilastatin alone in patients with complicated urinary tract infections. J. Antimicrob. Chemother. 2017;72:2616–2626.

Smith DA, Nehring SM.(2023). Bacteremia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan 19(22),1-6.

Spencer, J. D., Schwaderer, A. L., Becknell, B., Watson, J., & Hains, D. S. (2014). The innate immune response during urinary tract infection and pyelonephritis. Pediatric Nephrology, 29, 1139-1149.

Sperandeo P, Martorana AM, Polissi A.(2019). Lipopolysccharide Biosynthesis and Transport to the Outer Membrane of Gram-Negative Bacteria. Subcell Biochem.;92:9-37.

Stamm WE, Norrby SR. (2020). Urinary tract infections: disease panorama and challenges. J Infect Dis.;183 (Suppl 1):S1–S4

Stillie R, Farooq SM, Gordon JR, Stadnyk AW. (2019). The functional significance behind expressing two IL-8 receptor types on PMN. J Leukoc Biol.;86(3):529–43.

Støy S, Laursen TL, Eriksen LL, Grønbæk H, Vilstrup H, Sandahl TD. (2021). No Effect in Alcoholic Hepatitis of Gut-Selective, Broad-Spectrum Antibiotics on Bacterial Translocation or Hepatic and Systemic Inflammation. Clin Transl Gastroenterol ,12:e00306.

Stuart ME, Macuiba J, Heidrich F, Farrell RG, Braddick M, Etchison S. (2019). Successful implementation of an evidence-based clinical practice guideline: acute dysuria/urgency in adult women. HMO Pract;11:150-7.

Subramanian K, et al.(2019). Pneumolysin binds to the mannose receptor C type 1 (MRC-1) leading to anti-inflammatory responses and enhanced pneumococcal survival. Nat Microbiol 4, 62–70 .

Sundac, L. et al. (2020). Protein-based profiling of the immune response to uropathogenic Escherichia coli in adult patients immediately following hospital admission for acute cystitis. Pathog Dis 74, pp5-12.

Sundvall PD, Elm M, Ulleryd P, Mölstad S, Rodhe N, Jonsson L, Andersson B, Hahn-Zoric M, Gunnarsson R. (2014). Interleukin-6 concentrations in the urine and dipstick analyses were related to bacteriuria but not symptoms in the elderly: a cross sectional study of 421 nursing home residents. BMC Geriatr. Aug;14:88.

Tandogdu Z, Wagenlehner FM.(2016). Global epidemiology of urinary tract infections. Curr Opin Infect Dis, 29:73–9.

Tang M, Quanstrom K, Jin C, Suskind AM. (2019). Recurrent Urinary Tract Infections are Associated With Frailty in Older Adults. Urology. Jan;123:24-27.

Tannupriya, Vivek Kumar, Garg, A. (2023). review on traditional natural compounds and conventional methods for the treatment of UTI, URINE, Volume 5, Pages 13-22.

Taylor TA, Unakal CG. (2024). Staphylococcus aureus Infection. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan 26, pp21.

Tegegne KD, Wagaw GB, Gebeyehu NA, Yirdaw LT, Shewangashaw NE, Kassaw MW. (2023). Prevalence of urinary tract infections and risk factors among diabetic patients in Ethiopia, a systematic review and meta-analysis. PLoS One Jan 17;18(1):e0278028.

Tille, P. M. (2017).Bailey & scott's diagnostic microbiology 14 t h ed. Mosby, Inc., an affiliate of Elsevier Inc. China

Tiwari A, Balasundaram P. (2024). Public Health Considerations Regarding Obesity;7(41);271-278.

Torres-Sangiao E, Lamas Rodriguez B, Cea Pájaro M, Carracedo Montero R, Parajó Pazos N, García-Riestra C. (2022). Direct Urine Resistance Detection Using VITEK 2. Antibiotics (Basel). May 15;11(5):663.

Tramma D, Hatzistylianou M, Gerasimou G, Lafazanis , V. (2012). Interleukin-6 and interleukin-8 levels in the urine of children with renal scarring. Pediatr Nephrol;27(9):1525–1530

Traven, A. and T. Naderer, (2019). Central metabolic interactions of immune cells and microbes: prospects for defeating infections. EMBO Rep. 20(7): p. e47995.

Tsalkidou EA, Roilides E, Gardikis S, Trypsianis G, Kortsaris A, Chatzimichael A, Tentes I.(2013). Lipopolysaccharide-binding protein: a potential marker of febrile urinary tract infection in childhood. Pediatr Nephrol.1091–1097

Tsalkidou EA, Roilides E, Gardikis S, Trypsianis G, Kortsaris A, Chatzimichael A, Tentes I. (2013). Lipopolysaccharide-binding protein: a potential marker of febrile urinary tract infection in childhood. Pediatr Nephrol, Jul;28(7):1091-7.

Tuttle AR, Trahan ND, Son MS. (2022). Growth and Maintenance of Escherichia coli Laboratory Strains. Curr Protoc. Jan;1(1):e20. Erratum in: Curr Protoc. 2022 Aug;2(8):e551

Tyagi P, Moon CH, Janicki J, Kaufman J, Chancellor M, Yoshimura N, Chermansky C. (2018). Recent advances in imaging and understanding interstitial cystitis. F1000Res. Pp. 27.

van Buul L.W., Vreeken H.L., Bradley S.F., Crnich C.J., Drinka P.J., Geerlings S.E., Jump R.L.P., Mody L., Mylotte J.J., Loeb M., et al.(2018). The Development of a Decision Tool for the Empiric Treatment of Suspected Urinary Tract Infection in Frail Older Adults: A Delphi Consensus Procedure. J. Am. Med. Dir. Assoc;19:757–764.

Van den Boom L, Kalder Ms, Kostev K. (2021). Prevalence of urinary system, pelvic organ, and genital tract disorders among women with type 1 diabetes in Germany. Primary Care Diabete; 15: 257-261.

van der Zande HJP, Nitsche D, Schlautmann L, Guigas B, Burgdorf S. (2021). The Mannose Receptor: From Endocytic Receptor and Biomarker to Regulator of (Meta)Inflammation. Front Immunol. Oct 14;12:765034.

Van Leeuwen, A.M.; Bladh, M.L. (2019). Davis's Comprehensive Manual of Laboratory and Diagnostic Tests with Nursing Implications (8 ed.). F. A. Davis Company. ISBN 978-0-8036-9448-4.

Vilotić A, Nacka-Aleksić M, Pirković A, Bojić-Trbojević Ž, Dekanski D, Jovanović Krivokuća M. (2022). IL-6 and IL-8: An Overview of Their Roles in Healthy and Pathological Pregnancies. Int J Mol Sci. 2022 Nov 23;23(23):14574.

Vincent CR, Thomas TL, Reyes L, White CL, Canales BK, Brown MB. (2023). Symptoms and risk factors associated with first urinary tract infection in college age women: a prospective cohort study. J Urol;189(3):904-910.

Wagenlehner, F.M.E., Bjerklund Johansen, T.E., Cai, T. et al. (2020). Epidemiology, definition and treatment of complicated urinary tract infections. Nat Rev Urol 17, 586–600.

Wasnaa , J & Ibrahim, NoorAlhuda. (2017). Levels of IL-1β and IL-8 in Iraqi women with Bacterial vaginosis and Trichomoniasis. Cihan University-Erbil Scientific Journal, 253-264.

Watanabe, H., Katsura, T., Takahara, M. et al. (2020). Plasma lipopolysaccharide binding protein level statistically mediates between body mass index and chronic microinflammation in Japanese patients with type 1 diabetes. Diabetol Int 11, 293–297 .

Wesevich A, Sutton G, Ruffin F, Park LP, Fouts DE, Fowler VG Jr, Thaden JT. (2020). Newly Named Klebsiella aerogenes (formerly Enterobacter aerogenes) Is Associated with Poor Clinical Outcomes Relative to Other Enterobacter Species in Patients with Bloodstream Infection. J ClinMicrobiol. Aug 24;58(9):e00582-20.

Whiteman W, Topley C (1990). Topley and Wilson's Principles of bacteriology, virology and immunity : in 4 volumes (8th ed.). London: Arnold. p. 198. ISBN 978-0-7131-4591-5.

WHO . (2020). Fact sheet Antibiotic Resistance.

Woll C, Neuman MI, Pruitt CM, Wang ME, Shapiro ED, Shah SS, McCulloh RJ, Nigrovic LE, Desai S, DePorre AG, Leazer RC, Marble RD, Balamuth F, Feldman EA, Sartori LF, Browning WL, Aronson PL. (2018). Febrile Young Infant Research Collaborative. Epidemiology and Etiology of Invasive Bacterial Infection in Infants ≤60 Days Old Treated in Emergency Departments. J Pediatr. 2018 Sep;200:210-217.e1.

World Health Organization .(2021). Global Priority List of Antibiotic-Resistant Bacteria to Guide Research, Discovery and Development of New Antibiotics.

Xu K, Wang Y, Jian Y, Chen T, Liu Q, Wang H, Li M and He L. (2023). Staphylococcus aureus ST1 promotes persistent urinary tract infection by highly expressing the urease. Front. Microbiol. 14:1101754.

Y., & Li, D. (2019). Body Mass Index and the Risk of Rheumatoid Arthritis: An Updated Dose-Response Meta-Analysis. BioMed Research International, 2019.

Yamaji R, Friedman CR, Rubin J, Suh J, Thys E, McDermott P, Hung-Fan M, Riley LW. A (2018). Population-Based Surveillance Study of Shared Genotypes of Escherichia coli Isolates from Retail Meat and Suspected Cases of Urinary Tract Infections. mSphere. Aug 15;3(4) .

Yang, B; Foley, S. (2020). Female urinary tract infection in clinical practice. Springer Nature, Switzerland AG. Switzerland.

Yang, X., Chen, H., Zheng, Y., Qu, S., Wang, H., & Yi, F. (2022). Disease burden and long-term trends of urinary tract infections: A worldwide report. Frontiers in Public Health, 10.

YEH, E., PINSKY, B. A., BANABI, N. & BARON, E. J.(2009). Hair sheep blood, citrated or defibrinated, fulfills all requirements of blood agar for diagnostic microbiology laboratory tests. PloS one, 4, 6141.

Younis, K. R., & Al-bustany, D. A. (2017). Prevalence of obesity in rheumatoid arthritis and its association with disease activity and latex positivity in a sample of patients in Erbil. 21(2), 1726-1735.

Zaffanello M, Malerba G, Cataldi L, Antoniazzi F, Franchini M, Monti E, Fanos V. (2020). Genetic risk for recurrent urinary tract infections in humans: a systematic review. J Biomed Biotechnol:e321082.

Zalmanovici Trestioreanu A, Lador A, Sauerbrun-Cutler MT, et al. (2015). Antibiotics for asymptomatic bacteriuria. Cochrane Database Syst Rev.;4:CD009534.

Zarkesh, M., Sedaghat. F., Heidarzadeh, A., Tabrizi, M., Bolooki-Moghadam, K. and Ghesmati, S. (2019). Diagnostic value of IL-6, CRP, WBC and absolute neutrophil count to predict serious bacterial infection in febrile infants. Acta Med Iran 53(7), 408-411.

Zhu Z, Wang D, Jiao W, Chen G, Cao Y, Zhang Q, Wang J.(2017). Bioinformatics analyses of pathways and gene predictions in IL-1α and IL-1β knockout mice with spinal cord injury. Acta Histochem. Sep;119(7):663-670.

Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF. (2018). Development and validation of a bedside instrument to predict carbapenem resistance among gram-negative pathogens in complicated urinary tract infections. Infect Control Hosp Epidemiol ;39(9):1112–1114.

Appendices

Apendix 1: Questionnaire

Name;

Age;

Sex ; F ☐

M ☐

Code;

Height;

Weight;

Do you have any of the following symptoms?:

☐ Discomfort or pain passing urine

☐ Passing urine more frequently at night

☐ Urine that is more cloudy

☐ New discharge from the vagina

☐ New discharge from the penis

☐ None of the above

Do you have any of the following symptoms?:

☐ New pain in lower back

☐ Nausea

☐ Vomiting

☐ Fever

☐ Shivering

☐ Other symptoms

How long have you had these symptoms?:

○ Less than 3 days

- 3 days to 1 week
- 1-2 weeks
- More than 2 weeks

What have you done to manage your symptoms?:

- Painkillers eg, Paracetamol
- Antibiotics
- Cranberry products
- Drinking more fluids
- Other remedies
- None

Have you had a Urinary tract infection (UTI) before, these are sometime called a bladder or water infection?:

- Yes- In the previous 6 months
- Yes- In the previous year
- Yes- In the previous 3 years
- Yes- more than 3 years ago
- No

Is there a possibility you may be pregnant?:

- Yes
- No

Do you have a urinary catheter (This is a tube that is inserted into your bladder, which is used to empty the bladder and collect urine) :

- Yes
- No

Do you have any immunological disease :

- Yes
- No

Do you have hypertension disease :

- Yes
- No

Do you have diabetic mellitus disease :

- Yes
- No

Do you have cardiovascular disease :

- Yes
- No

Do you receive any vaccine :

- Yes
- No

Do you take any medication at this period : if yes what is ? :

- Yes
- NO
- ……

Do you have any family history for UTI :

- Yes
- No

Do you have any prostate issue :

- Yes
- No

الخلاصة

واحدة من أكثر أنواع العدوى انتشارًا في العالم هي التهابات المسالك البولية، أو عدوى المسالك البولية. ترتبط عدوى المسالك البولية بعبء سريري ومالي كبير بالإضافة إلى انخفاض نوعية حياة المرضى. يمكن أن يصاب كلا الجنسين بالتهاب المسالك البولية في أعمار مختلفة، وعادة ما تكون النساء أكثر عرضة للإصابة به من الرجال. ينبع الأساس المنطقي من الاختلافات في بنية وفسيولوجيا الجهاز البولي بين الجنسين. التهاب المثانة، أو عدوى المسالك البولية السفلية، والتهاب الحويضة والكلية، أو عدوى المسالك البولية العلوية، هما فئتان من التهابات المسالك البولية.

اجريت هذه الدراسة خلال الفترة من شهر تشرين الاول 2023 الى شهر شباط 2024 في مستشفى الامام الحسين ع في مدينة كربلاء المقدسة و مختبرات كلية العلوم الطبية التطبيقية/ جامعة كربلاء.

صممت الدراسة على اساس تصميم دراسة الحالة – السيطرة ، شملت الدراسة الحالية جمع عينات الادرار(لاستخدامه في فحص الادرار العام) و الدم (استخدام الدم مباشرة لقياس صورة الدم الكاملة ، والمصل لقياس البروتين التفاعلي الكروي ، انترلوكين واحد بيتا ، انترلوكين ثمانية ، بروتينات المرتبطة بالسكريات المتعددة الدهنية ، مستلم المانوز) من 70 مريض بالتهاب المجاري البولية (35 مريض لديه نمو بكتيري و 35 مريض ليس لديهم نمو بكتيري) اضافة الى 70 شخص سليم . وتم التحري ايضا عن المعايير العامة التالية : العمر ، الجنس ، الطول ، الوزن.

تراوحت اعمار عينات الدراسة بين 18 الى 77 سنة ، وكانت نسبة الاناث لكل مجموعة أكبر معنويا ($P<0.05$) من نسبة الذكور لكل مجموعة (نسبة الاناث 80% والذكور 20%) ، و اكثر الفئات العمرية بالتهاب المجاري البولية هي من 18 الى 37 سنة. ظهرت

البكتريا الموجبة لصبغة كرام بنسبة 51 % و السالبة لصبغة كرام بنسبة 49 %، تم الحصول على ثمانية انواع بكتيرية توزعت كالتالي: *Escherichia coli* (33 %) ، *Staphylococcus saprophyticus* (26 %) ، *Staphylococcus haemolyticus* و *Staphylococcus aureus* و *Klebsiella aurogenes* (10 %) لكل منها، و *Klebsiella pneumoniae* (5%) *Enterococcus faecalis* و *Enterococcus faecium* (3 %).

ومن اهم ما توصلت اليه الدراسة هو ارتفاع المعايير التالية : CRP, IL-1b, LBP, MR,وخلايا القيح لدى مرضى التهابات المسالك البولية مقارنة بمجموعة السيطرة. كما وجد ان ارتفاع تركيز MR,LBPفي مجموعة المرضى الذين لديهم نمو بكتيري إيجابي كان معنويا مقارنة بمجموعة السيطرة ومجموعة المرضى الذين ليس لديهم نمو بكتيري.

كما توصلت الدراسة الحالية الى وجود علاقة ارتباط طردية معنوية في مجموعة المرضى الذين لديهم نمو بكتيري بين كل من: (WBC و CRP) ، (WBC و Neutrophils) ، (Neutrophils و Lymphocytes) ، (Neutrophils و IL-8) . اضافة الى وجود علاقة ارتباط سلبية بين : (WBC و MR) ، (LBP و IL-1β). تشير الارتباطات بين العلامات في مجموعة المرضى الذين ليس لديهم نمو بكتيري إلى وجود ارتباط موجب فقط بين (LBP و IL-8).

جامعة كربلاء

العلاقة بين Lipopolysaccharide binding protein, Mannose receptor, IL-1β and IL8 في مرضى التهاب المجاري البولية

رسالة مقدمة

الى مجلس كلية العلوم الطبية التطبيقية - جامعة كربلاء

وهي جزء من متطلبات نيل شهادة الماجستير في التحليلات المرضية

كتبت بواسطة

آية حيدر قحطان آل سعودي

بكالوريوس تحليلات مرضية/ ٢٠٢١ كلية العلوم الطبية التطبيقية – جامعة كربلاء

بأشراف

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