

TURKISH REPUBLIC OF NORTH CYPRUS

NEAR EAST UNIVERSITY

INSTITUTE OF GRADUATE STUDIES

URINARY TRACT INFECTION DURING AND PRE COVID-19 PANDEMIC IN CHILDREN IN NORTHERN CYPRUS

ODAI RJOUB

MEDICAL MICROBIOLOGY AND CLINICAL MICROBIOLOGY PROGRAM

MASTER OF SCIENCE THESIS

SUPERVISOR

Assoc. Prof. Dr. Ayşe Arıkan SARIOĞLU

NICOSIA

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APPROVAL

We certify that we have read the thesis submitted by **ODAI RJOUB** titled "Urinary Tract Infection in Children During and Pre the COVID-19 Pandemic in Northern Cyprus" and that in our combined opinion it is fully adequate in scope and in quality as a thesis for the degree of Master of Medical Microbiology and Clinical Microbiology.

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STATEMENT (DECLARATION)

Hereby declare that the work in this thesis entitled "Urinary Tract Infection in Children During and Pre the COVID-19 Pandemic in Northern Cyprus" is product of my own research efforts under the supervision of Assoc. Prof. Dr. Ayşe Arıkan SARIOĞLU. I had no unethical behaviour in all stages from planning of the thesis until writing thereof, I obtained all the information in this thesis in academic and ethical rules, I provided reference to all of the information and comments which could not be obtained by this thesis study and took these references into the reference list and had no behaviour of breeching patent rights and copyright infringement during the study and writing of this thesis.

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Date:31-12-2021

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List of Abbreviations

CO: CHROM agar orientation (Type of chromogenic media) **CFU:** Colony Forming Unit **CLED:** Cysteine Lactose Electrolyte Deficient agar CPS ID3: Types of chromogenic media **GI:** Gastrointestinal tract HPF: High Power Field NICE: The National Institute for Health and Clinical Excellence TMP-SMX: Trimethoprim-sulphathiazole %: Percent sign USA: The United States of America **UTI:** Urinary Tract Infection **VUR:** Vesicoureteral reflux WBCs: White Blood Cells **AK:** Amikacin AMC: Amoxicillin-Clavulanic Acid **ATM:** Aztreonam CAZ: Ceftazidime **CFP:** Cefepime CIP: Ciprofloxacin **CRO:** Ceftriaxone **CTX:** Cefotaxime **EMB:** Eosin Methylene Blue EUCAST: The European Committee for Antimicrobial Susceptibility Testing **UTI:** Urinary tract infection

µg/mL: Microgram per Milliliter

TRNC: The Turkish Republic of Northern Cyprus

SPSS: Statistical Package for the Social Sciences

Gr (-): Gram-negative

Gr (+): Gram-positive

S. aureus: Staphylococcus aureus

E. coli: Escherichia coli

CTX: Cefotaxime

BA: BLOOD Agar

U. A: Urine analysis

CRP: C-reactive protein

CBC: Complete blood count

WBC: White Blood Cell

SXT: Trimethoprim / Sulfamethoxazole

TIGA: Tigecycline

TETRA: Tetracycline

VANCO: Vancomycin

TZP: Piperacillin-Tazobactam

TOBRA: Tobramycin

RBC: RED BLOOD CELL

°C: Celsius

HPF: high power field

CFU: Colony forming units

No: Number

µg/mL: Microgram per Milliliter

Mm: Micrometer

MER: Meropenem

ABSTRACT

ODAI A.A. RJOUB. Urinary tract infection during and Pre COVID - 19 pandemic in children in Northern Cyprus. Near East University, Institute of Graduate Studies, Medical Microbiology and Clinical Microbiology Program, M.Sc. Thesis, Nicosia, 2022.

Aim: Determine the prevalence of UTI in children prior to and during the covid-19 pandemic, to search for the main causes that led to an increase in UTI in children through the covid-19 pandemic, identify microorganism responsible for UTI in children in Northern Cyprus, Investigate the susceptibility antibiotics used to treat UTI in this phase group and Demographic variables and relationships with UTI include a gender, Investigate the Biochemical and Hematological test is have relationship is bacterial growth in urine culture to diagnosis UTI.

Materials and Methods: A total of 1488 samples for children were taken from the archives of the Near East University Hospital to study the prevalence of urinary tract infection in children before and during the COVID- 19 pandemic based on urine culture examination and identification of organisms that cause urinary tract infection in children by the BD Phoenix Automated Microbiology Identification System (Becton Dickinson, USA) and Vitex (Bio-Merioux, France).

Result: According to our results, the prevalence of UTI in children during the covid-19 pandemic was 30.3% higher than the prevalence of UTI in children before the covid-19 pandemic, where the prevalence rate before the covid-19 pandemic was 25.0%. *E. coli* as the most common urinary tract infection in children in North Cyprus with a rate of 39.4%, followed by *Klebsiella pneumoniae* at a rate of 19.5% the prevalence of UTI among females was higher than males). A significant correlation was found between leukocyte and nitrite positivity and growth in urine culture (p=<0.001). The resistance to the antibiotic Ampicillin before the COVID 19 pandemic was 120/97 (79.5%), and during the COVID 19 pandemic it was 176/110 (62.5%) P value is 0.001. While The resistance to the

antibiotic Ciprofloxacin before the COVID 19 pandemic was 22/122 (18.0%), and during the COVID 19 pandemic it was 14/190 (7.4%) P value is 0.004.In addition The resistance to the antibiotic Ertapenem before the COVID 19 pandemic was 11/132 (8.3%), and during the COVID 19 pandemic it was 4/185 (2.2%) P value is 0.011.

Conclusion: The prevalence of UTI in children in North Cyprus is 30.0%. The prevalence of urinary tract infection in children during the COVID- 19 pandemic increased to 30.3%, where it was 25.0% before the COVID- 19 pandemic, meaning that the percentage of urinary tract infection in children increased to 5.3%. Female children in North Cyprus are more likely to have a urinary tract infection. *Escherichia coli* is the most common UTI pathogen with an average of 39.1%. followed by *Klebsiella pneumoniae* (19.5%) and *Proteus mirabilis* (11.5%). significant correlation was found between leukocyte positivity and nitrite positivity with growth in urine culture. A correlation between an increase resistant antibiotic of Enterobacteriaceae family with COVID 19 pandemic.

Key Words: UTI infection, covid-19 Pandemic, Urine Test. Biochemical and Hematological Analysis, Antibiotics susceptibility test.

ÖZET

ODAI A.A. RJOUB. Kuzey Kıbrıs'ta çocuklarda covid-19 pandemisi sırasında ve öncesinde idrar yolu enfeksiyonu. Yakın Doğu Üniversitesi, Sağlık Bilimleri Enstitüsü, Tıbbi Mikrobiyoloji ve Klinik Mikrobiyoloji Programı, Yüksek Lisans Tezi, Lefkoşa, 2022.

Amaç: Çocuklarda covid-19 pandemisi öncesi ve sırasında İYE prevalansını belirlemek, covid-19 pandemisi sırasında çocuklarda idrar yolu enfeksiyonlarında artışa neden olan ana nedenleri araştırmak, çocuklarda İYE'den sorumlu mikroorganizmayı belirlemek Kuzey Kıbrıs'ta, . Bu yaş grubunda İYE tedavisinde kullanılan antibiyotiklere duyarlılık araştırılmalı ve demografik değişkenler ve İYE ile ilişkiler cinsiyet içermektedir, Biyokimyasal ve Hematolojik testlerin araştırılması İdrar kültüründe bakteriyel üreme ile İYE tanısı arasında ilişki vardır.

Gereç ve Yöntem: Yakın Doğu Üniversitesi Hastanesi arşivlerinden COVID-19 pandemisi öncesi ve sırasında çocuklarda idrar yolu enfeksiyonu prevalansını incelemek ve idrar kültürü incelemesine dayalı olarak çocuklara yönelik toplam 1488 örnek alındı. BD Phoenix Otomatik Mikrobiyoloji Tanımlama Sistemi (Becton Dickinson, ABD) ve Vitex (Bio-Merioux, Fransa) tarafından çocuklarda idrar yolu enfeksiyonuna neden olur.

Sonuç: Sonuçlarımıza göre, covid-19 pandemisi öncesi çocuklarda İYE prevalansı, covid-19 pandemisi öncesi çocuklarda İYE prevalansından %30,3 daha yüksek, covid-19 pandemisi öncesi prevalans oranı %25,0 idi. ., Kuzey Kıbrıs'ta çocuklarda en sık görülen idrar yolu enfeksiyonu %39,4 ile E. coli iken, bunu %19,5 ile Klebsiella pneumoniae izlemektedir.). Lökosit ve nitrit pozitifliği ile idrar kültüründe üreme arasında anlamlı ilişki bulundu (p=<0,001). Ampisilin antibiyotiğine COVID 19 pandemisinden önce direnç 120/97 (%79,5) ve COVID 19 pandemisi sırasında 176/110 (%62,5) idi. P değeri 0.001'dir. COVID 19 pandemisinden önce antibiyotik Siprofloksasin'e direnç 22/122 (%18,0) iken,

COVID 19 pandemisi sırasında 14/190 (%7,4) idi. P değeri 0.004'tür. Ayrıca COVID 19 pandemisinden önce antibiyotik Ertapenem'e direnç 11/132 (%8.3), COVID 19 pandemisi sırasında 4/185 (%2.2) idi. P değeri 0.011'dir. Tablo 5'i gösteriyor.

Sonuç: Kuzey Kıbrıs'ta çocuklarda İYE prevalansı %30,0'dir. COVID-19 pandemisi öncesinde çocuklarda idrar yolu enfeksiyonu prevalansı %30,3 iken, COVID-19 pandemisinden önce %25,0 iken çocuklarda idrar yolu enfeksiyonu yüzdesi %5,3'e yükselmiştir. Kuzey Kıbrıs'taki kız çocukların idrar yolu enfeksiyonu geçirme olasılığı daha yüksektir. Escherichia coli, ortalama %39.1 ile en yaygın İYE patojenidir. bunu Klebsiella pneumoniae (%19,5) ve Proteus mirabilis (%11,5) izlemektedir. idrar kültüründe üreme ile lökosit pozitifliği ve nitrit pozitifliği arasında anlamlı ilişki bulundu. Enterobacteriaceae familyasının artışa dirençli bir antibiyotiği ile COVID 19 pandemisi arasında bir korelasyon.

Anahtar Kelimeler: İYE enfeksiyonu, covid-19 Pandemisi, İdrar kültürü, İdrar analizi. Biyokimyasal ve Hematolojik Analiz, Antibiyotik suspitlite testi, Demografik değişk.

CHAPTER I

INTRODUCTION AND AIMS

Urinary tract infection is one of the furthermost communal bacterial infections in infancy. Both the upper and lower urinary tracts can be infected with what is known as pyelonephritis (mentioned to as cystitis). Unfortunately, it might be incredible to tell the difference between pyelonephritis and cystitis based on clinical signs and symptoms, especially in infants and children under the age two. Fever, dysuria, and lower abdominal pain (LAP) are all common symptoms of an contagion of the urinary tract, and kidney scarring are possible if the infection is not treated quickly (Chen, 2011).

Pathogen later recognized as *Escherichia coli* (*E. coli*) was discovered in 1885 by Austrian paediatrician Theodor Escherich (1857–1921), who practiced in Vienna. For the first time he discovered the important of urinary tract infections (UTIs) in children by analysing urine samples from young girls with lower urinary tract symptoms (Shulman et al., 2007).

Efforts to better understand the symptoms and etiologic of UTI have been made since then. However, the diagnose of urinary tract infections (UTIs) in new-borns and adolescent children is particularly challenging (Tullus, 2011).

Contaminations of the urinary tract can be acquired in the society or in a hospital setting. When a patient is diagnosed with a community-acquired urinary tract infection (CA-UTI), the term mentions to a contamination of the urinary system that occurs within 48 hours of admission, whether in the community or a hospital. The second most frequent microbiological illness in the population is a community-acquired urinary tract infection (UTI) (*Moyo: Antimicrobial Resistance among Producers and... - الباحث العلمي من - Google*, n.d.).

N-UTIs are infections of the urinary tract that emerge afterward 48 hours of hospitalization if the patient was not incubation at the admittance or within three days following discharge from hospitalization (Iacovelli et al., 2014).

Symptoms of urinary tract infections (UTIs) could range from symptomless to severe to chronic, and from complicated to uncomplicated, and the sternness of the contagion and a patient's aptitude to build an immune response are all factors that influence the UTIs' clinical manifestations. Because both silent and symptomatic UTIs threaten public health, they lower people's quality of life and increase the number of people who are unable to work (Olowe et al., 2015). A person's age and the region of a urinary tract infect can influence the symptoms of a urinary tract infect can influence the symptoms of a urinary tract infect and suprapublic discomfort, and pyuria (Odoki et al., 2019).

Recurrent UTIs can be affected by a variety of circumstances, including gender, age, race, circumcision, HIV, diabetes, the use of a urinary catheter, genitourinary tract anomalies, pregnancy, new-borns, the elderly, and hospitalization. When it comes to UTI pathogens, *E. coli* is the most communal, after that *K. pneumoniae, Staphylococcus, Proteus, Pseudomonas, and Enterococcus*. A total of 150 million people around the world get urinary tract infections per annum, estimate the healthcare system in excess of \$6 billion dollars. 4.5 percent of all patients treated to acute care units for more least 48 hours in Algeria were located to have a urinary tract infection (UTI). Patients hospitalized to the university hospital in Dakar, Senegal, had a incidence rate of 0.7%, with females having a greater rate than males (Odoki et al., 2019).

In Nigeria, a study of 12,458 urine tests found an incidence of 12.3% for society - acquired UTIs and 9.3% for nosocomial UTIs. The prevalence rates are 14.6% for females and 7.4% for males, respectively. Antenatal moms at Mulago hospital in Uganda had a medication resistance rate of 20–60 percent and had a prevalence of UTIs of 29/218 (13.3 percent). The incidence of urinary tract infections (UTIs) amongst people presence Mulago Hospital's evaluation centre was determined to be 38.8%, while age, feminine gender, and wedded status were all statistically significant factors. *E. coli* was the most communal bacterial uro pathogen in Bushenyi District, Uganda, through 41/67 (61.19 percent) after that *Staphylococcus aureus* (10/67), *Klebsiella pneumoniae* (4/67), *E. faecalis* (4/67), *M. morganii*

(3/67), *Citrobacter species* 2/67 (2.99 percent), *Acinetobacter* 1 (1.49 percent), *Enterobacter species* 1 (1.49 percent), and *P. aeruginosa* (1.49 percent). The most common bacterial uropathogens was *Staphylococcus aureus* with 45/103 (43.7 percent), followed by *E. coli* with 29/103 (28.2 percent), *Klebsiella species* with 28/103 (27.2 percent), and *Enterococcus species* 1/103 in a research paper of UTIs in diabetics in Bushenyi District, Uganda (1.0 percent) (Odoki et al., 2019).

With the spread of the COVID -19 pandemic in the world, many changes, controls, and standards have occupied place in order to limit the spread of the COVID- 19 virus, as many sectors have been affected, including the health sector. On the other hand, the restrictions and restrictions set by the government in terms of closure and lack of movement and movement sometimes, except for the utmost necessity, greatly affected people. For example, in terms of health, where the rate of infection with certain diseases and many other things that affect the population.

In this study, we decided to focus on UTIs in children before and during the COVID- 19 pandemic to find out the reasons that led to the increase in UTIs in children during COVID 19 pandemic, where they focused. This study is about several things.

1.1 Objectives of study

1. Determine the prevalence of UTI in children prior to and during the COVID- 19 pandemic.

2. Identify microorganism responsible for UTI in children in Northern Cyprus.

3. Demographic variables and relationships with UTI include age and gender.

4. Investigate the Biochemical and Haematological test is had relationship is bacterial growth in urine culture to diagnosis UTI.

5. Investigate the susceptibility antibiotics used to treat UTI in this age group.

6.To search for the main causes that led to an increase in urinary tract infections in children during the COVID- 19 pandemic.

CHAPTER II

LITERATURE REVIEW

2.1. Background

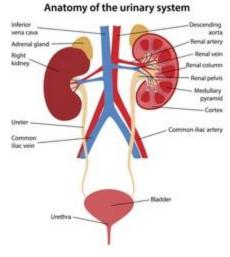
In infants and children, urinary contagions are the maximum public and serious bacterial contamination (Chen, 2011). In emerging republics, it is unity of the greatest frequently encountered bacterial contaminations via doctors (Tessema et al., 2007). At least \$6 billion is spent each year treating UTIs, which affect 150 million people (Sykes & Westropp, 2014). An estimated 7 million office visits and 1 million trips to ERs in 1997 resulted in UTI hospitalizations for a total of 100,000 patients in the USA. (Ghedira Besbes et al., 2004).

Vesicoureteral reflux (VUR) and neurogenic bladder are two conditions that can lead to a UTI in children. To evade lasting problems and decrease the risk of serious illness, it is critical to identify and treat children with UTI as soon as possible. UTIs that go unnoticed leading to renal damage, hypertension, and kidney failure (Sawalha, 2009).

Underdiagnosis, delayed diagnosis, or undertreatment of UTI in children may bring about hypertension and end-stage renal disease if the infection is misdiagnosed or neglected. (Sahsi & Carpenter, 2009) (Adjei & Opoku, 2004).

2.1.1 Structure and physiology of the urinary tract

In order to produce, transport, store and expel urine, the urinary system is consisting of two kidneys, two ureters, a bladder, and a urethra. Fig. 1-1 depicts an outline of the urinary system and the location of its major anatomical features.



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FIGURE 1 (Hickling et al., 2015)

2.1.2 Kidneys and the formation of urine

One of the kidney's primary homeostatic duties is to remove soluble waste from the blood, which is why the kidneys are bean-shaped. Approximately 10-12 centimetres is the length of a human kidney. They measure 5-7 centimetres in width and 3 centimetres in thickness and are located on either side of the spinal column between the peritoneum and posterior wall (Moinuddin & Dhanda, 2015). Due to the liver's anatomical superiority, the right kidney's position is slightly lower than the left kidney (Wood & Greenwell, 2010).

An 8-18-pyramidal medulla lies within the kidney's cortex, and a pelvis connects it to the ureter through the kidney's ureteropelvic. Nephrons, the kidney's primary functional filtering units, make up the cortex and medulla, which together contain about a million of these structures (*Wheater's Functional Histology - 6th Edition*, n.d.).

Bowman's capsule protects the glomerular capillary network of each nephron, which is surrounded by a tube around 5.5cm in length, separated into four sections by the convoluted tubule, loop of Henle, and the distal convoluted tubule and collecting duct. Minor calyces, which are 8-18 cup-like structures, are formed by a single collecting duct and several hundred papillary ducts that drain into them.

Minor calyces supply urine to 2-3 large calyces, which in turn drain pee into the renal pelvis (Hickling et al., 2015; Moinuddin & Dhanda, 2015).

Each nephron's Bowman's capsule is made up of an exterior parietal layer formed of simple squamous epithelial cells and an inner visceral layer of podocytes, which extend footlike projections called pedicels that wrap around the solitary endothelial cell layer of the glomerulus. Endothelial cells, the basal lamina, and the podocyte layer all play a role in filtering the glomerular filtrate. This region is filled with glomerular filtrate that separates the parietal from the visceral layers (Miner, 2011; *The Cell Biology of Renal Filtration / Journal of Cell Biology / Rockefeller University Press*, n.d.).

The proximal convoluted tubule consists of cuboidal epithelial cells with a brush border of microvilli that face the lumen and increase the surface area for reabsorption and release of glomerular filtrate. Henle loop and nephrons juxtamedullary include epithelial cells with cuboidal to low columnar morphology (*Wheater's Functional Histology - 6th Edition*, n.d.)

End of ascending limb contains columnar cells known as macular dense that are densely crowded. Distal convoluted tubule and collecting duct primary cells respond to various stimuli to control sodium and potassium transport, whereas intercalated cells, a smaller subset of cells, are involved in pH regulation, potassium and ammonia transport, and the innate immune system (Pearce et al., 2015; Roy et al., 2015).

In order to produce urine, water and solutes from the blood plasma are filtered out of the glomerulus by Bowman's capsule and along the tubule, and then reabsorbed back into the blood by tubular reabsorption. Wastes and ions are then secreted from tubular reabsorption and the tubules into the filtrate by tubular and collecting ducts. There are approximately 95 percent water molecules and 5 percent solutes (urea, creatinine and uric acid) that make up the final composition of urine. Other chemicals, such as hormones and fats also make up the rest of the composition (Robinson, 2018).

2.1.3 Ureters and the transport of urine

This combination of ureter contractions and hydrostatic pressure and gravity is responsible for ureter transport of urine as of each kidney to the bladder. The ureters are located in the retroperitoneum and range in length from 22 to 30 centimetres, with a small diameter of 0.1-1 centimetres. The ureterovesical junction (UVJ) is the place where each ureter enters the bladder wall obliquely, and the ureters continue up to the bladder lumen. Ureteral apertures are protected from vesicoureteral reflux (VUR) when the bladder is filled with urine, because of the pressure change that follows. Mucosa, muscularis, and adventitia are the three different layers of the ureter's wall. Known as the urothelium, the transitional epithelial cells seen on the surface of the mucosa are transitional epithelial cells (de Groat & Yoshimura, 2015, 2015).

An additional benefit of this layer is that it can expand to accommodate changes in urine volume, allowing the ureter and other structures to adjust to them. Small blood veins and lymphatic tissue make up the lamina propria in the mucosal layer of connective tissue. Circular and longitudinal smooth muscle fibres make up the outer layer of the muscularis, while an additional outer layer of longitudinal fibres is found in the distal third of the ureters. peristaltic movement. This connective tissue carries blood, lymph, and nerves to and from the adventitia (Notley, 1971; *Wheater's Functional Histology - 6th Edition*, n.d.).

2.1.4 Bladder and the storage of urine

The bladder's principal role is to accept, store, and then expel soluble waste from the urinary tract. The bladder is a hollow distensible organ situated anteriorly to the rectum in males and inferiorly to the uterus in females. When the bladder is empty, it takes on the shape of a tetrahedral cube. The peritoneum protects the superior surface, which is referred to as the dome. An inverted triangle is formed by placing the urethra's internal orifice at the apex, with the ureteric orifices on the right and left forming the other two corners (de Groat & Yoshimura, 2015). Mucosal layer, muscular layer, adventitial layer, and serosal layer are the four primary tissue layers of the bladder wall. The urothelium, a single-cell foundation membrane, and the lamina propria make up the innermost mucosal layer. An impermeable physical barrier to pee, the urothelium prevents water from exiting the cells into hypertonic urine during its outermost layer (Birder & Andersson, 2013).

Polyhedral umbrella (or facet) cells make up the urothelium's outermost layer, which is highly differentiated. uroplakins (particularly, UPIa, UPII, UPIIIa, and UPIIIb) form a plaque on the apical surface of these cells and cover the entire asymmetric unit membrane (AUM). It is while the bladder is full of urine that the bladder's umbrella cells take on the shape of cuboids, but when the bladder is empty these cells return to their cuboidal shape. Tight junctions, which separate the umbrella cells, help to build a barrier by preventing proteins, ions, and non-ions from flowing through. This layer is followed by intermediate cell layers and a basal layer that contains stem cells that can develop into other cell types (Apodaca, 2004; Khandelwal et al., 2009).

Laminin, fibronectin, and collagen type IV make up the basal membrane that covers the urothelium. The lamina propria is an extracellular matrix consist of a diversity of cell types, including the stellate-shaped interstitial cells of Cajal (ICC), fibroblasts, and adipocytes, and it is well-supplied with arterial, nerve, lymphatic, and elastic fibres. Smooth muscle cells in this layer create a delicate and often imperfect tissue known as muscularis mucosae. The detrusor muscle is consist of three distinct layers of smooth muscle fibres, each of which is called after its orientation (Birder & Andersson, 2013; J. S. Dixon & Gosling, 1983).

They're placed longitudinally, but with a circular orientation in the intermediate layer of smooth muscle cells. The internal urethral sphincter is consisted of the detrusor muscle, which are located in a neck of the bladder. It is the ring of muscles located right below the detrusor muscle that contracts as the urethra contracts to prevent urination. A layer of vascularized connective tissue called the adventitia covers is posterior and inferior bladder surfaces and extends from both ureters. An further layer of visceral peritoneum, called the serosa, covers the bladder's superior surface, which is comprised primarily of connective tissue and mesothelium (Andersson & Arner, 2004; *Wheater's Functional Histology - 6th Edition*, n.d.).

In addition to the sympathetic and parasympathetic nervous systems, the lower urinary tract is also supplied by the somatic nervous system. Internal urethral sphincter closure occurs because of sympathetic nervous system involvement in bladder detrusor muscle relaxation and sympathetic innervation of spinal segments T1-L2 during bladder filling. Sacral spinal segments S2-S4 are innervated by the parasympathetic nervous system, which is answerable for detrusor muscle contraction and relaxation throughout the voiding phase. S2-S4 of the sacral spinal column provide the somatic efferent neurons, which control pelvic floor muscle tone and external urethral sphincter striated muscle innervation (de Groat et al., 2015; Fowler et al., 2008; Hill, 2015).

Bladder pressure doesn't alter much when pee fills the bladder at a pace of 0.5-5ml per minute on average. Due to the bladder wall's capacity to fold and the detrusor smooth muscle's ability to expand, low intravesical pressure is maintained, which is known as compliance. During physical exertion, the afferent signalling is amplified, which blocks the parasympathetic pathway and the subsequent contraction of detrusor muscle while simultaneously inducing contraction of smooth muscle of internal urethral sphincter. Detrusor muscle parasympathetic route is suppressed by somatic innervation, while the external urethral sphincter muscle is stimulated to contract. Relaxed bladder muscles and closed urethras keep the bladder detrusor muscle in place (*Continence and Micturition: An Anatomical Basis - PubMed*, n.d.; Keane & O'Sullivan, 2000).

Intravesical pressure rises, urethral resistance increases, and urethral contractions of the external urethral sphincter slowly increase as the bladder fills up. The micturition centre in the brain receives sensory input when the bladder capacity (about 200-400ml) has been achieved, and the feeling of a 'full bladder' is subconsciously accepted. Detrusor muscle contraction inhibition is controlled cortically at this moment, and the urge to urinate can be overridden by voluntary control. The need to urinate doesn't kick in until about 75% of one's bladder capacity is used up. Activating the parasympathetic spinal cord outflow activates detrusor muscle contraction and causes the internal urethra to open. To further open

the internal urethral sphincter, somatic innervation is inhibited as a result of afferent signals, which further suppresses sympathetic outflow. When the bladder detrusor contracts and both urethral sphincters open, we are able to go to the bathroom and urinate (Keane & O'Sullivan, 2000; *Pathophysiology of Overactive Bladder - PubMed*, n.d.).

2.1.5 Urethra and the expulsion of urine

An aperture on the bladder floor known as the internal urethral orifice connects to an orifice on the bladder wall known as the external urethral orifice. Micturition occurs when the bladder releases pee through the urethra (and seminal fluid from the seminal vesicles in males). The architecture and placement of the urethras in men and women are vastly different. The external urethral orifice is situated between the clitoris and the vaginal aperture of the female urethra, which is about 4 cm length and 0.6 cm wide. This passageway is approximately 20 centimetres long, passing via the prostate, perineum and penis. Female urethral wall mucosa is made up of epithelium, lamina propria, and superficial muscularis of the female urethral wall (*Gray's Anatomy for Students - 4th Edition*, n.d.).

The transitional epithelium (urothelium) that lines the anterior urethral mucosa is continuous with the bladders. Non-keratinized stratified squamous epithelium is found near the external urethral orifice in the distal mucosa, while stratified columnar epithelium is found in the proximal area. Circular smooth muscle fibres make up the muscularis, which is also found in the bladder. The prostatic urethra, the membranous urethra, and the spongiosa urethra are all types of male urethra. In the prostatic urethra, the stratified columnar epithelium or pseudostratified columnar epithelium progresses to the stratified squamous epithelium towards the external urethra. The internal urethral sphincter of the bladder is formed by the circular smooth muscle fibres of muscularis of the membranous urethra form the external urethral sphincter of the bladder (Carlile et al., 1987; *Endoscopic Diagnosis and Treatment in Urinary Bladder Pathology - 1st Edition*, n.d.).

2.2. Definition of UTI

A urinary tract infection (UTI) is broad name that encompasses a wide range of clinical states , as of symptomless bacteria in the urine to undecorated kidney contamination with sepsis as a result (Sykes & Westropp, 2014). A UTI is too definite as the growth of a identified bacterial pathogen in the presence of a positive dipstick or urinalysis result in the incidence of in excess of 10,000 cfu/ml (Coplen, 2006).

Based on National Institutes of Health and Clinical Excellence (NICE) recommendations, UTI is definite via the attendance of bacteria in urine (Baumer & Jones, 2007). The clinical symptoms of urinary tract infection (UTI) typically include frequency, dysuria, pyuria, abdominal pain, back pain, fever, and earnestness(McLoughlin & Joseph, 2003) (Sahsi & Carpenter, 2009). However, these symptoms alone are not enough to establish a diagnosis of UTI in verbal children (Sahsi & Carpenter, 2009). A temperature of unidentified source in children is usually a sign of a urinary tract infection (UTI) (Dulczak & Kirk, 2005).

Contagions of the urinary tract are divided into two types: lower tract infections that affect the bladder and/or urethra (such as cystitis and urethritis) and upper tract infections that affect the ureters, collecting system, and parenchyma (such as kidney stones) (pyelonephritis) (Heffner & Gorelick, 2008). To get an accurate diagnosis, it's important to know the difference between the two types. Pyelonephritis is an contamination of the pelvis and kidney parenchyma, while cystitis is an inflammation of the urinary bladder itself. Dysuria, urgency, malodorous urine, enuresis, haematuria, and suprapubic pain are all signs and symptoms of cystitis. On the other hand, fever and anxieties, accompanied by costovertal or flank ache and soreness, along with pyuria and positive urine culture, are symptoms of pyelonephritis. Pyelonephritis is the furthermost serious form of urinary tract infection (UTI) in children, with a elevated rate of sickness and lasting damage (Dulczak & Kirk, 2005) (Sawalha, 2009). Intestinal pain, back pain, dysuria, frequency and new-onset incontinence are all symptoms of a urinary tract infection

(UTI), but they are not enough to establish a diagnosis in children who are verbal(Sahsi & Carpenter, 2009).

2.3. Risk factors of UTI

Children are at risk for developing UTIs because of both physical and physiological factors. A person's peril of evolving a UTI increases if urinary tract abnormalities that impede the flow of urine are present (Sykes & Westropp, 2014).Short urethras in women, vesicoureteral reflux (VUR), neurogenic bladder, and uncircumcision in boys are all anatomical abnormalities that can effect a person's aptitude to urinate. As the foreskin is warm, moist, and mucosal, bacteria are more likely to settle in the urethra and colonize the bladder of uncircumcised boys (Dulczak & Kirk, 2005) (Heffner & Gorelick, 2008). Another anatomical factor is the presence of posterior urethral valves, or bladder diverticulitis (Heffner & Gorelick, 2008). Constipation, infrequent urination, incomplete bladder emptying, and dysfunctional voiding are all examples of physiological causes. In persons who are constipated, stool collects in the rectum for a lengthy retro of time, which raises the risk of urinary tract infection (Dulczak & Kirk, 2005).

There are numerous things you can do to upsurge the chance of developing a UTI. These include urinary retention (such as urine stasis or reflux), UTIs and constipation are common side effects of long-term usage of antibiotics for an unstable bladder, as is sexual activity, chronic disease, and illness. Periurethral flora can be damaged by prolonged use of antibiotics, allowing Ur pathogens to infect and colonize the urinary tract (Sykes & Westropp, 2014). Individuals experience bacteriuria in different ways depending on their circumstances. A wide range of factors can influence teenage health, including age, gender identity, race, genetics, sexual activity, circumcision, nocturnal enuresis, and other hazardous habits. (Heffner & Gorelick, 2008).

At the extremes of life, bacteriuria is more common than urinary tract infections (UTIs). (UTIs) are bimodal, peaking in the first year of life and again in the late teens (Heffner & Gorelick, 2008). UTIs affect people of all races, but

epidemiological studies have found that the prevalence and complications of UTIs vary depending on race (Wein et al., 2011). According to extensive research, UTIs are more common in white people than in other races (Heffner & Gorelick, 2008). Studies conducted in emergency departments have found that Asian, Hispanic, and white infants are more likely than other races to develop UTI, with 22 percent, 16 percent, and 16 percent reported, respectively. Black infants, on the other hand, had a 4% lower rate of UTI than other ethnic groups. (Sahsi & Carpenter, 2009).

UTI is influenced by the gender of the patient (Wein et al., 2011). In the first year of their lives, boys are further probable to get a UTI than girls. After the first year of life, females are further probable than boys to become a urinary tract infection (UTI). (Sykes & Westropp, 2014). Bacteriuria risk may also be influenced by family history, as follow-up studies have shown that people with childhood UTIs are still at risk for adult UTIs regardless of whether they have vesicoureteral reflux. 42%Patients in research at the University Hospital in Bern, Switzerland, had a family history of urinary tract infections (UTIs). (Stauffer et al., 2004).

Sexual activity among adolescent girls is on the rise, and this, too, increases the risk of a UTI. Only a small ratio of young girls and females look to be in danger for intercourse- related infection, which is caused by the passage of bacteria as of the vagina to the urethra (Dulczak & Kirk, 2005) (Heffner & Gorelick, 2008). For religious, social, and medical reasons, when it comes to surgery, circumcision is a long-standing practice. According to ethnicity and culture, its incidence varies greatly. (Yang et al., 2009). There have been several studies that have suggested a link between urinary tract infections and being uncircumcised. Circumcision was found future significantly linked with a decreased peril of urinary tract infections in 144 children younger than five years old, despite criticism of these studies' methodology. (Watson, 2004). In the foremost year of life, uncircumcised males prosecute to ten times the peril of developing a urinary tract infection (UTI) than circumcised boys. (Wein et al., 2011). 2.4 percent of circumcised male infants below the stage of three months had a urinary tract infection (UTI), compared to 20.1 percent of uncircumcised males (Prendergast, 2009). After the first year of life,

the prevalence of (UTIs) decreases, making circumcision status in boys meaningless (Heffner & Gorelick, 2008). In a cross-sectional study in Iran that included 7562 child aged 5 to 18 years old, there is a robust association between (UTI) plus nocturnal enuresis. The incidence of UTI was 2.9% among the enuretic (Safarinejad, 2007).

These contagions can be caused by a wide diversity of reasons, either alone or in mixture with other predisposing factors. UTI may be caused by a person's urination and bowel movements. During the day, incontinence and urinary tract contagions can be attributed to a lack of micturition and incomplete bladder emptying in children (UTI), Changes in the incidence of moistening and urinary tract contagions were observed as a result of behavioural intervention in children (Lindstrom et al., 2000). 8 percent of school children (10-12 years old) report some frequency of daylight wetting with/without night time moistening, which is associated with bladder sphincter disfunction and frequent urinary tract contagions (Bakker et al., 2002). Day-wetting is a problem that affects one percent of healthy child in excess of the age of five, according to study. (Meadow, 1990). Study participants at Berne University Hospital's Department of Paediatrics, Switzerland, discovered that reduced hygiene and toilet behaviours can lead to contagions when they are joint with functional abnormalities for example insufficient fluid drinking, frequent urination, functional stool incarceration, or excretion disfunction (Mazzola et al., 2003). According to a different study, the way people use the restroom has a significant impact on the frequency and severity of UTI (Wan et al., 1995).

2.4. Epidemiology of UTI

It is important to know how common urinary tract contagions are in various peoples in order to determine the suitable level of doubt and the fitting work-up for these infections (Quigley, 2009). Due to underreporting, it is hard to accurately estimate the rate of UTI. This state is further complex because the precise diagnosis of UTI requires together the attendance of signs and a positive urine culture (Ghedira Besbes et al., 2004). In epidemiological studies, asymptomatic bacteriuria is a critical sign because it allows early detection of urinary tract infections (UTIs) and prompt administration of the appropriate prophylactic measures (Nurullaev, 2004). Via age, gender, race, and circumcision station of the patient, the epidemiology and incidence degrees of UTI are categorized (Sykes & Westropp, 2014) (Prendergast, 2009). The prevalence of urinary tract infections (UTIs) is bimodal, peaking in the first year of life and again in the adolescent years (Heffner & Gorelick, 2008). During babyhood, 8 percent of lasses and 2 percent of lads are in risk of evolving a urinary tract infection (UTI). (Alhaj & Bayoumi, 2020).

Throughout childhood, the risk of the incidence of UTI in feverish babies increases through age, with approximately 7% of feverish new-born having a indicative, culture- established urinary tract contamination by the age of six ages (Alper & Curry, 2005). In children under the age of 4, UTIs are more likely to cause scarring or reduced kidney growth. Infants in their primary year of life are particularly susceptible. Between 3% and 5% of infants admitted to the ER with a fever are diagnosed with a urinary tract infection (UTI) (Shaw & Gorelick, 1999). White lasses , uncircumcised lads , and those with no other possible cause of fever are more likely to develop UTIs than those who are circumcised (Shaw & Gorelick, 1999).

Urinary tract infections affect children under the age of 12 at a rate of 0.7 percent per year (Gaspari et al., 2005). In a report conducted in Sweden in 1999, children younger than 2 years old were found to have a cumulative incidence of 2.2% and 2.12% for both boys and girls, respectively. The mean incidence was found to be 1.1% for both genders, with a range of 0.33%-3.9% and 0.4%-2.99%, respectively (Jakobsson et al., 1999). Males 9 times are further probable than females to contract UTIs through their firstly age of life (Wein et al., 2011). Based on a meta-analysis paper shown by the University of Pittsburgh's general Academic Paediatrics division to measure the occurrence of UTI in infants with fever, there was an overall prevalence of 7.0percent of UTI in children 0–19 years old with signs of UTI. The incidence rate of feverish UTI in women aged 0–3 month were 7.5%, for those old 3-6 months it is 5.7%, and for those old 6–12 months it is 8.3% (Prendergast, 2009).

According to a paper published in the Urologic Nursing Journal, about 1 percent to 5 percent of female pre-schoolers and school-age kids have urinary tract infections (UTIs). Males have a much lower incidence of UTIs than females (Dulczak & Kirk, 2005). As a result, the incidence of UTI in school-aged kids in Campbell-Walsh urology ranges from 0.03 percent to 1.2 percent for boys and from 1% to 3% for girls (Wein et al., 2011). After puberty, females' incidence rises, while males' incidence is rare (Dulczak & Kirk, 2005). As adolescence progresses, the prevalence of (UTIs) in young women rises to 20%, while the incidence remains stable of young men (Sykes & Westropp, 2014).

UTI rates in girls begin to decline after the age of six, but begin to rise significantly again during adolescence as a result of increased sexual activity (Heffner & Gorelick, 2008). In a study via the Section of General Academic Paediatrics at the University of Pittsburgh in the United States, 7.8 percent of adolescents under the age of 19 who had urinary symptoms had a UTI (both febrile and afebrile) (Prendergast, 2009). In a study in Tunisia, UTI was found to be 1.85 percent in a group of kids aged 2 months to 14 age, by a mean age of 5 years (Ghedira Besbes et al., 2004).

Contagions of the urinary tract are more common in lads than in lasses [3% of lasses and 1% of lads experience UTI in the primary 10 years of their lives] (Evans, 2006). New-borns under the age of three months have a upper incidence of urinary tract infections (7.5% for lasses and 8.7% for boys) (Sahsi & Carpenter, 2009). Even though the exact incidence of UTIs is unknown, patterns in the northern United Kingdom propose that 3.6 percent of lads and 11.3 percent of lasses have had a UTI by the time they reach the age of 16 (*Management of Urinary Tract Infection - ScienceDirect*, n.d.).

2.5. Causative of organisms

2.5.1 Bacterial the UTI

Among the utmost prevalent causes of UTI are gram (-) bacteria such as *E. coli, Klebsiella species*, *P. mirabilis*, *Acinetobacter* and *Serratia*. More than 90% of UTI case are caused by Gram (-) bacteria and less than 10% by gram (+) bacteria. Gram (+) bacteria consist of *Enterococcus*, *Staphylococcus*, and *S. agalactiae*, all of which cause gram (+) bacterial infections. (Lazarević et al., 1998). Mon microbic infections in children's urinary tracts are common, accounting for 60–80 percent of cases, and are frequently caused by *E.coli, Proteus, Klebsiella, Enterococcus*, and coagulase-negative *staphylococci*. (Alper & Curry, 2005).

Escherichia coli is the utmost frequent gram(-) bacteria that causes UTIs. (Wein et al., 2011). *E. coli* bacteria are responsible for 75.5 to 87% of (UTI). (Ghedira Besbes et al., 2004) (Yüksel et al., 2006). *Escherichia coli* is to blame for at minimum 80% of all cases of simple cystitis and pyelonephritis (Sykes & Westropp, 2014). However, *Proteus mirabilis* infections account for 10% of all infections, whereas *Klebsiella pneumonia* infection accounts for 6% (Ghedira Besbes et al 2004) (Yüksel et al 2006) (Wu et al 2004). While bladder emptying and host defense responses can help flush out some organisms, in some situations, these organisms' adhesion qualities prevent them from being flushed out of the body. The existence of P. fimbriae, organelles that confer or cling to specialized receptors of uroepithelial cells and inhibit the washout of bacteria, causes violent strains of *Escherichia coli*.(Sykes & Westropp, 2014).

Girls are further probable to be infected with *E.coli* than boys, while *Proteus mirabilis* and *Klebsiella pneumoniae* are more common in lads (Ghedira Besbes et al., 2004). *Proteus spp, Klebsiella spp and Enterobacter spp.* have a high rate of UTI. Kids with repeated urinary tract infections (UTIs) and those taking antibiotic prophylaxis are more likely to contract an infection. Children with urogenital abnormalities are more susceptible to infection by pathogens such as Pseudomonas, Serratia, and Candida (Mangiarotti et al., 2000). Most community-acquired UTI are

affected via *E.coli*, with 12% of cases caused by *Klebsiella*; in hospital-acquired UTIs, 66% is affected via *E.coli* and other microbe (Ashkenazi et al., 1991).

2.5.2 Fungal and Viral UTI

Viruses and fungi can both cause contagions of the urinary tract. *Candida* is second utmost communal fungus of children's nosocomial UTIs. It can spread throughout the body systemically and be life-threatening (Alhaj & Bayoumi, 2020). Paediatric patients on long-term antibiotic therapy, those with compromised immune systems, and those who use IVs, grains, and catheters are all at risk for fungal infections (Dulczak & Kirk, 2005) (Alhaj & Bayoumi, 2020). Urinary tract anomalies are associated with a higher prevalence of *Candida* fungi infections in kids (UTA) (Yildiz et al., 2007). It is linked to urinary tract contagions following urinary tract instrumentation (Schlager, 2001). UTIs affected via *Candida* increased in prevalence as hospitalization wore on, reaching 27.2 percent (Parlak et al., 2007). Blocking antibiotics, deleting or replacing indwelling catheters, and beginning an antifungal treatment regimen, such as oral fluconazole, parental or intravesical amphotericin B, are all options for treating candiduric (Alhaj & Bayoumi, 2020). *Adenoviruses types* 11 and 21; *polyomavirus* BK; and *herpes* simplex viruses can all affect viral UTI (Alhaj & Bayoumi, 2020).

2.6. Methods of bacterial entry

Bacterial entry on the genitourinary tract can occur by two ways. UTIs in kids are usually affected via rising infections, but hematogenous spread may be more communal in children under 12 weeks of age (Alper & Curry, 2005).

2.6.1 The ascending route:

In utmost cases, pyelonephritis is brought on via bacteria ascending as of the bladder into the ureters and the parenchyma of the kidneys (Sykes & Westropp, 2014). Ascending bacteria from the perineum is the utmost communal cause of UTI (Heffner & Gorelick, 2008).

2.6.2 Hematogenous route:

Neonatal and immunocompromised patients are the most common victims of this condition (Sykes & Westropp, 2014). A hematogenous source can cause urinary tract contagion in babies as children as 8 to 12 weeks old. As a result, initial discovery of UTI in kids is critical because it serves as a biomarker for urinary tract faults in new-borns. Bacteraemia may be linked to a UTI that is hematogenous in origin (Schlager, 2001). The urinary tract is commonly infected by pathogens like *Staphylococcus aureus*, *Candida species*, and *Mycobacterium tuberculosis*, which move during the bloodstream (Sykes & Westropp, 2014).

2.6.3 Risk factors of UTI in children

A number of risk factors for urinary tract infections (UTI) have been found, including ethnicity and gender, vesicoureteral reflux, neurogenic bladder and phimosis. Urinary retention, increased residual urine volume, infrequent voiding, and voiding delay are all LUTS that have been linked to UTI in the literature. Bladder hyperactivity is the utmost frequent lower urinary tract disease.

2.7. Pathogenesis of UTI

The development of Urinary Tract Infections (UTIs), factors such as male circumcision status, periurethral flora, micturition, and bowel disorders, as well as local factors and hygienic measures, are significant (Mangiarotti et al., 2000). The most serious long-term consequences of UTI are end-stage renal disease and hypertension (Schlager, 2001). Of the 3 percent of lasses and 1 percent of lads whom develop a prepubescent UTI, 17% or further develop contagion - associated renal damaging , 10 percent to 20 percent develop hypertension, excluding only an infrequent children develops progressive renal disfunction leading to end-stage renal disorder (Wein et al., 2011). Bacterial bond and motility, as well as the host's immune response and genetic factors, influence of pathogenicity at bacteria in UTIs (Heffner & Gorelick, 2008).

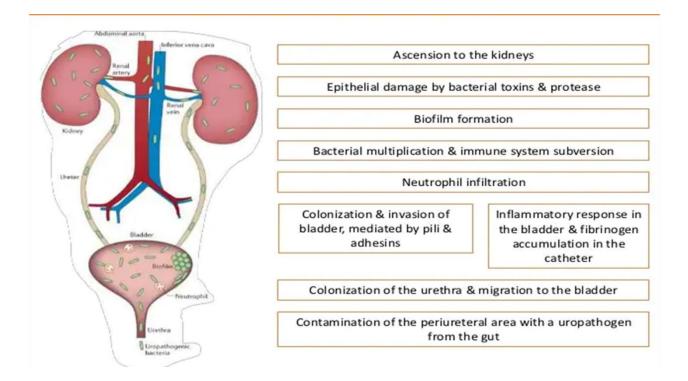


Figure 2. Pathogenesis of UTI (Keane & O'Sullivan, 2000)

2.8. Diagnosis of UTI

Clinical characteristics and the incidence of bacteria in the urine are used to define a urinary tract infection (UTI). Over 100,000 colony-forming units (cfu) of solo bacteria in cultured urine is another way to define this condition. It is possible to have together specific and nonspecific signs and symptoms in the course of a urinary tract infection (UTI). Correct diagnosis and medication of UTI are critical for reducing morbidity and mortality and avoiding unnecessary antibiotic use (Sykes & Westropp, 2014). Diagnosing UTIs in children and infants is particularly challenging. Children's UTIs are often characterized by symptoms such as feverishness, irritability, and vomiting that are also common in further infant viral infections (National Collaborating Centre for Women's and Children's Health (UK), 2007). Diagnosis of a UTI trusts on a mixture of laboratory tests and clinical symptoms. Both urinalysis and urinalysis culture are included in laboratory investigations.

2.8.1. Urinalysis

Urinary Tract Infection (UTI) in urine culture can be evaluated and screened quickly using urinalysis, which includes a dipstick test and microscopy (Dulczak & Kirk, 2005). A UTI urine culture screening was performed. When dipped into a urine sample, a urine dipstick made of chemical preserved paper shows diverse colours that indicate the existence of leukocyte esterase, nitrites, blood, and protein (Lamond, 2006). Nitrates can be found in most people's urine. The enzyme "reductase" produced by gram-negative bacteria in the urinary tract reduces nitrate to nitrite. A urinalysis may reveal nitrites, which may marker the presence of UTIs.

The breakdown of neutrophil white blood cells (WBCs) in the urine produces the enzyme leukocyte esterase (Lamond, 2006). Usually, after centrifugation, the urine is examined under a microscope for WBCs and bacteria. An infection is likely if there are above three WBCs per high-power field (Sykes & Westropp, 2014). The inflammatory response of the urogenital mucosa to colonizing bacteria results in an increase in the number of WBCs in the urine (Lamond, 2006). Enhanced urinalysis refers to the examination of urine samples that have not been centrifuged (Heffner & Gorelick, 2008).

CELLS OF THE BLOOD (WBCs) 0-4 WBC/HPF is considered normal.

After looking at the leukocyte distribution with a 40x objective,

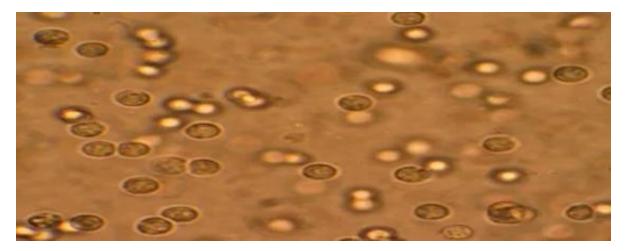


Figure 3. URINE OF MICROSCOPIC EXAMNATION (Kesson et al., 1978).

2.8.2. Urine culture

When a positive dipstick test result is in doubt, a urine culture is typically performed (Sahsi & Carpenter, 2009). to determine the etiologic of the UTI and the best course of action for treating it (Wein et al., 2011). The test for urine culture is performed on a sample of urine to determine whether or not infection-causing organisms are present in the urine. The Ur pathogens are detected and the numeral of bacteria colonies it can form of the culture plate is counted in colony-forming units each millimetre (CFU/ml) after 24 hours at incubation at 37 degrees Celsius in an incubator.(Wein et al., 2011). If your child has been diagnosed with acute pyelonephritis, has a high risk of severe illness, is child than 3 ages, has had a single positive result for leukocyte esterase or nitrite, or has had a recurrent UTI, you should send urine samples for culture (National Collaborating Centre for Women's and Children's Health (UK), 2007). Cultures of urine should be started right away, in a clean, dry container. To diagnose UTIs in child with a elevated level of clinical doubt, murky urine or urine dipstick test that demonstrates positive leukocyte esterase or nitrite activate, urine culture is necessary. (Alper & Curry, 2005).

Primary screening for urinary tract infections (UTIs) can be done using B agar, EMB agar, and chromogenic media. The use in chromogenic media of urine culture is a recent development. Isolates of bacteria can be identified and differentiated using this method. Different colored colonies are formed by the breakdown of chromogenic substrates by specialized enzymes in bacterial isolates. Ur pathogens *for example Escherichia coli, Klebsiella*, and *Enterobacter* can grow and be identified using this method. Gram(+) bacteria, for example *S. aureus and Enterococcus*, can thrive in this medium (*UTILITY OF URICHROM II – A CHROMOGENIC MEDIUM FOR UROPATHOGENS - ScienceDirect*, n.d.). Different chromogenic media, for example Chromogram Orientation (CO) and CPS ID3, differ of their specificity, sensitivity, and accuracy. To compare CPS ID 3 and CHROM agar with standard biplane technique, 91.9% and 100.0% of *Escherichia coli* and *Enterobacter* were identified direct on CO media, respectively, while 97.5 percent and 94.44 percent of *Enterobacter spp* were identified on CPS3 media, respectively, on the Taiwanese study (Chang et al., 2008).

Studying the uncovering and ID of urinary tract pathogens using three different chromogenic agar plates (CPS ID 2, Chromogenic UTI, and USA agar) found that the detect and identification rates of the three media were very similar, with just slight variances observed (Chaux et al., 2002). Inoculated urine specimens inoculated for one or two days were tested in Sweden to compare the results of four colorimetric urine culture media to source media; mild differences were observed between these media as 96 percent of the isolated strains were recovered on blood agar, 96 percent were recovered on CLED, and 92 percent were recovered on CLED. (Aspevall et al., 2002). Urinary tract infection (UTI) media evaluation and introduction has resulted in quality improvements, with enhanced discrimination of mixed cultures, and staffing and working time inefficiencies that counterbalance media costs (Bakker et al., 2002).



Figure 4. Urine CULTURE(Aspevall et al., 2002).

2.8.3 Creatinine Test

The creatinine levels in blood and/or urine are measured by this test. Your muscles produce creatinine as a byproduct of normal, everyday action. If all goes according to plan, your kidneys resolve eliminate creatinine from your blood and excrete it urine. If your kidneys aren't functional properly, creatinine levels in your blood can rise, and less of it will be excreted in urine. Creatinine levels can indicate renal disease if they are abnormally high or low in the blood and/or urine (Gounden et al., 2021).

Nephrons are the tiny blood-filtering units that make up each kidney. Filtration takes place in the glomeruli, a small cluster of blood vessels that form the nephrons. These structures remove waste, excess water, and other contaminants from the bloodstream. During urination, poisons that have been accumulated in the bladder are flushed out.

To determine if your kidneys are functioning properly, a creatinine test is administered. Blood urea nitrogen (BUN) or a complete metabolic panel may be ordered in conjunction with this test (CMP). A CMP is a collection of tests that provide information about various physiological systems and organs. An annual CMP is often included in a checkup (Gounden et al., 2021).

2.8.4 Urea Test

Urea nitrogen levels in the blood can be assessed with a blood urea nitrogen test (BUN). The amount of urea nitrogen in your blood is one indicator of how well your kidneys are functioning. Urea is a waste product that originates in the liver and travels via the blood to the kidneys, where it is removed from the circulation. It is then excreted from your body through the kidneys. It is normal to have a modest quantity of urea in your blood because of the continual nature of this process. A high level of urea suggests that the kidneys are not filtering waste correctly, which may point to a more serious issue (Seki et al., 2019).

2.8.5 C-Reactive Protein (CRP) test

C-Reactive Protein (CRP) blood test detects your body's amount of this protein. CRP is a liver-produced protein. Inflammation triggers its release into your bloodstream. When you've been harmed or infected, your body responds by inducing inflammation to defend your tissues. Injured or damaged areas may experience swelling, redness, and discomfort as a result. Inflammation is a symptom of some autoimmune and chronic diseases. Your blood normally contains low concentrations of c-reactive protein. A significant rise in these levels could be an indication of an infection or other ailment ("C-Reactive Protein (CRP) Test-Uses, Procedure and Result Interpretation," 2015).

In 1930, Tillett and Francis identified C-reactive protein (CRP). When the "c" carbohydrate antibody of the pneumococcus capsule interacted with the CRP found in the serum of individuals with acute inflammation, it was given the term CRP. When inflammation occurs, the liver produces CRP, a pentameric protein that raises in concentration. At the beginning of an inflammatory/infectious disease process, Inflammatory response protein CRP is primarily triggered by IL-6, which has a

significant effect on the gene that encodes CRP. SLE's pathogenesis may be aided by a dysregulation of CRP's involvement in a clearing of apoptotic cells and cellular debris, but this has yet to be established conclusively. Animal investigations on alveolar tissue in alveolitis have shown that it can reduce neutrophil-mediated damage to alveoli and protein leakage into the lungs (Nehring et al., 2021).

2.8.6 Complete blood count (CBC) TEST

It is one of the utmost commonly requested lab test in medicine. Blood cell counts, hemoglobin concentrations and distributions, reticulocyte counts, differential white blood cell counts, and platelet counts are all included in this analysis. Helpful in the diagnosis and monitoring of hematological diseases and other medical conditions (L. R. Dixon, 1997).

For CBCs, the WBC count is often included. Routine blood tests may include these assays. An essential component of the immune system is the white blood cell, or leukocyte. From there, they go through the body's circulatory system. These cells aid in the battle against infection by destroying bacteria, viruses, and germs that enter the body. Immune deficiencies, autoimmune diseases, and blood disorders can all be detected by a simple white blood cell count, which can help your doctor rule out more serious health issues that might be lurking beneath the surface. This test also aids doctors in monitoring the efficacy of chemotherapy, radiation therapy, and other cancer treatments (Walters & Abelson, 1996).

The complete blood count with differential is a frequent CBC variant. There are five types of white blood cells: neutrophils, lymphocytes, macrophages, and granulocytes Inflammatory and infectious disorders are fought by neutrophils, which make up the majority of WBCs and are created in the bone marrow. B-cells and T-cells, two types of lymphocytes, are largely found in the lymphatic system and are responsible for fighting off bacteria and other pathogens in the blood (L. R. Dixon, 1997).

Together with neutrophils, monocytes fight infections and other diseases by eliminating damaged or dead cells from the body. As a response to allergens and some illnesses, the white blood cells known as eosinophils become activated. When it comes to infection detection and treatment, basophils play an important role. An initial CBC with differential may be part of the first blood workup, or it may be performed if the original standard CBC results were unfavorable. The CBC with differential can be used to discover aberrant levels of specific white blood cell types, which may indicate an underlying health risk (Walters & Abelson, 1996).

2.9 Urine collection

Two considerations must be made when collecting urine samples: the method used and the amount of time elapsed until the sample is tested (Heffner & Gorelick, 2008). There are four methods for obtaining urine samples from children. Suprapubic aspiration, catheterization, or the bagged specimen, which is a plastic bag assigned to the perineum (Wein et al., 2011). NICE recommends that urine samples be collected using a clean catch in the middle of the stream. If possible, In the event that urine samples cannot be examined and cultured immediately after collection, they should be refrigerated or preserved using boric acid. (National Collaborating Centre for Women's and Children's Health (UK), 2007). When stored in the refrigerator, urine can be kept fresh for up to 24 hours (Sykes & Westropp, 2014).

2.10 Treatment of UTI

Urinary tract infections (UTIs) necessity be diagnosis and treat quickly. Acute UTIs can be banned by the usage of an appropriate antibiotic. Understanding UTI pathophysiology and developing new diagnostic tests and antibacterial medicines has allowed doctors to customize treatment for each patient. (Sykes & Westropp, 2014). Children's age, site of the infection, etiology of infection, severity of sickness, and antibiotic efficiency all play a role in determining how to treat a urinary tract infection (UTI) (Heffner & Gorelick, 2008) (Gaspari et al., 2005). (Gaspari et al., 2005). Health child and old infant can treat as outpatients, while sick

children and newborns below the age of three months should be admit ion to the hospital as inpatients (Santen & Altieri, 2001). A number of factors, including antibiotic sensitivity patterns in the practice area, the medical status of the patient, and the availability of close follow, should be considered when selecting the most appropriate antimicrobial for a particular patient's condition (Schlager, 2001).

Antibiotics are the primary treat for a UTI. When it comes to UTIs, the utmost communal pathogen is *E. coli*, which usually originates in the gastrointestinal tract. Antibiotics prescribed must be effective against these microorganisms, and broader spectrum antibiotics must be used if a child is seriously ill. The vast major of patients benefit from oral antibiotics, but intravenous antibiotics may be necessary for certain patients, such as those who are critically ill or septic, infants younger than 1 month old, or those who have vomited. Antibiotics are typically given for seven to ten days to treat acute pyelonephritis, but for lower tract UTIs, a shorter treatment period of three to four days works just as well (Smith, 2004). For the treat of a UTI , antibiotics must be able to combat urinary pathogens that are resistant to the antibiotics, be able of side effects, be edible, sugar-free, and be readily accessible (Smith, 2004).

Fluroquinolones (e.g., Ciprofloxacin) are also used to treat UTIs, as are Sulphamethoxazole, Trimethoprim, Nitrofurantoin, Amino glycosides (e.g., Gentamicin, Amikacin), Cephalosporin, and Aminopenicillins (e.g., Ampicillin and Amoxicillin) (Sykes & Westropp, 2014). Treatment of UTIs in children is best done with antibiotics like trimethoprim/Sulphamethoxazole, cephalosporins, and amoxicillin-clavulanate, rather than with quinolones, which can affect joint development, and amoxicillin, which has an elevated dominance of resistance to *E.coli* in many societies (Heffner & Gorelick, 2008). Resistance to antibiotics is an issue in the treat of UTI in child (Ghedira Besbes et al., 2004). Antibiotics are given on the basis of clinical suspicion, which necessitates testing each patient's microorganisms for distribution and susceptibility prior to administration. In addition, every five years, policies for treating urinary tract infections in children should be reevaluated (Raz et al., 2000) (Pape et al., 2004). Initial empirical therapy

with antibiotics is not recommended if their resistance rate is less than 10% to 20% (Warren et al., 1999).

Urinary Tract Infection (UTI) isolates were found to have a high level of antibiotic resistance due to long-term use, which can damage the microbiome and allow pathogens to colonize and infection of the urinary tract, exit doctors with limited options for treating urinary tract infections (Sykes & Westropp, 2014) (Tessema et al., 2007). Prevalence of antibiotic resistance varies as of country toward country, based on the incidence of antibiotics. UTIs affected by Enterococci and Pseudomonas spp. are not commonly treated with Trimethoprim-Sulphamethoxazole. Deficiencies in folate can be caused by it. It's both highly effective and reasonably priced (Sykes & Westropp, 2014). The number of TMPuse SMX's has dwindled as the prevalence of bacterial resistance has risen (Sykes & Westropp, 2014). Increasing rates of bacterial resistance mean that antibiotics like ampicillin, cephalexin, and TMP-SMX cannot lengthier be use as first choice treatments for common urinary tract infections (UTIs). (Raz et al., 2000).

There are regional variations in antibiotic resistance due to the consumption habits and laws that govern antibiotics in a given region. Trimethoprim-sulfamethoxazoleresistant gram-negative pathogens appear to be 6.5 percent in the United States, while 55.2 percent appear to be the case in Taiwan, according to a research conducted by the University of Florida's Department of Emergency Medicine (McLoughlin & Joseph, 2003) (Wu et al., 2004). Resistance to trimethoprimsulfamethoxazole is further communal in older child and those who has previously used antibiotics than in the general population (McLoughlin & Joseph, 2003). Ampicillin and sulfamethoxazole/trimethoprim resistance has been progressively enlarging above the last few decades (Wu et al., 2004). In many cases, medication with Trimethoprim and Ampicillin was futile because of significant resistance rates to these medications in *E. coli* and other urinary infections. At the Fattouma Bourguiba Hospital in Tunis, researchers were able to determine the prevalence of various antimicrobial susceptibility of bacteria. It has been found that 65% of the strains are resistant to Ampicillin; 67% of the strains are resistant to Amoxycillin; and only 34% of the bacteria are resistant to Amoxycillin/Clavulanic Acid.. (Ghedira Besbes et al., 2004).

Cotrimoxazole and first-generation cephalosporins have seen a 20% increase in resistance rates (Pape et al., 2004). Cephalosporins and amino glycosides from the third generation are still effective against the vast majority of bacteria (Ghedira Besbes et al., 2004). Isolated gram (-) bacteria like *E. coli, K. species, P. mirabilis,* and *P. aeruginosa* were found to be particularly sensitive to amino glycoside antibiotic treatments during research conducted at the University Children's Hospital in Belgrade between 1986 and 1995. (Amikacin and gentamicin). However, *Klebsiella species* have a natural resistance to ampicillin, which has shown an increase in resistance rates in *E. coli and K. species. Proteus mirabilis* species can be affected by amino penicillin (Lazarević et al., 1998).

Common antimicrobials commonly used in the treat of UTI have varying levels of resistance to *E. coli*, with ampicillin having the highest rate of resistance (74.2 percent), after that co-trimoxazole (61.3 percent). Nitrofurantoin had the lowermost rate of resistance (2.2 percent), after that amikacin (4 percent), ceftriaxone (7.5 percent), and ciprofloxacin (7.5 percent) (12 percent) (Yüksel et al., 2006). In another study, 54 percent of the respondents showed resistance to sulfamethoxazole and trimethoprim (55.2%), gentamicin (24.9 percent), and cefazolin (82.2 percent). Trimethoprim-Sulphamethoxazole and cephalothin, on the other hand, are more effective against a wide range of pathogens than ampicillin (Ashkenazi et al., 1991).

Because their resistance rates are higher than those of amikacin and gentamicin, its use of ampicillin and co-trimoxazole as standalone treatments for urinary tract infections (UTI) may be of little use., which has enormous benefits as an experiential treat of Urinary tract infection in infants aged more than one year of age. In older children, nitrofurantoin may also be an appropriate empirical treatment for lower urinary tract infections (UTI) (Yüksel et al., 2006). Microbial resistance is on the rise because of the unsuitable use of antibiotic prophylaxis, selfmedication with various antibiotics, and under-dosing of these antibiotics (Mangiarotti et al., 2000) (Adjei & Opoku, 2004). Reduce the frequency and clinical manifestation of UTIs such as VUR by using antibiotics properly, resolving any underlying pathology (Mangiarotti et al., 2000).

2.11. Prevention of UTI

The detection and correction of urinary tract abnormalities is an imperative part of a prevention of recurrent Urinary tract infection. Children thru a history of recurring Urinary tract infection are further probable to experience less symptomatic UTI if they receive treatment for constipation and voiding dysfunction (Wu et al., 2004). Constipation and other symptoms of a malfunctioning elimination system in children with a UTI should be addressed. and they should be fortified to drink an passable amount of water, as recommended by the NICE guidelines (National Collaborating Centre for Women's and Children's Health (UK), 2007).

CHAPTER III

MATERIALS AND METHODS

This section defines the sort of study, identify of the people and sample size, as well as the setting, ethical considerations, instruments, and database well as experimental work.

This research was carried out retrospectively based in the information and statistics for patients present in Near East University Hospital. Where we collected and analyzed them for the work of this study.

These techniques on which the research was based, we collected from archives of a NEU Hospital, and we did not implement them, as the data was clearly present.

The cross-section research is design to measure the prevalence of Urinary Tract Infection between child in old group from 0-17 years in Northern Cyprus between 1.01. 2019 -31.07. 2021. 1488 children under the age of 17. The subject of this study before and during the COVID- 19 pandemic, we investigated whether there is an increase or not in UTIs in children in Northern Cyprus between 1.01. 2019 -31.07. 2021 In our study, we used many laboratory tests to diagnose urinary tract infections, included dipstick test, microscopic examination, urine culture, CBC test, biochemical test and anti-susceptibility test. both dipstick tests and microscope examinations for equally white blood cells and bacteria were performed in the laboratory. After centrifugation at 1000 rpm/5 minutes for each urine sample. A microscope was used to analyze all of the urine samples that tested positive for leukocyte esterase and nitrite. Incubation at thirty-seven °C of 18-24 hours is then carried out for a blood and EMB culture media. After the microorganisms on the urine culture plate were identified and counted, a sensitivity test is performed a examine the sensitivity patterns in the various microorganisms responsible for UTI. The automated Vitek2 system was used to conduct sensitivity tests on various antibiotics use in a treat of UTI Based on how many children were included in our calculations and how many positive samples were collected, we arrived at this

result., we determined a total prevalence of urinary tract infection in children in Northern Cyprus. Finally, SPSS software was used to analyze and compile all of the collected data.

3.1 Sample Size

The study's sample size included1488 children who had urinary tract infections both before and during the COVID- 19 pandemic.

3.2 Inclusion criteria:

- 1. Child (0-17) years of age.
- 2. Child positive urine culture before the COVID- 19 pandemic.
- 3. Children positive urine culture during the COVID-19 pandemic.
- 4. The research includes male and female children.

3.3 Exclusion criteria:

Child who took antibiotics in the same period during which samples were taken to calculate the prevalence of UTI were excluded from our calculations.

3.4 Data Collection

Samples stored before the COVID- 19 pandemic were taken from an archive of the NEU Hospital. Patient samples were collected after the COVID- 19 pandemic and analyzed, and some patient reports were taken from an archive of the NEU Hospital.

3.5 Tool of data collection

Research was conducted using two primary instruments.

3.5.1 Previous data

Samples for symptomatic children with urinary tract infections before the COVID-19 pandemic were taken from the archives of the NEU Hospital from 01.01.2019 to 31.07.2021.

3.5.2 Urine testing

Urine analysis, urine culture, and examinations related to urinary tract infection in children were conducted during the COVID- 19 pandemic, and some samples were taken from an archive of the NEU Hospital during the COVID- 19 pandemic from 01.03.2020 to 31.07.2021.

3.6 Materials used in urine testing:

- 1. Microscope (OlympusCX31, USA).
- 2. Centrifuge (Thermo scientific).
- 3. Sterile calibrated loops 10 (ml).
- 4. Incubator (Heraeus).
- 5. Autoclave (Muve steam art).

6. CBC machine (Abbott CellDyn ruby hematology analyzer, Abbott laboratories, USA).

7. CRP, Creatinine, Urea machine (Abbott Architect c8000 Biochemistry Analyzer, Abbot laboratories, USA) for these tests.

- 8. EMB Agar.
- 9. Blood Agar.
- 10. Antimicrobial susceptibility test by VITEK 2 (Biomerieux, France).
- 11. Urine multitasks (SD UROCOLOR TM, INDIA).

3.7 Methods:

3.7.1 Collection of urine samples

Samples were collected in the period between 01.01.2019 and 31.07.2021

3.7.1.1 Collecting a sample from children BY

Child and infants' sample in diapers or pads can be collected for testing with cotton wool and gauze.

Using a urine collection bag.

3.7.2 Urinalysis:

Urine samples were examined within a few hours after being collected. These specimens underwent urinalysis.

3.7.2.1 Dipstick screening technique

Dipsticks of SD Uro Color 10®SGL (SD UROCOLOR TM, INDIA) for leukocyte esterase and nitrite were used to test urine samples

3.7.2.2 Microscopy exam

The mid-stream urine sample obtained analyzed for the appearance, density, nitrite, pH, leukocyte esterase, microscopy (more than 5 leukocytes in each area, more than 5 erythrocytes, bacteria, leukocyte clusters, leukocyte casts) after bacterial culture. For this purpose, the urine samples will be centrifuge in a normal method; 10ml of urine will be spined at the rate of 2500 rpm for 20-30minutes. The supernatant will be decanted off and the sediment will be resuspended in the remaining 0.2ml. The sediment will be examined below a microscope.

3.7.3 Culture

A laboratory test that determines whether or not the urine contains bacteria, yeast, or other microbes. Microorganisms that cause an infection can be identified using urine cultures.

3.7.3.1 Blood agar

When the prepared medium is dissolved in 1000 ml of water, approximately 40 grams of it is added. To dissolve the medium completely, the suspension is heated to the boiling point. Afterwards, it is autoclaved at 15 lbs. of pressure and 121°C for about 15 minute to sterilize the product. Removed from the autoclave and chilled to 40–45°C, the medium is ready for use. Sterilized defibrillated blood is added aseptically and thoroughly mixed into this mixture. Under sterile conditions, the medium is poured into sterile Petri dishes. In order to eliminate any remaining dampness from the plates afore used, place them in the hot air oven for a few minutes after the media has solidified. Then we culture the bacteria on blood agar for identification

3.7.3.2 Eosin methylene blue agar (EMB)

Pour 1000 ml of distilled water over 35.96 grams. Add more water if necessary to achieve a homogeneous suspension. To completely dissolve the medium, bring the water to a boil. 15 pounds of pressure for 15 minutes at a temperature of 212 degrees Fahrenheit is sufficient for sterilization (121 degrees Celsius). Do not overheat. The flocculent precipitate can be suspended by cooling the medium to 45–50 °C, shaking it, and allowing the methylene blue to oxidize (restoring its blue color). Using a Petri dish, pour the mixture into the container. Ensure that you serve your food on dishes that are at room temperature. Before inoculation, the agar surface should be dry. The specimen should be inoculated and streaked immediately after collection. To isolate a swab specimen, roll the swab on the agar surface and streak it with a clean, sterile swab. 18–24 hours at 35–37°C in an aerobic setting is recommended for incubation of plate samples, with light shielded. Then I cultured the bacteria on EMB agar for identification.

3.7.4 Biochemical Test

The quantities CRP test, urea, creatinine tests start Preparation for the assay by machine automated that called is architect machine (Abbott Architect c8000 Biochemistry Analyzer, Abbot laboratories, USA).

3.7.5 CBC test

The complete blood count analyzed by a CBC analyzer by machine called Abbott CellDyn ruby hematology analyzer, Abbott laboratories, USA

3.7.6 Phoenix and Vitek bacteria identification panels

Urine samples that are sent to Microbiology Laboratory inoculated to blood agar and EMB agar. It incubated bout 24-48 hours at 37°C. The Vitek 2 technology used to identify bacteria and determine their susceptibility to antibiotics (Biomatrix, France).

The antibiotic discs that were tested in the studied; amikacin ampicillin, cefixime, ceftazidime, ceftriaxone, ciprofloxacin, ertapenem, gentamycin, imipenem, meropenem, TZB, SXT, ESBL

3.7.7 Statistical analysis

All statistical analyses performed by using Statistical Package for the Social Sciences (SPSS) version 25,0 (SPSS Inc. Chicago, IL, USA).

3.7.8 Ethical issues:

This study was carried out with URINE samples taken from patients who were followed up between 1.01. 2019 -31.07.2021. at the Near East University Hospital.

All samples sent to the microbiology laboratory were evaluated retrospectively. Ethics committee approval was obtained from NEU Faculty of Medicine Ethics Committee with NEU in date 27.01.2022, with the decision number 2022/99-1483.

CHAPTER IV

RESULT

The results of our study that we carried out were as we divided it into two periods, the first period was pre pandemic. It was the second period during pandemic.

Totally, 1488 pediatric patients aged 0-17 (0-215 months) who admitted to the Near East University hospital with symptoms of urinary tract infection (UTI) between January 2019and July 2021, were included in the study. The mean age of the patients was 4.27 ± 4.91 years (56.09 ± 59.68 months). Five hundred and forty-six (36.7%) of the patients included in the study were male; 942 (63.3%) were female, and their mean age was 3.47 ± 4.94 years (45.84 ± 60.19 months), 4.74 ± 4.83 years (62.04 ± 58.60 months), respectively. The rate of UTI in children younger than 18 years of age was determined as % (416/1488, 30%). UTI was diagnosed in 136 (24.9%) boys and 280 (29.7%) girls It was found that UTIs were more common in girls compared to the boys (p=0.046). Bacterial growth was detected in 416 (28%) of the urine cultures, while no growth was obtained in 1072 (72%). The rate of UTI increased significantly during the pandemic period (p=0.025).

	Pre pandemic n (%)	Pandemic n (%)	p value
Bacterial growth	164 (%25.0)	252 (%30.3)	0.026*
No growth	491 (%75.0)	581 (%69.9)	
Total	655 (%100)	833 (%100)	

Table 1. The rate of bacterial growth in urine cultures in pre pandemic period and during the pandemic period.

*Statistical significance

Escherichia coli (39.4%), *Klebsiella pneumoniae* (19.5%) and *Proteus mirabilis* (11.5%) were most frequently isolated pathogens in urine cultures. The distribution of microorganisms grown in urine cultures is shown in Table 2.

Bacteria	Pre pandemic	Pandemic
Dacteria	n (%)	n (%)
Escherichia coli	73/164 (44.5)	91/164 (55.5)
Klebsiella penumoniae	37/81 (45.7)	44/81 (54.3)
Enterobacter cloacae	8/21 (38.1)	13/21 (61.9)
Pseudomonas aeruginosa	13/34 (38.2)	21/34 (61.8)
Enterococcus faecium	8/19 (42.1)	11/19 (57.9)
Proteus mirabilis	18/48 (37.5)	30/48 (62.5)
Staphylococcus aureus	0/3 (0)	3/3 (100)
Morganella morganii	0/5 (0)	5/5 (100)
Serratia marcescens	0/5 (0)	5/5 (100)
Enterococcus faecalis	4/22 (18.2)	18/22 (81.8)
Enterobacter aerogenes	1/3 (33.3)	2/3 (66.7)
Klebsiella oxytoca	1/4 (20)	3/4 (80)
Citrobacter freundii	0/2 (0)	2/2 (100)
Staphylococcus saprophyticus	1/2 (50)	1/2 (50)
Citrobacter koserii	0/2 (0)	2/2 (100)

Table 2. The distribution of microorganisms grown in urine cultures.

Urinalysis

Urinalysis was performed on 1385 (93.1%) children and leukocyte positivity was determined 20.1% (279/1385). A significant correlation was found between leukocyte positivity and growth in urine culture (p=<0.001). Moreover, a statistically significant correlation was observed between nitrite positivity detected

in urine analysis and growths in urine culture (p=<0.001). Accordingly, bacterial growth was detected in 90.9% (30/33) of the nitrite-positive patients.

Biochemical and Hematological Analysis

Complete blood count was requested in 171 (41.1%) children with UTI. The leucocyte (white blood cell-WBC) parameter was high in 85 (49.7%) of the children. The mean WBC values were 10.66 ± 4.56 (between 3.40-26.70). There was no significant correlation between the mean WBC levels of the patients with and without growth in the urine culture (p=0.104). In addition, C-reactive protein (CRP) test was requested from 160 (38.5%) of the patients with growth in their urine cultures, and CRP was found to be high in 113 (70.6%) of them. No significant correlation was found between the elevation of CRP and the presence or absence of growth in the urine culture (p=0.527). Table 3 shows the WBC, CRP, urea and creatinine values in patients who had growth and no growth. Blood urea test was performed on 425 (28.5%) patients and 36 (8.5%), 360 (84.7%) and 29 (6.8%) of them had low, normal and high urea levels, respectively. The creatinine test was evaluated in 428 (28.8%) patients and 8 (1.9%) of them had low, 385 (90%) had normal and 35 (8.2%) had high creatinine levels.

	Growth	No growth	p value
WBC	10.66±4.56	9.96±4.93	0.104
CRP	2.20±4.59	2.49±5.17	0.527
Urea	21.91±18.84	23.10±11.48	0.437
Creatinin	0.49±0.12	0.59±0.60	0.090

Table 3. WBC, CRP, urea and creatinine values in patients who had bacterial growth and no growth.

*WBC: White blood cell; CRP: C-reactive protein

In Table 4, the distribution of children with bacterial growth in urine culture according to their gender before and during the pandemic, is given.

	Pre pandemic	Pandemic	p value
	n (%)	n (%)	
Male	46 (28)	90 (36)	0.103
Female	118 (72)	162 (64)	
Total	164 (100)	252 (100)	

Table 4. The distribution of children with bacterial growth in urine culture.

In Table 5 Resistance status of Enterobacteriaceae family, a bacterium before and during the COVID 19 pandemic is given:

Antibiotic	Before pandemic	During pandemic	p value
Amikacin	1/137 (0.7)	4/196 (2.0)	0.316
Ampicillin	97/122 (79.5)	110/176 (62.5)	0.001
Cefixime	35/121 (28.9)	41/180 (22.8)	0.229
Ceftazidime	27/127 (21.3)	34/196 (17.3)	0.380
Ceftriaxone	30/129 (23.3)	31/186 (16.7)	0.146
Ciprofloxacin	22/122 (18.0)	14/190 (7.4)	0.004
Ertapenem	11/132 (8.3)	4/185 (2.2)	0.011
Gentamicin	14/132 (10.6)	12/196 (6.1)	0.140
Imipenem	4/131 (3.1)	9/192 (4.7)	0.463
Meropenem	6/136 (4.4)	2/194 (1.0)	0.056
TZP	8/132 (6.1)	18/193 (9.3)	0.287
SXT	39/123 (31.7)	55/196 (28.1)	0.487
ESBL	30/137 (21.9)	35/197 (17.8)	0.348

Table 5. Resistance status of Enterobacteriaceae family.

CHAPTER V

DISCUTION

Urinary Tract Infection (UTI) was identified via the incidence of a contagion in the sterile posterior urethra, bladder, ureters, renal pelvis, or renal parenchyma (Evans, 2006). If a urine culture is positive, epidemiological research on UTIs can proceed. Furthermore, to pyuria (On microscopy, more than five white cells per high-powered field.) and bacteriuria, the conventional diagnostic of UTI (100,000 cfu/ml) is used A paediatric urinary tract infection diagnosis. Both pyuria and bacteriuria are strongly indicative of a urinary tract infection (UTI) (Watson, 2004).

After screening and studying the urinary tract infection disease in children for 1488 children at the NEU Hospital in North Cyprus, pre and during the COVID- 19 pandemic together .The general prevalence of UTI was calculated in the period between 1.1-2019 to 31.7.2022 The results indicate 416/1488 children by bacterial growth of the urine culture of UTI, which is 28 % of the children who were studied, while the number of children who not bacterial growth of urine culture in Urinary Tract Infection 1072/1488, or 72.% of those studied in Northern Cyprus.

In Jordan, a study was showed to determine the prevalence of UTI in children in the age group from 0-16 years, where the prevalence rate was 14.2%, and In another study conducted in Sudan to determine the prevalence of UTI in child, the incidence rate is 29% between child aged 2-15 years (Alhaj & Bayoumi, 2020).

A results in our study were higher than their results in Jordan, because our study was more comprehensive, as the study period was longer and the number of samples was greater, in addition to the presence of the results of laboratory analyzes of patients ... while their results in Sudan were higher than our results, and this may be related to the fact that the spread of Urinary tract infection varies greatly by region in developing countries, depending on the location and demographics of the country and the level of health care is underdeveloped in developing countries. The percentage of UTI in child in Northern Cyprus pre a COVID- 19 pandemic was calculated from the date of 1.1.2019 to the date of 29.2.2020. The number of children suffering from urinary tract infection was 164/414, or 25%. While the percentage of children suffering from urinary tract infection during the COVID- 19 pandemic in the period from 1.3.2020 to 21.7.2021 was 252/414, which is equivalent to 30.3% in Northern Cyprus.

The cause of the increase in urinary tract infection in child during the COVID- 19 pandemic is due to the influence of the COVID- 19 pandemic on the children lifestyle significantly, a most important of which is physical activity. The closure of schools and play areas on the children movement and thus affected the children immune system and the children ability to resist pathogens greatly.

Where the movement of the child and sports are important, where movement and sports in children strengthen the immune system and activate its cells and make it in a state of stimulation by sending more immune compounds to the blood to resist bacteria and viruses and also works to stimulate blood circulation and a greater amount of oxygen is delivered to the brain and thus the pituitary gland is activated Responsible for the happiness hormone, the level of stress and depression in children decreases which are considered as a reason for weakening the immune system.

In addition to that, movement and sports in children increase the percentage of stem cells in the blood and raise the rate of tissue regeneration. The amount of oxygen produced during movement and sports work on reviving dormant stem cells, their division and multiplication, and the production of new stem cells that resist bacteria and viruses. In addition, sleep has become in children My randomness is unorganized and insufficient ... as the children are not sleeping enough. They stay up late on TV and video games, and when they do not sleep enough, the body does not produce hormones that help and rejuvenate the vital system, thus weakening the functions of the immune system.

The influence of the COVID- 19 pandemic has also been on me. Feeding the children, so children sleep late and do not wake up in the morning, and thus neglect breakfast, which is important for the growth of the child In addition to the consumption of fast food, soft drinks, processed foods and crackers, which greatly affects the ability of the immune system to resist diseases.

The second objective of this study is to identification the bacteria that causes of UTI in child a North Cyprus.

E. coli was the utmost communal cause of UTI a 39.4% of children, followed by *Klebsiella pneumoniae* with 19.5%, *Proteus mirabilis* with 11.5% is most frequently isolated pathogen in urine culture.

In a study conducted in Israel, Gram (-) bacteria was to blame for 98% of causing Urinary tract infections in children. *Escherichia coli* was responsible for 87% of urinary tract infections, after that *K. pneumonia* with 4% and *P. mirabilis* at 4%. This research comprised 151 child under the age of 14 years (*[Community Acquired Urinary Tract Infection among Hospitalized Children in Northern Israel*, n.d.).

Enterococcus spa. *Escherichia coli,., and Morganella morganii Proteus spp* are a highest isolated bacteria child in 1-18 years old (Lewczyk et al., 2001).

Out cases in the age range of 1.5-65 years (mean age 28.2) participated in a prospective study in northwest Iran over a 14-month period to collect 5136 urine samples to investigate the causative agents of UTI and their antimicrobial susceptibility. The causal 47agents in the age ranges included in our research were: To put this into perspective: in the 0–9-year-old age range, the utmost communal pathogens were *E. coli*, 80 percent; *Klebsiella*, 11 percent; *Enterobacter*0% *Proteus* 1.3 percent; *P. Aeruginosa*, 6.7 percent; *S. Aureus*, 1.3 percent; *S. Saprophyticus*, 4 percent; whereas the 10–19-year-old age range, the most common path *E. coli* 78.2%, *Enterobacter spy* 0%, *K. Pneumonia spp* 11.5%, *Pseudomonas aeruginosa* 1.3%, *Proteus spp* 1.3%. *Staphylococcus Saprophyticus* 6.4% *Staphylococcus aureus* 0%, (Farajnia et al., 2009).

Urine samples from patients under the age of 17 were obtained in an emergency department by researchers at the University of Florida in the United States and cultures with more than 100,000 cfu/ml of a solo organism were grown on a MacConkey and blood agar. Each patient with no signs or symptoms of a UTI were excluded. 81 patients satisfied the inclusion criteria for this study after all exclusions were made 89% percent of these patients were infected with E.coli, Proteus1.2% and Citrobacter 1.2%, whereas 3.7 percent were infected with Klebsiella and Enterococcus respectively (McLoughlin & Joseph, 2003).

In Jordanian research of 121 paediatric patients with recurring or severe urinary tract infections, *E. coli* is shown to be the furthermost communal bacterium in 71% of cases of recurrent Urinary tract infection and a 47% of cases of complicated UTI. A higher prevalence of *Proteus, Pseudomonas, and Candida Spp.* was found in individuals with complex Urinary tract infection (Younis et al., 2009).

Ur pathogens responsible for UTI in the age range of 5 to 15 years were as follows in a Jordanian study conducted by the Princess Haya Hospital Jordan's department of paediatrics: More than two-thirds (76%) of infections are cause by *E.coli*, followed by *K. Pneumonia* (13%) and *Proteus* (6.5%), followed by *Staphylococci* (2.2%), and *Pseudomonas* (2.2%) (*Al-Momani: Microbiological Study of Urinary Tract... - الباحث العلمي من* Google, n.d.).

In our study, result of Urine analysis (Microscopic examination) was calculated. To search for leucocytes in the urine sample under the microscope, Urine analysis was conducted in our study in 1385 children, or (93.1%), where we noticed a correlation between the presence of positive leukocyte and bacterial growth in urine culture, where the percentage was (20.1%). A correlation between an increase in leukocyte and a positive culture is due to the fact that when inflammation or infection occurs along the urinary tract, when inflammation occurs, the body sends immune cells to the urinary system to find out the infection so the leucocyte shows in urine. Where bacteria are one of the most communal reasons of inflammation or infection in the

urinary system. Therefore, there are a relationship between the positive urine culture and the presence of positive leukocyte in the urine.

Also in urinalysis, there was a relationship between positive nitrates and positive urine culture in 30/33 children, or 90.9% of the children. Urine that contains nitrites, indicator of bacterial illness in the urinary tract, indicates that you have an infection. A urinary tract infection is the most common term for this (UTI). Nitrates are converted to nitrites by an enzyme found in some bacteria. Nitrites in urine are therefore an indication that you may have a UTI.

Therefore, there was an association between a positivity of nitrates and a positivity of urine culture due to the conversion of nitreates to nitrites due to bacteria, which is a strong indicator of its presence and its occurrence in a UTI.

A fast diagnosis for UTI can be made using urine leukocyte nitrite and bacteria count per high-power field, which perhaps useful if urine culture is unavailable. If at all possible, aberrant urinalyses could be accustomed determine the course of an experiential antibiotic treatment. This examination was very important as it is an indication of a defect, inflammation or infection in the urinary system and is also used to monitor the effectiveness of the therapeutic process with antibiotics.

In our study the high or normal of the CRP test was calculated in the samples in which the test was used in 160(38.5%) samples of patient grow in urine culture, 113(, 70.6%) samples were is high, we found no significant correlation found between elevation CRP with growth bacteria in urine culture.

In our study, in calculating the high and normal of the WBC in CBC test, where the number of samples that were used in the study was 171(41.1%) samples for children with UTI, the WBC parameter was high in 85(49.7%) and the mean WBC value is 10.66 ± 4.56 (between 3.40-26.70). so, there was no significance between mean WBC level with bacterial growth in urine culture.

According to a finding of this investigation, CRP and WBC were appeared to be neither extremely sensitive nor highly special for the detect of UTIs or the place of their origin. An additional set of testing guarantees that a UTI is detected and that it is located. For the diagnosis of a UTI and the location of the infection, tests in the lab, such as a panel of urinary markers (such as urinary albumin, urine urea nitrogen, urine interleukin-6, urine procalcitonin, and so on) is required, as well as a via medical history and physical examination. It is also possible to distinguish an upper UTI from a lower one by using biomarkers. Since the diagnosis of UTIs can be difficult, we recommend the usage of additional and more additional tests alone or in combination.

Simple, non-invasive assays such as the CRP and peripheral WBC count are used to diagnose invasive bacterial infections and to estimate the severity of a UTI. Patients with acute pyelonephritis have higher levels of WBC and CRP, according to some research, than those with acute cystitis. Some research, on the other hand, does not stress the role of haematological variables in identifying upper from lower UTIs.

The Complete Blood Count (CBC) and C-Reactive Protein (CRP) TEST no significant with growth bacteria in urine culture that referred to CBC and CRP examination are two general inflammatory examinations inside the body, meaning when inflammation occurs anywhere inside the body, their value increases. They are affected by any inflammation inside the body. Therefore, they cannot be considered as accurate examinations for diagnoses UTI and determining a location of the infection. There two examinations are considered a general indicator of the occurrence of inflammation. In the body and the severity of the inflammation, but they cannot determine the location and cause of the inflammation.

White Blood Cell (WBC) IN CBC TEST and CRP TEST is an important indicator of the presence of inflammation in the body. It is general evidence of the presence of inflammation, but it does not determine the location of inflammation, but it can be used to monitor inflammation during treatment. If the patient is improving or worsening, it is used to monitor inflammation. In our study, we also studied urea and creatinine and their relationship with the positive urine culture .We found that there is no relationship between urea and creatinine test with positive urine culture. The urea test was performed in 425 patients. The urea test was high in 29 (6.8%), normal in 360 (84.7%), and low in 36 (8.5%). While the creatinine test was performed in 428 patients, the serum creatinine was elevated in 35 (8.2%), normal in 385 (90%), and low in 8 (1.9%).

These results are due to the fact that creatinine and urea have no relationship with positive urine culture. They rise only if an inflammation was in the upper urinary tract and the inflammation is complicated. But if the inflammation is in the lower urinary tract or uncomplicated, they are not affected.

Third in this research we wanted to see if there was any link between UTI and demographic factors such as gender.

In our study to find the related between UTI in children and gender pre and during pandemic, we found that the number of males children with bacterial growth in urine culture that before pandemic 46 (28%) and in pandemic is 90 (36%), while the number of females children with bacterial growth in urine culture that before pandemic is 118(72%) and in pandemic is 162 (64%).

During the COVID 19, the incidence of bacteria growth is increased based on urine culture, so the increase in male children and female children together for bacteria growth on urine culture.

The high rate of bacterial infection in female children was higher than that of male children before and during the COVID 19 pandemic in both cases BUT the increase in the percentage of disease among males was higher compared to the increase in the percentage of females after COVID 19, where in males the percentage increased from 28% to 36%, while in females it decreased from 72% to 64% and this is due to the fact that the number of male children who attended the hospital during COVID 19 was More than male children who attended hospital before COVID 19

Pandemic. This means that both genders, female children and male children have been affected by the COVID 19 pandemic.

Girl's UTI risk was 8% throughout childhood, while boy's risk was 2%, according to the 7th module of Paediatric UTI from the Department of Urology and the University of Wisconsin School of Medicine (Alhaj & Bayoumi, 2020).

As it is the main reason for the increase in UTI in girls more than boys, the length of the urethra is shorter in females, which makes it easier for bacteria to reach the urinary system.

In our research of the distribution of bacterial resistance to antibiotics before and during the COVID 19 pandemic, we found a correlation between antibiotic resistance and the COVID 19 pandemic in the following antibiotics:

The resistance to the antibiotic Ampicillin before the COVID 19 pandemic was 120/97 (79.5%), and during the COVID 19 pandemic it was 176/110 (62.5%). P value is 0.001. While The resistance to the antibiotic Ciprofloxacin before the COVID 19 pandemic was 22/122 (18.0%), and during the COVID 19 pandemic it was 14/190 (7.4%). P value is 0. 004.In addition the resistance to the antibiotic Ertapenem before the COVID 19 pandemic was 11/132 (8.3%), and during the COVID 19 pandemic it was 4/185 (2.2%). P value is 0.011. It shows table 5

The reason for the high resistance to the three antibiotics before the pandemic is that the number of patients who were tested for antibiotic susceptibility test was higher than the patients during the pandemic.

And perhaps also, we can say that these antibiotics were poorly used in the past with patients who were before the COVID 19 pandemic, so their resistance was high.

When looking at children younger than 14 years old who were treated at the Queen Alia Military Hospital / Jordan from January 2006 to April 2007, a retrospective

analysis was conducted. A high percentage of Escherichia coli isolates (59.9%) were resistant to Ampicillin, sulfamethoxazole, and trimethoprim (TMP-SMZ).

Common antimicrobials commonly use in the treat of UTIs have varying levels of resistance to E. coli, with ampicillin having the highest rate of resistance (74.2 percent), after that co-trimoxazole (61.3 percent). Nitrofurantoin had the lowest rate of resistance (2.2 percent), followed by amikacin (4 percent), ceftriaxone (7.5 percent), and ciprofloxacin (7.5 percent) (12 percent) (Yüksel et al., 2006). In another study, 54 percent of the respondents showed resistance to sulfamethoxazole and trimethoprim (55.2%), gentamicin (24.9%), and cefazolin (82.2%). Trimethoprim-Sulphamethoxazole and cephalothin, on the other hand, are more effective against a wide range of pathogens than ampicillin (Ashkenazi et al., 1991).

CHAPTER VI

CONCLUTION AND RECOMMENDATIONS

Our study, which we conducted at the Near East University Hospital about urinary tract infection in children before and during the COVID -19 pandemic, concluded several things.

Firstly. The prevalence of Urinary Tract Infection (UTI)in children in North Cyprus is 30%.

Secondary. The prevalence of Urinary Tract Infection (UTI) in child during the COVID- 19 pandemic increased to 30.3%, where it was 25.0% before the COVID-19 pandemic, meaning that the percentage of UTI in children increased to 5.3%.

Thirdly. Female children in North Cyprus are more likely to have a UTI than male child.

Fourthly. *E. coli* is the most communal UTI pathogen with an average of 39.1%. followed by *Klebsiella pneumoniae* (19.5%) and *Proteus mirabilis* (11.5%).

fifthly A correlation between an increase in leukocyte and NITRITE in urine analysis with a positive culture of bacterial growth.

sixthly NO correlation between UREA.CRETAINEAIN.CRP WBC PARAMETERIN CBC TEST with a positive culture of bacterial growth.

Seventhly A correlation between an increase resistant antibiotic of Enterobacteriaceae family with COVID 19 pandemic.

6.1 Recommendation

We recommend in our study on many things, including:

1.Providing places for child during the period of the COVID- 19 pandemic within the health conditions and standards that allow children to move and play sports.

2. Educating parents about proper child care in terms of nutrition and proper behaviours for healthy habits during the COVID- 19 pandemic.

3. Encouraging doctors to advice their patients to do a urine culture test to accurate diagnosis of UTI infection.

4. Making TV programs that talk about how to take care of a child during the COVID-19 pandemic.

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APPENDICES

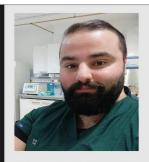
Appendix A

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Curriculum Vitae



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Microsoft Word	•	•	•	•	•	
Microsoft Excel	•	•	•	•	•	
Microsoft Powerpoint	•	•	•	•	•	

LANGUAGES

English Arabic Turkish

••••

CERTIFCATE

- 1 Immunological Test
- 2-RadiAnt Dicom Viewer
- 3- General Medicine
- 4-GIT Pathology
- 5- Kidney Function Test
- 6- Cancer
- 7- Hepatobiliary and pancreas pathology
- 8-Respiratory system pathology
- 9- Blood and lymphoreticular tissue pathology
- 10- CNS pathology
- 11-Endocrine pathology
- 12-Bone pathology
- 13- Anatomy of lymphatic system

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Egaft

Ethical Approval

YAKIN DOĞU ÜNİVERSİTESİ BİLİMSEL ARAŞTIRMALAR ETİK KURULU

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Yakın Doğu Üniversitesi Tıp Fakültesi öğretim üyelerinden Doç. Dr. Ayşe Sarıoğlu'nun sorumlu araştırmacısı olduğu, YDU/2022/99-1483 proje numaralı ve **"The Impact of COVID-19 Pandemic on Urinary Tract Infection Rate in Children"** başlıklı proje önerisi kurulumuzca değerlendirilmiş olup, etik olarak uygun bulunmuştur.

2-4 P a

Prof. Dr. Şanda Çalı Yakın Doğu Üniversitesi Bilimsel Araştırmalar Etik Kurulu Başkanı

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