TURKISH REPUBLIC OF NORTH CYPRUS
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EXTENDED-SPECTRUM BETA LACTAMASE RATES OF E. COLI FROM URINARY TRACT INFECTION IN RIZGARI HOSPITAL, ERBIL, IRAQ

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A THESIS SUBMITTED TO THE GRADUATE SCHOOL OF HEALTH SCIENCES

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BY

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DECLARATION

Hereby, I declare that this thesis study is my own study, I had no unethical behaviors in all stages from planning of the thesis until writing there for, 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 behavior of breeching patent rights and copyright infringement during the study and writing of this thesis

Mohamed Hussein Mohamed ALI

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LIST OF ABBREVIATIONS

UTI	**Urinary Tract Infection**
CAUTI	**(Catheter Associated Urinary Tract Infection**

ESBL	**Extended Spectrum Beta Lactamases**
UPEC	**Uropathogenic *E. coli***
AUC	**Acute Uncomplicated Cystitis**
IS	**Insertion Sequences**
Tn	**Transposons**
EHEC	**Enterohemorrhagic *E. coli***
EPEC	**Enteropathogenic *E. coli***
ETEC	**Enterotoxigenic *E. coli***
EIEC	**Enteroinvasive *E. coli***
EAEC	**Enteroaggregative *E. coli***
DAEC	**Diffusely adherent *E. coli***
UPEC	**Uropathogenic *E. coli***
NMEC	**Neonatal meningitis *E. coli***
TLRs	**Toll-like Receptors**
MPL	**Monophosphoryl Lipid**
GC	**Generation Cephalosporins**
PCR	**Polymerase Chain Reaction**
CA-FSM	**Comite Antibiogramme Francaise Societe Microbiologie**
EUCAST	**European Committee on Antimicrobial Susceptibility Testing**
DDST	**Disc Diffusion-Based Screening,**
IPDD	**Inhibitory Potentiated Disc Diffusion**
CLSI	**Clinical and Research facility Standards Founded**
NaCl	**Sodium Chloride**
CLED	**Cystine Lactose Electrolyte-Deficient Agar**
AES	**Advanced Expert System**

ÖZET

Mohamed Hussein Mohamed ALI

İrak Erbil, Rizgari Hastanesi'ndeki idrar yolu enfeksiyonu olan hastalardan izole edilen E. coli'lerin geniş spektrumlu beta laktamaz oranları. Yakın Doğu Üniversitesi Sağlık Bilimleri Enstitüsü, Tıbbi Mikrobiyoloji ve Klinik Mikrobiyoloji Programı, Yüksek Lisans Tezi, Lefkoşa, 2020

İdrar Yolu Enfeksiyonları (İYE), küresel olarak ciddi bir sağlık olarak kabul edilir. *E. coli,* piyelonefrit ve sistite neden olan en çok tekrarlanan enfeksiyona neden olsn patojendir. İYE ile ilişkili vakaların% 85-90'inin etkenidir. Hastane kaynaklı İYE'lerin yaklaşık% 50'sini. Toplum kaynaklı İYE'lerin yaklaşık% 85'i nin etkeni E. colidir. ESBL'ler,bazı bakteriler tarafından üretilen, geniş spektrumlu sefalosporinlere, aztreonam ve oksimino p-laktamlara direnç sağlayan ve klavulanik asit, sulbaktam ve tazobaktam gibi p-laktamaz inhibitörleri tarafından inhibe edilen enzimler grubudur. Çalışmamız, Erbil şehrindeki Rizgari Eğitim Hastanesi laboratuvarında idrar kültürü için ürolog tarafından sevk edilen 192 hastayı içermektedir. Hastalar poliklinik ve hastanede yatanlar olmak üzere iki gruba ayrıldı. Klinik olarak idrar yolu enfeksiyonu olduğu düşünülen hastalardan standart orta akım "temiz yakalama" yöntemi ile idrar örnekleri alındı. Bakterilerin izole edilmesi ve idantifikasyonunda diferansiyel kültür besiyeri olan CLED agar kullanıldı ve Vitek 2 ile de değerlenirildi.

Örneklerin % 64,1'i ayaktan tedavi gören,% 35,9'i ise hastanede yatan hastalardan alındı. Toplamda % 30,2'si erkek ve % 69,8'i kadındı. % 18.2'sinde E. coli üredi% 81.8'inde ise üreme olmadı

E. coli üreyen hastaların % 8.9'u ESB pozitif ve % 9.9'u ESBL negatif olduğu saptandı.

Çalışmamız, Erbil-Irak'ta ESBL üreten E. coli prevalansının olduğunu göstermiştir. ESBL üreten E. coli için risk faktörleri, uzun süreli bir bakım tesisinde tedavi görme,

üriner kateterizasyon, olası önceki antibiyotik kullanımı, ileri yaş, cinsiyet ve hasta tipi idi. Bu nedenle, doktor bu yüksek riskli hastaların farkında olmalı ve ESBL üreten E. coli'ye bağlı ölüm oranını en aza indirmek için başlangıçtaki uygun ampirik antimikrobiyal tedaviyi hedeflemelidir.
Anahtar Kelimeler: İdrar yolu enfeksiyonu. Escherichia coli, Genişlemiş Spektrumlu Beta-Laktamaz,

ABSTRACT

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Extended-spectrum beta lactamase rates of *E. coli* from urinary tract infection isolated from patients in Rizgari Hospital, Erbil, Iraq. Near East University Institute of Health Sciences, M.Sc. Thesis in Medical Microbiology and Clinical Microbiology Program, Nicosia, 2020.

Urinary tract infections (UTIs) are considered a serious health affecting problems globally. And the *E. coli* is most repeated bacterial pathogen that causing pyelonephritis and cystitis. *Escherichia coli* (*E. coli*) is related to 85–90% of the cases associated with UTIs, and represents about 50% of hospital-acquired UTIs. Nearly 85% of community-acquired UTIs. ESBLs are group of enzymes which confers resistance to extended spectrum cephalosporins, aztreonam, and oxyimino β-lactams and are inhibited by β-lactamase inhibitors such as clavulanic acid, sulbactam, and tazobactam. Our study included (192) patients, divided to two groups (outpatient and inpatient) referred by urologist for urine culture at laboratory of Rizgari Teaching Hospital in Erbil city. urine

samples were taken (by standard mid-stream “clean catch” method) from patients with clinical suspected urinary tract infection. CLED agar is used as a type of differential medium optional to growth better of bacteria and especially for diagnostic pathogenic bacteria in urinary tract, in addition Vitek 2 used in bacterial evaluation. Among the patients that included to this study 64.1% them were out patients and 35.9% of them were in patient, 30.2% was male and 69.8% was female. 18.2% were diagnosed as *E. coli* 81.8% of other was free of *E. coli* infection. Among those patients that have *E. coli* 8.9% of them were ESBL positive and 9.9% of them were ESBL negative. In addition to 81.3% were Non-ESBL. Our study showed the prevalence of ESBL-producing *E. coli* in public of Erbil-Iraq. Independent risk factors for ESBL-producing *E. coli* were, residence in a long-term care facility, urinary catheterization, possible previous antibiotic use, older age, gender and type of patients. Therefore, the physician should be aware of such high-risk patients and target the initial appropriate empirical antimicrobial therapy to minimize the mortality of those with infections due to ESBL-producing *E. coli*

Keywords: Urinary Tract Infection, *Escherichia coli*, Extended Spectrum beta lactamase

CHAPTER 1

1. INTRODUCTION

1.1. Background

The urinary tract of a human being, is a hollow organ which is highly prone to infection. Its main function is to first collect, and then transport, store, and finally eliminate urine out of the body regularly. The whole process is highly controlled. And as an end result, the human body makes sure that the products of metabolism and toxic substances are entirely removed by the kidneys through the urinary tract. Urine flowing in the upper part of the tract and being eliminated from the lower part, has an important role in cleaning and removing the microbes which might have invaded the tract already. At the time that urine is not being eliminated, the urinary tract is like a closed system, in which microorganisms will not be able to reach it. Proximally, the urinary tract is made up of; papillae, pelvis, ureters, bladder, and urethra. Each of which has a distinct function and a particular anatomical feature.

1.2. Epidemiology

Urinary tract infection or UTI, could be one of the very usual bacterial infections. 150 million people will be victims of this infection annually. A few years ago in the US, about ten million patients visited clinics for UTI symptoms, and two to three million presented to the ED. Health managements and losing the ability to work costs the UTI patients about four billion every year. This infection is one of the noteworthy causes of agony in male infants, all females and old men. Complications of UTI may include;

recurrent infections, pyelonephritis, permanent kidney damage, antibiotic resistance due to regular use of antibiotics. Some studies show:

- low rates of ESBL-producing Enterobacteriaceae which accounts about 3 to 8 percent., seen in: Singapore, Japan, and Sweden.

- Higher rates are noted in:

- Portugal - 34 percent,
- Italy - 37 percent
- USA - 44 percent.
- Latin American countries – 30 to 60 percent.
- Turkey – 58 percent
- Saudi Arabia - 8 to -38 percent
- Kuwait – 31 percent
- United Arab Emirates – 41 percent

The most common bacterial infection in children, is considered to be UTI. During the first 6–12 months of life, up to 30% of infants and children who experience recurrent infections have UTI. Symptoms vary among patients in many ways. For instance, there is a higher incidence among very young infants, especially in male. *Escherichia coli* is known to be the most common cause of the infections, however, in the first year of life, *Enterobacter*, *Klebsiella pneumonia*, *Pseudomonas*, and *Enterococcus* are much more frequent than later in younger age, with a higher risk of urosepsis compared with adulthood. Main causative factors for UTI in the community are age, diabetes, history of UTI, and sexual activity. Records show elevation in UTIs with age in men. In contrast, with women, there is a decrease in UTIs at middle ages, but an increase after the sixties.

Among people who are not committed to an institution, the incidence is about 14 percent in women and 10 percent in men. There is a record showing that one third of women who are older than 85, are diagnosed within one year, and two thirds are diagnosed in 5 years. History of previous UTI in young women, could be associated with an increased risk of developing a CAUTI (Catheter Associated Urinary Tract Infection). A study shows that after menopause and up to 75 years old, subsequent UTIs with a frequency of more than five times was the strongest factor of a new UTI. A major, independent, confirmed risk factor for UTI is having sexual intercourse in the previous 48 hours, in women of ages. A recent study carried out among young women presented that the rate of physical intercourse, is strongly proportional with the increased incidence of this type of infection.

1.3. Etiology

Urinary tract infections (UTIs) are considered a serious health affecting problems globally. The most common UTI bacteria that affect human beings are *K. pneumonia, E. coli, E. faecalis, P. aeruginosa, S. marcescens, S. aureus, Proteus mirabilis* and *S. saprophyticus*. *E. coli* represents about 50% of hospital-acquired UTIs and nearly 85% of community-acquired UTIs, and. Considering other factors like gender, age, urological instruments and immuno-suppression probably affect the spreadiest of UTIs. One of the most dangerous health risks is Catheter-associated UTIs which causing 34% of all infections associated in healthcare. The outgrowth of broad-spectrum beta-lactamases were dangerously affecting the experimental use of ciprofloxacin and cephalosporins. There are various mechanisms by which Microorganisms use to develop resistance to medications, as in horizontal gene transfer, the chromosome level when foreign recombining the DNA of the bacteria, also genetic material alteration. The Resistance of microorganisms pattern varies among different countries, governorate to governorate,

small hospitals compared to large hospitals and even community to hospital (Sabir, Anjum et al. 2014).

In the city of Erbil, the problem of antibacterial resistance might be due to overuse and misuse of antibiotics as an experimental therapy for UTIs. A higher resistant in Multi-drug showed to be less prevalence among non-ESBL-producers than ESBL-producing *E. coli*. Other findings were similarly reported among several recent studies. In fact, ESBL, which produce by organisms of *Enterobacteriaceae's* family were basically considered as MDR started in the hospitals. The last few years ago an increasing of such ESBL-producers were detected in the settings of outpatient, specifically those connected to UTIs, thus having choices to reduce treatment for a restricted number of anti-biotics. It's difficult to Treat ESBL-producing organisms infections. This is due to its opposition to other agents of antimicrobial coded by plasmids, and also associated with the opposition to the extended-spectrum cephalosporins itself (Aka and Haji 2015). When dealing with UTI causing pathogens, it's essential to test for their resistance to commonly prescribed antibacterial medications in clinical setups to enhance the effectiveness of experimental treatment. The goal of current study is to find out the opposition form of *E. coli* isolates and to highlighting the bacterial etiology of UTIs (Sabir, Anjum et al. 2014).

1.4. UTI Pathogenesis

Pyelonephritis is referred to the infection that attack the upper urinary tract while cystitis is referring to the lower urinary tract infections. The most repeated bacterial pathogen that causing pyelonephritis and cystitis is Escherichia coli (*E. coli*), and it's related to 85–90% of the cases. The originate of Uropathogenic *E. coli* (UPEC) are known to come through the fecal flora, then spreading in the perineum, then later to entering the bladder

from the urethra. Investigation extensively of UPEC pathogenesis intermediate cystitis has been done from the two perspective of the pathogen and host .The interested reader can referred to the reviews recently addressed on this topic (Becknell, Schober et al. 2015). UTI's are not only highly recurrent, but also common. Specifically, the elderly, women that sexually active, and also pre-pubertal children are highly exposed to chronically recurrent UTI, which results negatively affecting on the quality of life and an increased use of antibiotics. About 20–30% with an initial UTI of adult women will experience a recurrence within 3–4 months. About one in three children before the age of one experiencing a UTI will also experience a recurrence within the next three years, in fact within a few months about 18% will have a recurrence (O'Brien, Hannan et al. 2016).

1.5. Complicated and Uncomplicated Urinary Tract Infections

A complicated UTIs can be identified as UTIs associated with other factors which compromising the host's defense system or the urinary tract , and those factors include the obstruction of the urinary tract, neurological disease induced urinary keeping, transplantation of renal, pregnancy, immunosuppression, renal failure and the being of foreign bodies presence like in residency catheters, calculi or different drainage devices. (Flores-Mireles, Walker et al. 2015). While uncomplicated urinary tract infections (UTIs) were have the highest occurrence infections that encountered among outpatient settings. And this is why antibiotics are prescribed as they are the most common reason. After Infections of the respiratory tract. Uncomplicated UTIs consist both acute uncomplicated cystitis (AUC) and also acute uncomplicated pyelonephritis (AUP). Lately, because of the resistance degree of uncomplicated UTI caused the pathogens to rise significantly. Considering this rising, the world of medicine has turned to be more cautious to the direct effects of antibiotics that applied systemically. The use of variety antibiotic agents is exerting a different selective pressure on both the innocent observer botany at the same

site and the infection-causing pathogens. Understanding this fact has led to re-evaluation an internationally the therapeutic recommendations of antibiotics in uncomplicated UTI (Wagenlehner, Hoyme et al. 2011).

1.6. *E. coli* Classification

There are many subdivision systems of *E. coil*. Here, we are mentioning the common subdivision that is not in accordance of serotype relatedness but based on surface antigens O antigen part of lipopolysaccharide layer H. However, the only important one to be mentioned is the serogroup, for example, the O-antigen. The number of serogroups that are identified recently are around 190. In the laboratory, the strain that is noticeable is usually associated to the alternation that constrains creation of an O antigen. Taxonomically speaking, the kingdom and domain of both bacteria and *Escherichia coli* exactly matches and the reason is this fellow are cellular microorganisms. To be continued, the phylum of both proteobacteria and *Escherichia coli* matches and the reason is this group fellows are Gram-negative bacterium with having membrane outside that is made of lipopolysaccharides mainly. However, in terms of class**,** the class of both the Gammaproteobacteria and the *Escherichia coli* matches since this group fellows are anaerobic G-ve bacterium, and also the Enterobacteriales and bacteria *Escherichia coli* order fits well into each other and this is because this set fellows are anaerobic G-ve bacterium with rod-shapes. Moreover, the Enterobacteriaceae and the family *Escherichia coli* are matched since it has motile capacity via peritrichous flagella that can expand fine at 37oC, is Catalase positive, Oxidase negative, and diminishes nitrates. Furthermore, the genus of both *Escherichia coli* and *Escherichia* matches because fellows of this group are taking immediate advantages and it settles in the mammal's colonic area, the species bacteria are one of five ones known under the Genus Escherichia. The natural actions that mark E. coli measured exceptional (owns lysine decarboxylase, ferments lactose, is Vogus-Proskauer negative, creates indole, doesn't raise on nitrate, and doesn't create

H2S) (http://bioweb.uwlax.edu/bio203/s2008/moder_just/classification.htm, Donnenberg, M)., (2013; Samaranayake, L., 2018).

1.7. Genetic and Chromosome-mediated resistance

There are two reasons that might lead to avoidance of Bacteria to drugs and those two reasons are chromosomal alteration ability and the achievement of movable genetic elements (transposons, plasmids, integrons) protecting resistance genes (Ojdana, Sieńko et al. 2018). In current years, it is determined that producing (ESBLs) short for extended-spectrum beta-lactamases has a great role in raising the *E. coli* resistance to third-generation cephalosporin. Aminoglycosides are types of antibiotics that are crucial and used to treat harsh contagions that are caused by Gram-negative bacteria, like *E. coli*. In the past couple of years, aminoglycoside ability resistance has been improved among ESBL-producing *E. coli*, (Ojdana, Sieńko et al. 2018). As mentioned above, both chromosomal ability of alteration and having moveable genetic elements (plasmids, transposons ,integrons) protecting resistance genes can result in Bacterial avoidance to aminoglycosides antibiotics. (Carattoli 2009, Ramirez and Tolmasky 2010).

1.8. Resistance of plasmid-mediated

Escherichia coli has gotten stronger and established a resistance to some different antibiotics. this action is happening mostly because of the efflux pumps intrusion and refusal genes that are placed on plasmids (Szmolka and Nagy 2013). Plasmid reflects the focal path in gaining and spreading of multi-resistant, which is either genotypically and phenotypically. Also, plasmids might be either nonconjugative or conjugative. Plasmid-encoded antibiotic resistance presently used related antibiotics classes, such as

Extended-Spectrum Cephalosporins, Aminoglycosides, and Fluoroquinolones.(Carattoli 2013).

1.9. Resistance of Transposon-mediated

(IS) short for Insertion sequences and (Tn) short for transposons are two distinct DNA segments. These two segments has ability to transfer themselves and related resistance genes to new places in the same DNA or different molecules of DNA and this action is done nearly arbitrary within one single cell. (Partridge, Kwong et al. 2018).

1.10. UPEC Virulence factors

commensal, *E. coli* rather stays safely to the colonic lumen and hardly causes disease since it is harmless. However, in the case of having weak immune hosts, or having the gastrointestinal barriers desecrated, even nonpathogenic-commensal strains of *E. coli* will have ability to cause contagion (Kaper, Nataro et al. 2004). It is important to know that some of *E. coli* strains may depart from their partners, starting an added pathogenic nature. These strains of *E. coli* require exact reasons (via DNA horizontal transfer of transposons, bacteriophages, pathogenicity island, and plasmids), that lets the bacteria having more capacity to lead to a wide-ranging illness with having capacity to adjust to new positions. The strains of pathogenic *E. coli* are generally categorized as these two which are enteric *E. coli* or (ExPEC) extraintestinal *E. coli.* ExPEC type *contained of Six* different *E. coli* "pathotypes," and they contain (EHEC) which is short for enterohemorrhagic *E. coli*. (EPEC) enteropathogenic *E. coli*, (ETEC) enterotoxigenic *E. coli*, (EIEC) enteroinvasive *E. coli*, (EAEC) enteroaggregative *E.*

coli, and (DAEC) diffusely adherent *E. coli*. The two well-known ExPEC pathotypes are (UPEC) short for uropathogenic *E. coli* and (NMEC) short for neonatal meningitis *E. coli.* There are numerous pathotypes of enteric *E. coli that* produce gastroenteritis, even though it is unusual for them to cause disease in the outside of the colonic area. Nevertheless, the extraintestinal *E. coli* strains can live and stay in the gut and not giving an outcome, but to not forget that they could distribute and attack other host places like the blood, and the vital nervous system, and of course causing infection (Bien, Sokolova et al. 2012).

1.11. Adhesion and colonization

The uninfected people's pee is clean because of the pee stream and healthy process of lithic corrosive. The normal stream of pee prevents microbes to settle in the renal system. Nevertheless, bond of the *Escherichia coli* till the layer of lining cells would make them to submerge the outcome of urine stream. For most harmful microbes, this is regarded to be the first step in the invasion procedure(Parvez and Rahman 2018). Anyhow the Bacterial attachment to the organism tissues is a complicated procedure that mostly engagement of a number of definite adhesins are included, in which all of them may work together at the same time or differently according to the stages of invasion (Ofek and Doyle 2012). Additionally the Pili are a collection of moderators between bacteria and biofilm establishment, or moderate distinct identification of invaded-cell receivers (Rendón, Saldaña et al. 2007). Mostly carbohydrates are receptors for fimbriae. their fimbriae make fimbriae first type, P pili , and flimsy collection of fimbriae (Parvez and Rahman 2018). The structural part which makes the first extension of harmful bacteria to the lining cells and succeeding successful invasion of the organism are polymeric sticking fibers termed ‘‘fimbriae’’. as for commensal bacteria it has been obvious that the pili accomplish the biological function of settling distinct recess and controlling organism's normal opening methods. This is thought that a number of

harmful *E. coli* breed utilize fimbriae type one or *E. coli* to invade living organisms' cell groups. However, the genomic series scanning *Escherichia coli* with some hostile *Escherichia coli* types has been demonstrating the availability of different putative pili operons, recommending the formation of other pili by harmful and regular greenery *Escherichia coli* inside organisms gastrointestinal (Rendón, Saldaña et al. 2007).

1.11.1. Fimbriae

The inclusion of clinical devices innately encourages the cells that contain bacteria enter body places that are typically nonproductive, and the creation of biofilms by supply an abiotic layer. The shortcomings of structured cure of biofilm-related infections are the inborn obstruction of biofilms hostile to the host resistance method and antibiotics treatment. So, one of the important guide reason of being diseased inside the environment of hospitals and care homes are biofilm-linked invasions, making extra medical management price run over $1 billion/year in the United States (Reisner, Maierl et al. 2014). Fimbriae moderate various responsibilities, along with attachment and biofilm creation. They are lengthy biomolecular complexes which stretch out outside of numerous microorganisms. The pieces that bacterium utilize to aim an exact layer and show tissue tropism are Fimbrial attachment; they are regularly put at the tip of the organelle, that mostly identifies distinct receptor aim in a familiar way. Different sorts of attachment pilus are explained in thin-layer and thick-layer bacteria (Wurpel, Beatson et al. 2013). although, the link is typically moderated by attachment pilus, that are filamentlike supplement set outside of the microbes, most of polypeptide pattern, that develop distinct holding on receiver to the host cells which is Eukarya, they are able to create biofilms on sterile layers like as flexible tube(Garcia and Le Bouguénec 1996), and its availability is dedicated to serious human contamination (Barnhart and Chapman 2006). Fimbria has the capability to specially work with the organism's complex polypeptide like cold-insoluble globulin, domain IV, and endothelial to start the

procedure of attaching and settling the host. Gram-negative bacteria shows substance combination to indicator color as stated by to Hammar et al., and this quality is utilized to specify attachment pilus availability in the attachment examination phenotypically (Barnhart and Chapman 2006). The urinary tract invention capability of UPEC and turning into disease is mostly linked with the declaration of fimbriae attachment (Klemm, Hancock et al. 2010). UPECs attachment to the lining cells disables it to allow efficient approach strength of pee movement along with activate organisms and ways that signal cells containing bacteria, and accomplish invasion. between the specialized heterogeneous group linkages, and Gram-negative bacteria correspond along with lining cells with moderate holding to special receiver inside the renal system (Wullt, Bergsten et al. 2000). UPEC P fimbriae are generally involved in settlement of the upper part of the urinary tube (Roberts, Marklund et al. 1994), with heterogeneous group stretches that make kidney swellings normally send number of duplicates of pyelonephritis pili genome collections in their gene. pyelonephritis pili dedicate for invasion via holding to the diary sugars receive antigen within lipids inside carbohydrate's CD77 antigen available renal system and on Red blood cell. pyelonephritis pili identifies their receivers by the help of the cellular structures –put attachment, and they are accurately held to various antigenic. pyelonephritis pili dedicate to surface cell attachment and placement of inside immune reactions in animals and humans. So, occupy pyelonephritis pili adhesion might stop renal system invasion by *E. coli*, and also may stop the settlement of swelling in the kidney which could cause severe harmful noticed in event of chronic (Watts, Tan et al. 2012).

1.12. Toxin

Apparently 30–50% of the *E. coli* separated from the pee of infected people with kidney swelling create accomplishing poison, Alpha-toxin. This poison harms the layer of the cell by creating holes within the cell, therefore clears a way for the microbes to pass in

the outer way. We expand these assessments in our recent research, to recognize Apo-1 poisons more. It is recommended that poisons like lipoglycans, cytostatic Flesh-eating bacteria and alpha-toxin are considerably the essential severe causes in *Escherichia* invasion. One of the surface membrane parts of the *E. coli* microorganism cell borders is called lipopolysaccharide which encourages the organism reactions and makes lymphokine formation of fertilization inside and outside of the cell. lipoglycans has immediate poisonous causes on cells in the kidney by their living vital element endotoxin molecule (Chen, Tofighi et al. 2006).

1.13. Siderophores

Gram-negative utilizes Fe for the moving, saving dephlogisticated air, deoxyribonucleic acid production, electron movement, with digestion of peroxides. However, the ratio of Fe accessibility would be decreased in the organism's renal system through cystitis (Henderson, Crowley et al. 2009). In reaction to this, *Escherichia* own some alternative structures with a number of practicality that moderate Fe usage by producing oligosaccharides bonding of ions, that are called iron carriers (Olson, Justice et al. 2015). iron carriers moderate iron use, that is important for settlement of the renal system by heterogeneous group (Hagan and Mobley 2009). four of them exist special iron carriers systems available in Escherichia (Neilands, Bindereif et al. 1985). Although their structures include some genome like-ent genome sending Enterochelin, iuc genome sending siderophore, and iro genome sending structures like-ent. Nevertheless, all these structures are uttered when Fe ratio is low and are inappropriately controlled by iron containing and iron III utilization controller Fur (Hagberg, Jodal et al. 1981).

1.14. Membrane

The main function of a membrane is to surround and save the bacterium from different unwanted situations also the organizations immune system, that is primarily composed of polysaccharide (Bien, Sokolova et al. 2012). The layer offers safety for the encounter of entrapment and supplement-moderator bactericide outcome in the organism, and adding biostatic refusal with serum shock inability (Bien, Sokolova et al. 2012, Jahandeh, Ranjbar et al. 2015). Certain capsular, such as phylloquinone, Keratin 5, resist an appropriate antibody-mediated immunity reaction of the invaded organism by demonstrating a molecular similarity to tissue parts (Bien, Sokolova et al. 2012). The capsular *Escherichia coli*, a one-form neuraminic acid acetal, have an essential function in International Building Code improvement also within a number of periods of harmful urinary tract infections (Agarwal, Srivastava et al. 2012, Olson, Justice et al. 2015).

1.15. lipoglycans and endotoxins

lipoglycans and endotoxins (LPS) are parts of the cell's essential components surface formatted by the greatly protected lipoglycans and replicate endotoxins distinct components which vary essentially within stretches produced by the sugar remaining and their normal link inside the recurring distinct components (Bower, Eto et al. 2005, Sarkar, Ulett et al. 2014). lipoglycans would be highly considered to encourage organism's reaction and to make nitrogen monoxide and lymphokine (IL-1, TNF-α) formation, which encourages the provokation reaction (Emody, Kerenyi et al. 2003). This makes the production of special immunoglobulin to the bodily antigen and apply an immunity aid outcome that improves the fluid protection reaction to another immunogen. of the harmful microbes. Nevertheless, specific immunity components of lipoglycans are also included in stopping harmful to the execution cause of the healthy human serum (Cirl, Wieser et al. 2008). by the help of a research conducted on model organisms, severe renal abortion because the lipoglycans rely on the structural reaction to lipoglycans. It does not rely on the utterances of functional lipoglycans receiver, Toll-

like receptor 4, in renal system. It is still doubtful whether lipoglycans are responsible for moderating a renal abortion and severe allogeneic transplant damage in infected people with renal system infection (Bien, Sokolova et al. 2012).

1.16. Motility

The flagellum is defined as an organelle which is accountable for bacterial motility. Flagellum also has a great part in the original adhesion phase of creation of biofilm (Ong, Ulett et al. 2008). According to a study that is done recently, motility affects the infections when they transfer to kidneys from the bladder (Lane, Alteri et al. 2007). Flagellated UPEC is a reason of all urinary area contagions for around 70–90%, and pathogenesis contains links between epithelial cell surface of the urinary area and the bacteria (Bien, Sokolova et al. 2012). Though, flagellar motility can increase the capability of *E. coli* through adjustable replies to beautiful or disgusting environmental stimuli (Emody, Kerenyi et al. 2003).

1.17. Immunity against *E. coli*

1.17.1. Innate Immunity

Both males and females generative areas are vital to the internal mucosal facing of the human body, and those mucosa with those of lung mucosa and gastrointestinal is alike, they also have the ability of increasing a complete range of immune replies. In both men and women the generative area's immune system has different alterations in order to see the serious physiological tests of both well keeping complete guard against microbial

invasion. The typical structures of the male and female genital areas are the categorize of immunity system and replies of mucosal immune. The features that regulate immune replies result in generative area contain cellular relations with mechanisms that create the generative tract immune system also the resident microenvironment which is conquered by a matchless microbiome and sex hormones (Wira, Fahey et al. 2005, Kaushic, and Ferreira et al. 2010). The immune system of humans is basically distributed into two main divisions, which are called the adaptive (specific) and the innate (non-specific) immune system. Though those two both have a defensive job in contradiction of invading pathogens, they vary in period to respond or react, the cells included, type, effector devices, and specificness of receptors. The inborn system of immune establishes the first reply to contagion and joins quickly after working with contagious agents, because of this cause it has a crucial part in host protection (Janeway Jr and Medzhitov 2002, Wira, Fahey et al. 2005). The stable responsibility of the system of immune is to protect the surfaces of epithelial to discriminate and execute pathogenic microorganisms. Basic responses are produced by pathogen-acknowledgment receptors ligation in and on cells of epithelial and started by cells of immune. These results begin and resist phagocytes, particularly neutrophils and macrophages (polymorphonuclear leukocytes), that has ability to finish bacterial pathogens at path point.

One of the ways to become ill and repel the immune recognition, the dissimilar types of microorganisms all of them have gotten a collection of molecular devices to decline and prevent mammalian basic immunity. The authority of these microorganisms is normally diverse between Gram-negative bacteria. In several kinds of pathogens even these three, *Yersinia*, *Salmonella*, and *Vibrio*; actual proteins interfering the hint of the cell of host like, post-translational modification, kinase activation, cytoskeletal reorganization, and dissimilar actions are assumed to the host cell by discharge type III. Later on, we goal the core cause for urinary tract infections, that is the specific immune modulation actions

of (UPEC) short for UroPathogenic *Escherichia coli* (Olson and Hunstad 2016). The growing level of overview of UroPathogenic *Escherichia coli* (UPEC) or pathogenic microorganisms inside the mammals urinary area reasons an inflammatory response, fundamentally happened by rouse of (TLRs) Toll-like receptors. Stimulation of TLRs by (LPS) short for bacterial lipopolysaccharides passes the path of NF-κB , activating the announcement of neutrophil chemo attractants and cytokines including IL-6, for example, IL-8 (CXCL1), that has ability to be predicted in human and mice urine by using UTI (Hedges, Anderson et al. 1991, Samuelsson, Hang et al. 2004). Uroepithelial cyclic AMP increment, rouse by TLR4-induced growths in intracellular [Ca2+], the result is independent NF-κB- development of IL-6 and IL-8 appearance (Song, Duncan et al. 2007). Bacterial flagellin energized TLR5 has ability to penetrating irritation throughout UTI (Andersen-Nissen, Hawn et al. 2007, Smith, Varley et al. 2011). neutrophil response broadcast may be determined by cytokines, e.g. IL-17, that has a significant career in joining inborn to versatile immunity (Peck and Mellins 2010) and it proceeds duty of the innate response through the UTI test (Sivick, Schaller et al. 2010). A minor, cationic antibacterial peptide, that is recognized as human cathelicidin LL-37 is visible in urine of human in cystitis, and mice lacking in its orthology (CRAMP) prove enlarged vulnerability to pyelonephritis (Chromek, Slamová et al. 2006). Though it may paradoxically promote bladder contagion (Danka and Hunstad 2015). From the defensing class of antimicrobial peptides some differ entities are formed locally, during UTI (Becknell, Spencer et al. 2013, Nielsen, Dynesen et al. 2014), and the presence of these available molecules in host-pathogen talk remains a fertile zone for learning. Neutrophils to the bladder is a central outcome of the soluble inflammatory reply. Furthermore, a diagnostic hallmark of human UTI is the discovery of neutrophils located in the urine. The phagocytic boundary of neutrophils shows an elementary part in governing UTI and UPEC, as displayed in dissimilar inquiries (Olson and Hunstad 2016).

1.17.2. Adaptive Immunity

When the wide innate immune responses of the urinary area are extra open to infection, the adaptable immune responses, particularly in the bladder, will in common be forced. UTIs that advancement to the kidneys have ability to lead to the formation of antibodies for the specific infection. Diseased patients limited to the bladder unpredictably disregard to make an antibody response (Abraham and Miao 2015). This seeming fault in the antibody reply of the bladder may perhaps be a main cause for the amazing reappearance of UTIs. This thought clinically was lately replicated in mouse in which UTIs that were severely restricted to the bladder made no or tiny antibody reply to the contaminating bacteria, while a considerable antibody reply was made during contagions of kidneys and the bladder both. The fundamental origin of the incapability of the bladder to stand an adaptive reply was related to developed local IL-10 creation, as mice IL-10-deficient displayed considerable antibody replies to bladder contagion. As it is deliberated before, mast cells are a main basis of IL-10 in the bladder resulting bacterial contagion. Though these secretory cells have a vital role in starting an immune of vigorous reply in the recent phases of bladder contagion, mast cells appear to contrary their action about 6 h after infection by swapping to IL-10 creation to finish this reply (Chan, John et al. 2013). Mast cell-generated IL-10 has capacity to stop the appearance of molecules of co-stimulatory on DCs and thus bound their ability to task as actual antigen-presenting cells while they traffic to demanding lymph nodes. Therefore, steady with the part of mast cell-derived IL-10 in weakening inborn immune reply, the incapability of the bladder to stand an antibody reply to bacterial contagion possibly will be a by-product of its effort to stop damaging adaptive immune replies to the insides of urine, also to ease the fast renewal of its epithelium succeeding infection-induced harm (Abraham and Miao 2015).

1.17.3. Immune escape

To settle the area of host urinary successfully, UPEC strains direct a range of virulence aspects. These contain flagella to ease bacteria movement and adhesins for add-on to the uroepithelium, permitting struggle to the movement of stable urine. Iron-acquisition systems for example, siderophores are doing a job which is permitting UPEC to gain iron in order to guarantee their development. Also, some type of toxins with some aspects like creating a capsule, gives allowance to the bacteria to effect the host immune reaction to flee (Bower, Eto et al. 2005, Dhakal, Kulesus et al. 2008). For the perseverance of contagion, UPEC create biofilms for example, for attachment to bladder catheters or even create intracellular colonies (Anderson, Palermo et al. 2003). It is better for the intracellular UPEC to be safe from antibiotics and cells of immune, allowing their perseverance (Dhakal, Kulesus et al. 2008). In opposition, it is important know that the system of immune is not inactive, and it has devices like to prevent the avoidance UPEC strategies, Based on the pathogens discovery by (TLR4) short for toll-like receptor 4 and other form appreciation receptors, a number of soluble aspects are unknown like for example, antimicrobial proteins and peptides, plus chemokines). Moreover, the bacterial contagion encourages caspase-dependent apoptosis of epithelial cells with sickness to decrease the bacterial weight. Lastly, immune cells of local sentinel for example, mast cells, , dendritic cells, natural killer cells and macrophages) feel the contagion and hide several cytokines to employee other immune cells from the blood flow, particularly neutrophils, to remove the contagion (Abraham and Miao 2015). This battle that is happening between both the bacteria and the host organism matches the evolutionary hypothesis of Red Queen. focusing on one specific species and improving it assure co-evolution in terms of a difficult and varied guard and preventing other species. These researches that are done on the immune response against UTI give the clearance and put a spot on UTI pathogenesis (Schwab, Jobin et al. 2017).

1.17.4. Immunomodulation of urinary tract

Continues in persons who in usage of type of antibiotic known as broad spectrum consumes may managed to occur the development of some type of antibiotic resistant among various bacteria which mostly related to the urinary tract as a significance, the managing of viable type of contagions establishes a severe in addition to developing medical challenge. In order to controlling the both controlling type of innate in addition adaptive human body resistant organizations pertaining in urinary tract region might be possibly take significant therapeutic insinuations for the fix the condition which related to UTIs. Since the lining of the urinary tract is exceedingly enhanced in TLR4 particles, regulating TLR4 particular ligands straightforwardly to the UTI seem trigger TLR4 intervened type of immune response termed as innate immune reactions subsequently improving nearby reactivity and resistance to disease.(Ashkar, Yao et al. 2004, Nurkkala, Nordström et al. 2007). These perceptions recommend to stimulate of the TLR4 flagging passageway within UTI that can be in effect restorative operators in contradiction of current contagions. Besides, the fundamental and it is in order to utilize TLR4 ligands in stimulus of promoting to beginning of the passageway needed. Indeed, in the event that TLR4 ligands which utilized for treatment use and it is impossible that LPS to be ligand of special ever since LPS has inherent toxicity. Moreover, the TLR4 ligand per enormously moved forward protection outlines as monophosphoryl lipid (MPL) may be used in in place (Evans, Cluff et al. 2003). Since the immune element both type of B in addition to T cells are facilitate type of immune which term adaptive immunity disapprovingly reliant on indications resulting after the type of innate immune of human being, modulators that improvement the type of innate immune answers may be of value in increasing major of the adaptive immune responses (Pasare and Medzhitov 2005, Parker, Prince et al. 2007) Certainly, the innate immune defiance at

present regularly being combined as ‘adjuvants’ to improvement immunity to vaccines (Ishii and Akira 2007, Tse and Horner 2007).

1.18. Clinical significance of *E. coli*

Escherichia coli has long been used as a model organism for exploring gene regulation in bacteria, and has become the most thoroughly studied organism in the world. *Escherichia coli* is an enteric, gram-negative rod that belongs to the Enterobacteriaceae family. *Escherichia coli* is typically motile by peritrichous flagella, although some strains are nonmotile. The bacterium is a facultative anaerobe that can grow on a variety of complete laboratory media. However, *E. coli* can produce in minimal media by utilizing glucose as sole carbon source to make all macromolecules necessary for growth (Reuter 2012; Ronald 2002). Moreover, there is indication for an abdominal environment for uropathogenic bacterial infection (Goetz, Mahmood et al. 1999), as type of strains of human uropathogenic *E. coli* consume been originate in the colonic microflora and there are new molecular have recognized 29 virulence genes of *E. coli* bacteria (Johnson and Stell 2000). Moreover, there are many research associating with UTI to non-immuno-compromised, immune-compromised and renal complication individuals establish *E. coli* was the greatest frequently inaccessible pathogen to all groups (Kärkkäinen, Ikäheimo et al. 2000). Moreover, the virulence issues of bacterial *E. coli* are more public between non-immunocompromised versus immune-compromised individual and it is recommended less infectious *E. coli* can reason for the UTI additional regularly in immune-compromised patients with renal complication (Ronald 2002).

1.19. Antibiotic resistance

1.19.1 Extended-spectrum β-lactamases

Extended spectrum beta lactamases (ESBL) enzymes were to begin with depicted in Germany in 1983 from *Klebsiella pneumonia*. ESBL chemicals are as a rule plasmid intervened and pick up wide resistance to cephalosporins: (cefotaxime, ceftazidime, ceftriaxone), and monobactams (aztreonam) (Altayar, Thokar et al. 2012). A modern course of ESBL, called CTX-M proteins, has developed amid late 1990 and early 2000s, which was broadly recognized among *Escherichia coli* confines. This ESBL-producing *E. coli* are able to stand up to penicillins, cephalosporins and are found generally in urinary tract contaminations UTI(Aka and Haji 2015). These days, the predominance of ESBL-*E. coli* carriage within the community setting is evaluated to extend between (10% and 50%) with concurring to the geological regions. This predominance has been particularly watched to be the most elevated in creating countries, as a conceivable result of ineffectively controlled anti-microbial utilization and problematic cleanliness conditions. ESBL-producing urinary pathogens are associated with higher morbidity and mortality amongst hospitalized patients (Toner, Papa et al. 2016). In condition related to treatment management of urinary tract which commonly in progress of the empirically that previous knowledge toward the occurrence of various causative representatives in addition to susceptibility of the anti-microbial profilesin a particular situation is indispensable (Alqasim, Abu Jaffal et al. 2018). The ESBLs encompass numerous mediation related to the plasmid products like (TEM, OXA, and SHV) (Trevino, Losada et al. 2016). Since2000, a new group of ESBLs, named CTX-M (ex., “active on CefoTaXime, first isolated in Munich”), has occurred (Caron, Wehrle et al. 2017). Since at that point, CTX-Mβ-lactamases have been the overwhelming ESBL sort around the world. Inside the CTX-M family, CTX-M-15 is right now the foremost predominant CTX-M genotype (Lee, Lee et al. 2018). This antimicrobial resistance which associated with ESBLs group that related with widespread to numerous type antibiotics chose, counting Beta-lactam mediators for instance (carbapenems, penicillin’s, cephalosporins, monobactams) (Sanchez, Adams et al. 2013; Arpin, Quentin et al. 2009). This expanding

of UPEC condition relate to their amount of the resistance of antimicrobial which extraordinary apprehension then it can constrain restorative selections utilized for treating common bacterial diseases such as UTIs and highlights the developing danger of rise of resistance of the pan drug related to UPEC conditions (Lee, Lee et al. 2018).

1.20. ESBL

1.20.1. TEM

The local TEM-1 of the Beta-lactamase discusses strongly resistance to various type of antibiotic. The chemical agents which mindful for 90% in E. coli have ability of ampicillin resistance separates (Livermore 1995). Moreover, changes inside the blaTEM-1 basic quality, apparently over antibacterial determination and it have the permitted of protein among grow amount of the hydrolysis competences to specific amplified range (aztreonam in addition to cephalosporins). However, keeping up its unique hydrolysis abilities. The variation of the TEM-2 is considered to be primary variation depicted, varied occur in location 39 of glutamine by lysis processes in TEM-1 over the replacement. Be that as it may, TEM-2 isn't measured an ESBL as the substrate outline is indistinguishable to TEM-1. Subsequently, amino acid replacements at 12 isolated from locations, temporary unaccompanied or in performance with other organizational quality (Rupp and Fey 2003).

1.2.2. SHV

The primary gene which distinguished within the 1970s was blaSHV-1 gene within *E. coli* bacteria. The encoded chemical sulfhydryl reagent variable for SHV-1, demonstrated the action in contradiction of penicillins drug to begin with era cephalosporins (Liakopoulos, Mevius et al. 2016). The foremost likely predecessor of

plasmid intermediated for SHV−1 may be a chromosomal type specific for penicillinase identified in stool separates from neonates (Haeggman, Löfdahl, et al,. 1997). Cchemical appeared commonplace antibiogram through penicillin instead of cephalosporin opposition and a checked restraint by clavulanic corrosive. (Liakopoulos, Mevius et al. 2016; Tzouvelekis and Bonomo 1999), monobactam and carbapenems. As it were a little extent is biochemically and/or hereditarily characterized SHV Beta-lactamases mostly divided between three category or subgroup in side of pertaining molecular characteristics useful possessions: (i) Subgroup 2b (n = 37), have ability to make hydrolyze to penicillins and early cephalosporins in addition to strongly hindered by both of the antibiotic known as (clavulanic acid and tazobactam). (ii) subgroup 2br (n = 7), are recognized by broad-spectrum β-lactamases obtained resistance to clavulanic acid. (iii) subgroup 2be (n = 46), encompasses the ESBLs that can moreover hydrolyze more than one and/or more oxyimino Beta-lactams. There are additional than half of these variations (n=99) has not remained categorized however in line for to nonattendance of chemical account (Liakopoulos, Mevius et al. 2016).

1.21. Phenotypic detection of ESBL

ESBLs are group of enzymes which confers resistance to extended spectrum cephalosporins, aztreonam, and oxyimino β-lactams and are inhibited by β-lactamase inhibitors such as clavulanic acid, sulbactam, and tazobactam (Limbago and Swenson 2015). encoded by mutated TEM1, TEM2 and SHV genes on plasmids (Thomson, Sanders et al. 1999). Various phenotypic methods have been recommended for routine use to detect ESBL production in gram negative bacilli. These employ a β-lactamase inhibitor, usually clavulanate, in combination with third generation cephalosporins (3GC) such as ceftriaxone, ceftazidime or cefotaxime (Chaudhary and Aggarwal 2004).

1.22. Genotypic detection of ESBL producing bacteria

Polymerase chain reaction (PCR) is a valuable technique in the diagnosis of bacterial infection. Molecular methods might be superior to bacterial culture in providing the etiologic diagnosis (Morgenstern, Renz et al. 2018). Generation of ESBLs is one of the foremost predominant resistance components in Gram-negative bacilli. At first, ESBLs were transcendently described in *K. pneumoniae* and *E. coli* strains, but as of late the chemicals were found in other genera of the Enterobacteriaceae family (Shaikh, Fatima et al. 2015). Within the 1980's, the term was connected to mutants of the as of now common plasmid intervened β-lactamases such as SHV and TEM. One of the primary identified, which started in France, was TEM-3 ESBL which had been assumed to have been chosen within the human have taking after the presentation and utilize of cefotaxine. Both of the 'parent' genotypes of this β-lactamase qualities blaTEM-1 blaTEM-2 were broadly dispersed among restoratively important individuals of Enterobacteriaceae and Acinetobacter spp. and it appeared consistent. The extended spectrum shape of the β-lactamase would ended up much more broadly disseminated all through the world beneath the particular weight of the utilize of third generation cephalosporins (Ungo-Kore, Bulus et al. 2019) There are also non-significant spread of genes into the extra general environmental of Enterobacteriaceae, in current place where ESBL is predominant (Iredell, Brown et al. 2016).

1.23. Infection control measures of ESBL

Hypothesized components for the presence and it is supply resistance of the antimicrobial in clinics incorporate of taking after: (i) presentation of safe living being an already helpless populace. (ii) securing type resistance and it is related to susceptible strain (through unconstrained transformation and/or genetic exchange). (iii) appearance relate with directed resistance as of now presents within the populace. (v) determination of a resistant subpopulation. (iv) dispersal or spread of safe living beings (Murthy 2001).

Whatever the ICUs give a singular setting, encouraging the development and blowout of resistance for a many explanations: (1) near the quarters or in height recurrence of the health worker deal with patient interaction give chance to increase patient to patient connection. (2) the way to transmission of pathogens agent due to deficiency of hand hygiene and handwashing degrees decrease through expanded assignment). (3) substantial determination weight by broad-spectrum anti-microbial utilize. (4) natural defilement giving encourage occasion for transmission of pathogens through polluted tools and health hospital care specialists (Murthy 2001).

1.24. ESBL detection

The discovery of ESBLs could be stable for schedule of microbiology research facilities in asset restricted situations and discovery of a reduction insusceptibility to oxyimino-cephalosporins isn't adequately delicate to distinguish ESBL strains. Moreover, the rules created by the `Comite de I'Antibiogramme de la Societe Francaise de Microbiologie` (CA-FSM) and `European Committee on Antimicrobial Susceptibility Testing` (EUCAST) (Harwalkar, Sataraddi et al. 2013). It is suggest screening for ESBL separates depended on diminished helplessness amplified spectrum of the cephalosporins in essential anti-microbial disc diffusion examination lengthways through single extra assenting test. Be that as it may, the foremost sensitive strategy for the phenotypic discovery of ESBL remainders unidentified (Garrec, Drieux-Rouzet et al. 2011). Standing phenotypic strategies ESBL discovery incorporate `disc diffusion screening the twofold disc co-operative energy test` (DDST), `inhibitory potentiated disc diffusion` (IPDD). As Clinical and Research facility Standards Founded (CLSI) rules, starting monitor for decreased helplessness to additional than one of five pointer cephalosporins taken after by a assenting test can make strides the sensitivity of discovery. The advance recognizable proof the particular qualities related with the generation of ESBLs can be accomplished utilizing exact nucleic acid measures. Be that

as it may, these molecular tests are constrained to resource rich settings past the possibility of schedule microbiology research facilities (Garrec, Drieux-Rouzet et al. 2011).

1.24. ESBL treatment

The nearness of ESBLs complicates the determination of anti-microbials, especially in patients with genuine diseases such as bacteraemia (Paterson and Bonomo 2005). The reason for this is often that ESBL-producing microbes are frequently multiresistant to different anti-microbials, and CTX-M-producing confines are co-resistant to the fluoroquinolones (Pitout, Nordmann et al. 2005). Anti-microbials that are routinely utilized for observational treatment of serious community-onset diseases, such as the third-generation cephalosporins (ex, cefotaxime and ceftriaxone), are frequently not effective in contradiction of ESBL-producing microbes (Paterson 2000; Hyle, Lipworth et al. 2005, Tumbarello, Sali et al. 2008). few considers have famous a diminishment in clinical impact against ESBL-producing microbes with a few β-lactam operators in spite of testing helpless in vitro, though other considers have appeared great clinical result with β-lactam–β-lactamase inhibitor combinations (Lagacé-Wiens, Nichol et al. 2006, Mugnaioli, Luzzaro et al. 2006; Rice, 2001). Anything the urinary tract disease could be a common and painful to the human sickness that, unfortunately not responsive to commonly, it is utilized anti-microbials within the current practice. Escherichia coli and Klebsiella pneumoniae are the leading common pathogens causing UTI. Extended-spectrum beta-lactamase delivered by ESBL-*E. Coli* and *Klebsiella pneumoniae* decreases the total number of best therapeutic choices for the contagion produced by the pathogenic agent (Gupta 2003, Falagas, Polemis et al. 2008; Paterson and Bonomo 2005), which are frequently used for UTI. Carbapenems resistance is also growing concern which poses a severe threat to the health. Infection with carbapenems resistant enterococci was accompanying with a four-fold rice the risk of getting IET which in

opportunity improved rate of mortality, length of stay and prices (Tulara 2018; Pitout and Laupland 2008). The antibiotic of choice in ESBL-producing *E. coli* or Klebsiella pneumoniae-related infections is generally carbapenems. NFT, fosfomycin, tromethamine, quinolones or TMP/SMX may be alternative choices. Approximately there are about 60% is assured to proteins of the plasma metabolized within the liver organ; Ca bout (30–50%) of the given dose is defecated by means of the urine. Taking after verbal organization. The drawbacks contain prerequisite of treating q6h and little tissue concentrations. The detail of NFT is compelling together in vitro and in medical thinks about against ESBL-producing E. coli proposes might be imperative (Tasbakan, Pullukcu et al. 2012).(Nurkkala, Nordström et al. 2007)

1.2. Aim of the study

1. To measure the percentage of UTI caused by *E. coli* in Rizgary Hospital
2. To determine the prevalence of ESBL in UTI patient in Rizgary Hospital

CHAPTER 2

2. MATERIAL AND METHOD

2.1. Material

2.1.1. Devices and Tool

Equipments	Company	Country
Incubator	WTB-Binder	Germany

Oven	**Memmert**	**Germany**
Medical Refrigerator	**Sanyo**	**Japan**
Autoclave	**Sakura**	**Japan**
Sensitive balance	**Shimaduz**	**Japan**
Centrifuge	**Hettich**	**Germany**
Microscope	**BH2**	**Japan**
Disposable Petri dishes plate	**The Science**	**USA**
Disposable test tube 10 ml	**The Science**	**USA**
Safety cabinet II	**DALTON**	**Japan**
Slides	**The Science**	**USA**
Cover slip	**The Science**	**USA**
Vitek 2 GN	**Biomerieux**	**France**
Vitek 2 AST-GN76	**Biomerieux**	**France**
Vitek 2 Compact	**Biomerieux**	**France**
Inoculation loops	**The Science**	**USA**

2.2. Specimen collection

The study included (192) patients divided to two groups (outpatient and inpatient) referred by urologist from urology department for urine culture at laboratory of Rizgari Teaching Hospital in Erbil city from January to April 2020. urine samples were taken (by standard mid-stream "clean catch" method) from patients with clinical suspected urinary tract infection (UTI) according to (Al-Mayahi 2014). After the patient's consent we are collect the following data: Gender, Out Patient or In Patient, Age, Surgical history, Medical history, and chronic disease.

2.3. Media preparation

2.3.1. Blood agar medium

Is **enriched medium** used to cultivation of fastidious bacteria

and determination of hemolytic reaction.

Composition of agar arrange **per liter:**

Agar = 15.0 gm

Beef extract = 10.0 gm

Peptone = 10.0 gm

Sodium Chloride (NaCl) = 5.0 gm

Sheep blood, defibrinated = 50.0 mL

pH 7.3 ± 0.2 at 25°C

2.3.1.1. Preparation of Blood Agar

1. Add the components (40 gm), to distilled water and bring volume to 950.0 mL, following mixing.
2. Heat with agitation and boil for 1 min.
3. Autoclave for 15 min at 15 psi, 121°C.
4. Cool to 45°- 50°C.
5. Aseptically add 50.0 mL of sterile, defibrinated sheep blood.
6. Mix t and pour into sterile Petri dishes.

(Source)
https://www.asm.org/getattachment/7ec0de2b-bb16-4f6e-ba07-2aea25a43e76/protocol-2885.pdf

https://www.bd.com/europe/regulatory/Assets/IFU/Difco_BBL/211086.pdf

2.3.2. MacConkey Agar

The media is selective to differential media used for the isolation and differentiation of non-fastidious gram-negative rods. The arrangement of MacConkey Agar**:**

Peptone`Pancreatic digest of gelatin`=17gm

Proteose peptone (meat and casein) = 3 gm

Lactose monohydrate = 10 gm

Bile salts = 1.5 gm

Sodium chloride = 5 gm

Neutral red = 0.03 gm

Crystal Violet = 0.001 g

Agar = 13.5 gm

Add D.W to 1 Liter, adjust pH (7.1 +/− 0.2)

2.3.2.1. Preparation of MacConkey Agar

1. Suspend 49.53 grams of dehydrated medium in 1000 ml purified/distilled water.
2. Heat to boiling to dissolve the medium totally.

3. Sterilize by autoclaving at 15 lbs pressure (121°C) for 15 minutes.
4. Let it to cool to 45-50°C.
5. Mix and pouring into plates.

(Source): Archived copy. *Archived from* the original *on 2010-12-03*. Retrieved 2011-03-20.

2.3.3. CLED agar

Is one of the most type of media that used commonly in UTI patients, the Cystine Lactose Electrolyte-Deficient Agar (CLED) Agar is used as a type of differential medium optional to growth better of bacteria and especially for diagnostic pathogenic bacteria in urinary tract. The medium provisions the development of all type of urinary pathogens and delivers separate colony morphology. The Composition of agar arrange:

L-Cystine 0.128 gm, Bromothymol Blue 0.02 gm, Agar 15 gm

Lactose = 10 gm

Enzymatic Digest of Gelatin = 4 gm

Enzymatic Digest of Casein = 4 gm

Beef extract = 3 gm

2.3.1.1. Preparation CLED agar

1. Droop 36 g of medium in to 1 liter of water.
2. Make heat with keeping agitation, following boiling 1 minute in order to dissolve medium.
3. Put inside of autoclave 15 minutes at 121°C for.
4. After the autoclave let media cooling then mix and distribute into plate,
5. It must stored at 8-15°C, pH 7.3 ± 0.2 at 25 °C

Reference

Analytical, Fluka. "55420 CLED Agar (Cystine-Lactose-Electrolyte Deficient Agar; Bromothymol-blue Lactose Cystine Agar)" (PDF). *Fluka Analytical*. Retrieved 18 October 2014.

2.4. Methods

2.4.1. Pyuria detection

The term of pyuria are used in case of determination white blood cells in urine samples by quantified microscopically measuring, the counting may perform by hemocytometer, calculating WBCs in urine samples using leukocytes in a centrifuged specimen, the benefits of these detection in urine by microscopy are directly can be detect the WBCs caste with other cellular associated with urine (Wilson and Gaido 2004). Urinalysis was carried out with emphasis on the presence and count of leukocyte in the sediment after centrifugation at 3000 rpm for 5 minutes. One drop of centrifuged urine was placed on a clean slide and covered with a coverslip. The slid was examined for leukocyte count under microscope, using high power field (HPF). The presence of leukocyte (5-10 WBC/HPF) was considered to be the cut-off for defining pyuria. The pyuria samples were immediately cultured for bacterial growth.

2.4.2 Urine culture

Culture method is a golden stander method which are used in detection of the UTIs infection, which are very necessary for those who have history with urinary tract infection because the method are support with antibiotic resistance and it is susceptibility to help in treat urine infection, moreover, performing urine culture help in reggeization type of microorganism which caused current infection which is very

useful in diagnosis type of infection with easy management in order to cure the UTIs infection. After shaking the urine container, 5 µl urine using micropipette was transferred and streaked on the `cystine lactose electrolyte deficient` (CLED) agar widely used in evaluation of the uropathogenic complication (Parajuli, Maharjan et al. 2017). Or sometimes we used (Blood agar and MacConkey agar) instead of cystine lactose electrolyte deficient (CLED) agar for the isolation and identification of significant uropathogens. After that all plates incubated aerobically at 37C° for 24-48

hours. The most commonly used criterion for defining significant bacteriuria is the presence of $\geq 10^5$ cfu per milliliter of urine (Wilson and Gaido 2004).

2.4.2.1. Bacteriuria detection and isolates

After 24 hours incubation, the plates were checked for bacterial growth. The positive growth indicated bacteriuria when the plate counts showed a 10^5 cfu/ml. The blood agar is one of the most method usage in amid to detected the pathogenic microorganism in medical field especially to recognize the specific agent in order to give better idea to treat complicated health situation in specific medical sample, moreover, the most media uses since 1905 in medical laboratory media to differentiated microorganism is MacConkey's agar which distinguish the gram negative pathogens since it is not support the development of bacterial agent associate with urinary tract, but both of Blood agar and MacConkey agar are used in order to investigate the pathogenic relate to the UTIs (Parveen, Saha et al. 2011). Different option are available for isolation bacterial *E. coli*, the processes are depend on kind of the stain used in possesses and isolation objective, following the ability to fermentative lactose give an option to use MacConey agar to discriminate *E.coli* from non-lactose ferment bacteria, the pink round media size colony recognized as *E.coli* also the strain can capture on MacConey media and this method gives wide spectrum of strains to work on it (Merlino, Siarakas et al. 1996). Opaque yellow colonies with a slightly deeper yellow center, colonies are picked as E. coli suspected. For recognized *E.coli* bacteria the study designed to use Vitek 2 because it is cards contain an ESBL test which monitors susceptibility of *Escherichia coli* to cefepime, ceftazidime and cefotaxime alone and in combination with clavulanic acid (Harwalkar, Sataraddi et al. 2013).

2.4.2.2. Vitek 2 for bacterial identification

Microbiological instrument knows as Vitek 2, it is Vitek 2 ID-GNB card contain a 64-well card intended for the automated documentation of greatest clinically significant fermenting and non-fermenting gram-negative bacilli. The ID-GNB card is a 64-well card that holds 41 biochemical tests there are 13 extra substrates than the number counted in the GNI card, moreover, there are two negative regulator wells for control. the 41 biochemical tests, 21 are with conventional substrates in addition to twenty wells cover preformed enzymes, other wells are remaining unfilled. There are variances in the substrates among this card and GN card can be understood by consulting the respective creation insertions.

The sample swab bacterial pellet was composed with a cotton swab to arrange among the 0.5–0.63 McFarland suspension in 3.5 mL of 0.45 % normal saline by means of the Densichek Vitek2 colorimeter. The time interval between suspension preparation and card filling was less than 30 min to avoid changes in turbidity. In following operation the Vitek2 cards injected with the next the orders of the manufacturer procedure and the cards selection contingent on Gram stain for example when Gram-negative rods were detected, GN documentation cards stayed used. (O'Hara and Miller 2003).

2.4.2.3. Vitek 2 Result Interpretation

After performing the procedure the result will be assisted in period of time, and the result observation will show as various range and or categorize such as levels of excellent, very good, good, acceptable, following the estimation are nearly will show nearly to current profile relate to specific taxonomy in addition other taxa in the database, moreover, the specific and currency of detectation are nearly will be between ranges from 99.9 to 80.0% and this significance is generalized from the index how narrowly the corresponds profile to the maximum typical set of responses for each taxon following algorithm calculation, the specific stander relate to detectation index range vary between 0 – 1 is in reverse comparative to the number of different type of tests. The self-assurance level of excellent is a combination the ratio

of documentation currency level of 99.9%, index of 0.75, moreover the acceptable combines level of the

percentage among documentation 80.0%, index of 0, when low amount taste is proposed.

2.4.2.4. VITEK 2 detection of ESBL-producing bacteria (AST-GN76)

After prepare a 0.5–0.63 McFarland suspension in 3 mL of 0.45 % normal saline using the Densichek Vitek2 colorimeter, we prepare second Densichek Vitek2 colorimeter for Antibacterial Susceptibility Test (AST) by adding 3mL of 0.45 % normal saline using the Densichek Vitek2 colorimeter, after that we take 145 µl from identification tube to AST tube, AST-GN76 cards were used. The VITEK 2 instrumental cards consist of ESBL assay in order to detect the bacterial pathogenic susceptibility relate to ESBL production such as *E. coli* and *Klebsiella* species. The principal logarithmic discount of development inside the wells covering with clavulanic acid and other that does not cover with clavulanic acid designates countenance of an ESBL enzymatic production, moreover the test merger with the VITEK 2 Advanced Expert System (AES) and duration of examination totally take 5 to 19 hours in aimed to put out the result (Numanovic, Hukic et al. 2013). The processes of procedure Vitek 2 requirements a definite identification to create report of conclusive results. Advanced Expert System analyzation of identification and susceptibility reliable by look up of the phenotype characteristic descriptions inside instrumental database and it is essential to improvement in the MIC to whole justification, moreover the AES response for changing result between the different interpretation such as resistant (R), sensitive (S) to intermediate (I) depending on the mechanism of resistance detection in order to prevent failure of current treatment, the instrument also consist of ID-GNB cards each of them are contain the bar-coded name that's scanned into the recollection data chip before the cards are loaded into the conforming slot. Following the processes of the reading based on automatically and it is collaborating with the memory chip which deal with the dilution concentration that essential for the susceptibility of fills the test cards, it is take incubates the cards 3 h, after the processes finished the automation software

run the card and analysis complete then processes end with print the results (Bruins, Bloembergen et al. 2004).

2.4.3. Other methods available for ESBL detecting

-Double-disk synergy test

-Three-dimensional test

-Inhibitor-potentiated disk-diffusion test

-Cephalosporin/clavulanate combination disks on iso-sensitest agar

-Disk approximation test

-E Test

-MicroScan panels

2. Statistical Data Analysis

Data analysis was performed using SPSS version 25.0 (SPSS). The present study data contain categorical were compared using perform the test associated with data suitable with Person Chi square test as appropriate. All p values were two-tailed; a p value < 0.05 was considered statistically significant.

2. Ethical Acceptance

RESEARCH ETHICAL COMMIITTE APPROVAL SHEET UNDER THE:

Title of the project: Extended-spectrum beta lactamase rates of Escherichia coli from urinary tract infection in Rizgary Hospital, Erbil Iraq (Apendix A)

CHAPTER 3

3. RESULTS

3.1. Study Population

A total of 192 patients with suspected urinary tract infection (UTI) were included in this study. In the period from January to April 2020 urine samples were collected from patients using the standard mid-stream "clean catch" method and urine culture was performed in the laboratory. The prevalence of the study population according to gender was analyzed and statistical analysis were performed. Results show that 69.8% of the patients were females, which was significantly higher than male patients (30.2%). Out of 192 UTI patients, 55.2% females and 26.0% males had a non-ESBL UTI infection, but ESBL-positivity rate was also higher in the female group (4.7%) than the male group (4.2%). Therefore, the rates of *E. coli* in UTI and ESBL production among these infections were statistically higher in female than male patients (p-value 0.005), also there are 30.2 % of them have history with surgical operation and 36..5 % of them have chronic disease infection, moreover 60.9% of total patents was used long medication usage, 18.2% were diagnosed as *E.coli* by Vitek 2 for bacterial identification and (81.8%)of other was free of E.coli infection, therefore those patients have *E.coli* positive there was (8.9%) of them was ESBL positive, following (9.9%) of them was ESBL negative, in addition to (81.3%) was Non-ESBL.

Table 3.1: Questionary of total study population

Parameter		Count	%
Age	**teen**	9	**4.7%**
	Adult	151	**78.6%**
	Old	32	**16.7%**
Gender	**male**	58	**30.2%**
	female	134	**69.8%**
long term medical	**Yes**	117	**60.9%**
	No	75	**39.1%**
Chronic disease	**Yes**	70	**36.5%**
	No	122	**63.5%**
Surgical History	**Yes**	58	**30.2%**
	No	134	**69.8%**
Patient have E. coli	**Yes**	35	**18.2%**
	No	157	**81.8%**
ESBL	**Positive**	17	**8.9%**
	Negative	19	**9.9%**
	Non ESBL	156	**81.3%**
Out.or.INpatient	**Out patient**	123	**64.1%**
	In patient	69	**35.9%**

Table 3.2: Prevalence of *E. coli* in UTI and ESBL according to gender

Parameter		**ESBL**						**(p-value)**
		Positive		**Negative**		**non.ESBL**		
		Count	**%**	**Count**	**%**	**Count**	**%**	
Gender	**male**	8	**4.2%**	0	**0.0%**	50	**26.0%**	**10.765 (0.005)***
	female	9	**4.7%**	19	**9.9%**	106	**55.2%**	

A total of 192 patients with suspected urinary tract infection (UTI) were included in this study. Urine samples were collected from patients using the standard mid-stream "clean catch" method and urine culture was performed in the laboratory. The prevalence of the study population according to gender was analyzed and statistical analysis were performed. Results show that 69.8% of the patients were females, which was significantly higher than male patients (30.2%). Out of 192 UTI patients, 55.2% females and 26.0% males had a non-ESBL UTI infection, but ESBL-positivity rate was also higher in the female group (4.7%) than the male group (4.2%). Therefore, the rates of *E. coli* in UTI and ESBL production among these infections were statistically higher in female than male patients (p-value 0.005).

Table 3.3: *E. coli* in UTI and ESBL according to IN & OUT patient

Parameter		ESBL						(p-value)
		Positive		Negative		non.ESBL		
		Count	%	Count	%	Count	%	
patient	Out patient	7	3.6%	9	4.7%	107	55.7%	7.556 (0.023)*
	In patient	10	5.2%	10	5.2%	49	25.5%	

This table show the Prevalence of *E.coli* in UTI and ESBL according to IN & OUT patient, the statistical analysis show there are 64 of total study population was out patients and 36% was In-patients, those who have non-ESBL are 55.7 % when comparing to in-patient 25.5% it show lower than out patient, also in ESBL patient the result determine the high rate in Positive ESBL in In-patient 5.2 % higher than Out-patient 3.2 %, also in Negative ESBL patient comparing result between two group In-

patient 5.2 show highest than Out-patient 4.7 %, and statistical P-value between two group according to ESBL was significant (P-value 0.023).

Table 3.4: *E. coli* in UTI and ESBL according to *E. coli* infection

Parameter		ESBL						(p-value)
		Positive		Negative		non.ESBL		
		Count	%	Count	%	Count	%	
Patient with E.coli	Yes	16	8.3%	19	9.9%	0	0.0%	185.68 (0.000)**
	No	1	0.5%	0	0.0%	156	81.3%	

In this study from total (192) patients who have clinical suspected urinary tract infection (UTI), therefore the urine culture at laboratory test perform in order to recognized the prevalence of whole study population percentage of *E.coli* infection in UTIs related to the ESBL production, according to the statistical analysis we found there are 18.2 % have been infected with *E.coli* comparing to non-*E.coli* infection was 81.8 %, in Non-ESBL group the rate of patients that have *E.coli* 0.0 % but in patient who have No *E.coli* infection was 81.3 %. But in the result was different in patients who have *E.coli* infection with positive result of ESBL 8.3 % higher when comparing to Non-*E.coli* infection was 0.5 %, also the negative ESBL in group that have *E.coli* was 9.9 % it is also high when evaluated with Non-*E.coli* group 0.0%, therefore and it is according to statistical significant value we can say the *E.coli* and ESBL production are significant higher from *E.coli* patients than the Non-*E.coli* group (p-Value 0.005).

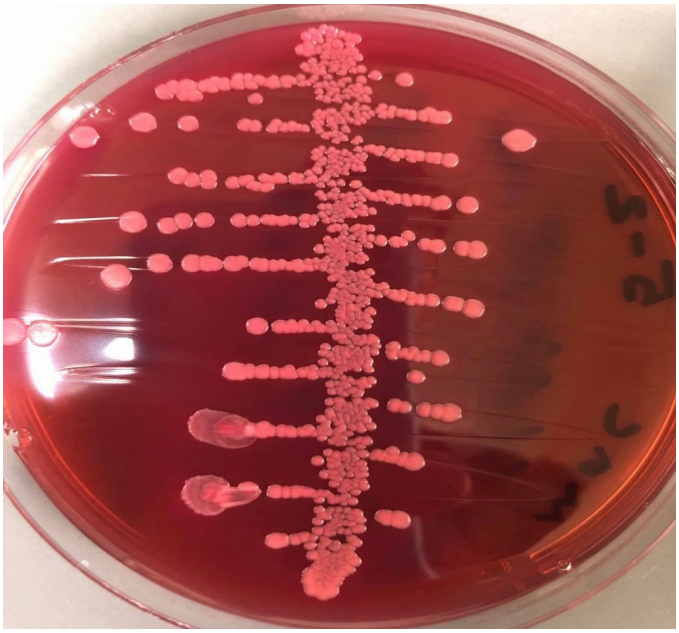

Figure 3.1: *E. coli* on MacConkey Agar

Figure 3.1: *E. coli* on Blood Agar

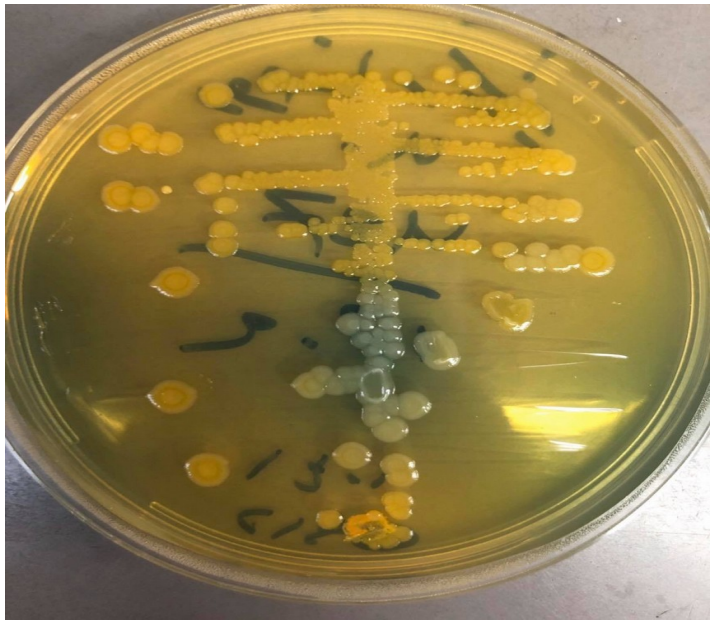

Figure 3.1: *E. coli* on CLED Agar

CHAPTER 4

4.1 DISCUSSION

In present study all in-patient and out patient's urine samples received in Rzgari Hospital Erbil-Iraq when patients suspected to have urinary tract infection in order to evaluated either it *E.coli* ESBL product positive or negative, later on comparing group of gender and type of patients, the culture study perform to the 192 of urine specimen following the administered all the samples in order to screen and evaluate the causative agents that relate to UTI especially those who relate to Extended Spectrum Beta Lactamase. for wholly samples culture examination of UTI perform to detect ESBL production, in previous experiment which conducted by the Azap, in 2010 the total positive samples were found for UTI with percentage of 21%. In height occurrence can be recognized and the data handed from various out patient to in patient associated with dissimilar sections of hospital who harbor the infection with urinary tract, also the *E. coli*-ESBL has developed the most troublesome causative agent of community-acquired UTIs. The previous study Azap demonstrate the prospective followers study estimating the prevalence of and risk factors for both uncomplicated and complicated UTIs. ESBL positivity was detected in 6.3% of E. coli isolates from uncomplicated UTIs and in 17.4% of *E. coli* isolates from complicated UTIs (Azap, Ö. K., et al, 2010).

In our study the results were divided to three categories (Gender, type of patient, UTI with *E. coli*) in order to comparing these groups to ESBL production. In the first section result was between the gender and ESBL production the result according to the statistical analysis was found that the rate of females 69.8 % are significantly more high than male 30.2 % out of 192 samples of UTI shows there was 55.2 % was females corespoding to male was 26.0 % have UTI infection without ESBL, but those patients have ESBL positive also high in female group than male (Female 4.7%) and (Male 4.2%), therefore according to statistical significant value we can say the E.coli in UTI and it is ESBL production are significant high in female

than male (p-Value 0.005). Also, in *Laupland, K. B.,* study perform on 247 patients mention that the rate of

mentione the females were at higher risk as compared to males (Laupland, K. B., et al, 2008).

The second aim was clarify the type of the In-patient and Out-patents among to *E.coli* in UTI, in our statistical analysis show there are 64% of total study population was pertaining to group of out patients and 36% in patients, those who have non-ESBL are 55.7 % when comparing to in-patient 25.5% it show lower than out patient, also in ESBL patient the result determine the high rate in Positive ESBL in In-patient 5.2 % higher than Out-patient 3.2 %, also in Negative ESBL patient comparing result between two group In-patient 5.2 show highest than Out-patient 4.7 %, and statistical P-value between two group according to ESBL was significant (P-value 0.023). Also there are many experimental study show that the rate of patients who have *E.coli* infection with ESBL production are higher in In-patient when comparing to Out-patient group, in *Al-Assil, B.,*mention the In-patient value was 35 (79.54%), when comparing to Out-patient group 20 (33.33%) we can also see the high different between two group among to *E.coli*-ESBL production (Al-Assil, B., et al, 2013).

In this study from total (192) patients collected in order to comparing *E.coli* infection and it is production ESBL enzyme or not, after sample collection the present study show the result according to the statistical analysis there are 18.2 % have been infected with *E.coli* comparing to non-*E.coli* infection was 81.8 %, in Non-ESBL group the rate of patients that have *E.coli* 0.0 % but in patient who have No *E.coli* infection was 81.3 %. But in the result was different in patients who have *E.coli* infection with positive result of ESBL 8.3 % higher when comparing to Non-*E.coli* infection was 0.5 %, also the negative ESBL in group that have *E.coli* was 9.9 % it is also high when evaluated with Non-*E.coli* group 0.0%, therefore and it is according to statistical significant value we can say the E.coli and ESBL production are significant higher from *E.coli* patients than the Non-*E.coli* group (p-Value 0.005). also in *Melzer, M., & Petersen, I.* mention that the rate of mortality following bacteraemic infection caused by ESBL producing *E. coli* was significantly higher than non-ESBL producing

E. coli which is mean the *E.coli* and ESBL production are significant higher from *E.coli* patients than the Non-E.coli group (Melzer, M., & Petersen, I., 2007).

CHAPTER 5

5. CONCLUSION AND RECOMMENDATION

5.1. Conclusion

In the current study according to data observation result show the total frequency of enzymatic ESBL of bacterial *E. coli* within public of Erbil-Iraq. Self-governing the hazard issues of ESBL were habitation in an extended period repair capability urinary catheterization, probable forgoing antibiotic practice especially relate with older age, gender and type of patients. Consequently the doctor must take care in side of high-risk patients in addition to aim of the early suitable experiential antimicrobial treatment to decrease the amount of the mortality with public bloodstream contagions which relate to the *E. coli* and it is ESBL-producing.

The experimental result shows the prevalence of UTI out of 192 urine specimens divided to two groups (outpatient and inpatient) collected from patients complaining of signs and symptoms of UTIs at Rizgari teaching hospital. (64.1%) were out patient and (35.9%) were in patient, all patients age history period was between 4-86 years divided to three groups (teenage less 4.7%, adult 78.6% and old 16.7%), according to gender the population was divided to 30.2% of male and also 69.8% was from female. In the period from January to April 2020, urine samples were taken (by standard mid-stream “clean catch” method) from patients with clinical suspected urinary tract infection (UTI), also there are 30.2 % of them have history with surgical operation and 36..5 % of them have chronic disease infection, moreover 60.9% of total patents was used long medication usage, Thirty-five (18.2%) were diagnosed as *E.coli* by Vitek 2 for bacterial identification and (81%)of other was free of *E.coli* infection, therefore those patients have *E.coli* positive there was seventeen (8.9%) of them was

ESBL positive, following nineteen (9.9%) of them was ESBL negative, in addition to (81.3%) was Non-ESBL.

In this study the prevalence of whole study population related to the genders and it is ESBL production according to the statistical analysis show that the rate of females 69.8% are significantly more high than male 30.2 %, also the Prevalence of *E.coli* in UTI and ESBL according to IN & OUT patient, the statistical analysis show there are 64 of total study population was out patients and was in patient 36%, moreover the result show the prevalence of whole study population percentage of *E.coli* infection in UTIs related to the ESBL production, according to the statistical analysis we found there are 18.2 % have been infected with *E.coli* comparing to non-*E.coli* infection was 81.8 %.

5.2. RECOMMENDATION

1. It is quite alarming to note the high prevalence of extensively resistant ESBL producing isolates in our setup, which is posing a major clinical crisis of treatment failure with β-lactam antimicrobials.

2. screening for ESBL detection should perform to all patient who have UTIs infection

3. Also the antibiotic susceptibility checking should be preform to limit the evolvement of highly resistant strains

4. improve the treatment and management of UTI.

5. The genetic recombination of ESBL producing strains of all over the country to improve the knowledge regarding such fastidious organisms.

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APPENDIX

Appendix A

Hawler Medical University
College of Health Sciences

Meeting code: E5
Ref. No: HMM 48
Date: 10/4/2020

HAWLER MEDICAL UNIVERSITY
College of Health Sciences

RESEARCH ETHICS COMMITTEE APPROVAL SHEET

Title of the project: Extended-spectrum beta lactamase rates of Eschrichia coli from urinary tract infection in Rizgary Hospital, Erbil, Iraq.

Principle investigator: Mohamed Hussein Mohamed Ali

Co-investigators: Dr. Warkaa Faraj Ahmad, Dr. Sahar Mohammed Zaki Abdullah

Head of Committee
Prof. Kochar M. Shareef

Committee Member
Dr. Fatmen A. Ali

Committee Member
Dr. Runak A. Hwaiz

CURRICULUM VITAE

Mohamed Hussein Mohamed

Basic information:

Age: 25 years old Sex: Male

Nationality: Iraqi State: Single

Tel. No. (009647503760600) Address: Erbil

Education State and Certification:

(Bachelor in Pathological Analysis Department)

(Faculty of Science)

Languages Talking and Writing:

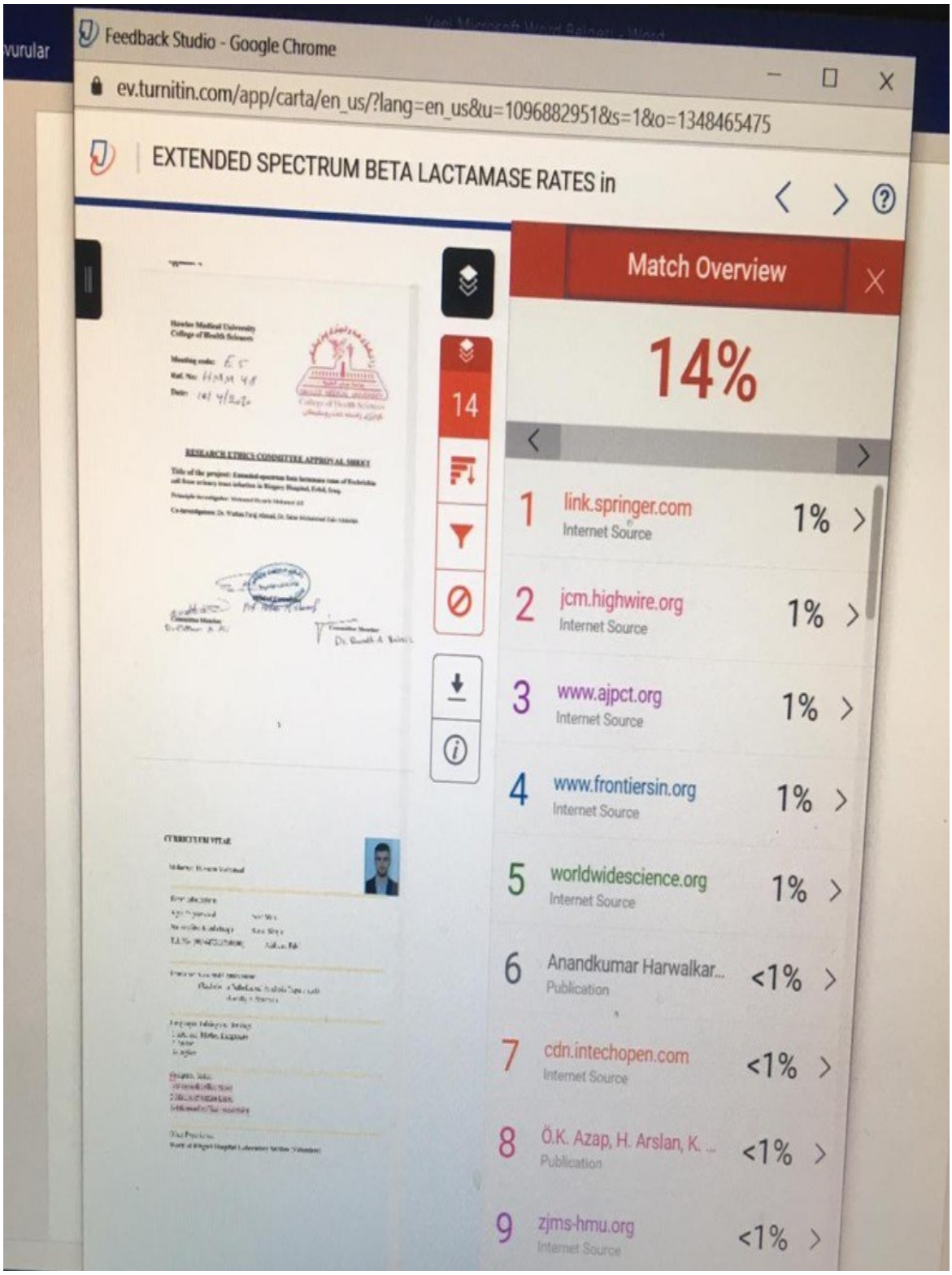
1-Kurdish (Mother Language)
2-Arabic
3-English

Computer Skills:

1-Microsoft Office Word
2-Microsoft Office Excel
3- Microsoft Office PowerPoint

Other Experience:

Work at Rizgari Hospital Laboratory Section (Volunteer)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EXTENDED SPECTRUM BETA LACTAMASE RATES in
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