Prevalence of Adhesive Pap Gene (Pyelonephritis Associated Pili) among Uropathogenic *Escherichia Coli* Strains Isolated from Out Patients and in Patients with Urinary Tract Infection in Ain Shams University Hospital

Thesis

Submitted for Partial Fulfillment of Master Degree in Basic Medical Sciences
(Medical Microbiology and Immunology)

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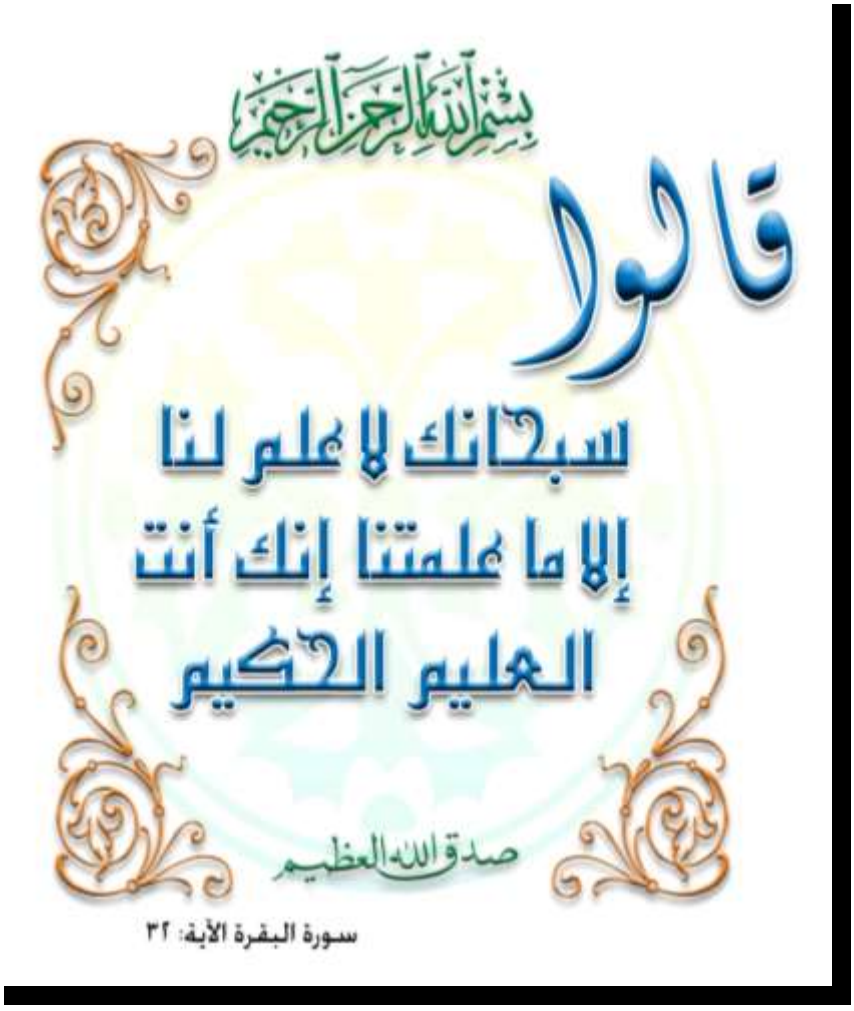
2018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Acknowledgments

First and foremost, I feel always indebted to **Allah**, *the* ***Most Beneficent*** *and* ***Merciful*** *who gave me the strength to accomplish this work.*

My deepest gratitude to my supervisor, **Prof. Dr. Mahmoud Khalil El Sayed,** *Professor of Medical Microbiology and Immunology, Faculty of Medicine, Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision.*

I would like to express my great and deep appreciation and thanks to **Dr. Dina Mohammad Erfan,** *Assistant Professor of Medical Microbiology and Immunology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work. I greatly appreciate her efforts*

I must express my deepest thanks to **Dr. Ahmed Kamal Mohamed,** *Lecturer of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, for guiding me throughout this work and for granting me much of his time to accomplish this work.*

Special thanks to all members of my **Family** *members for their continuous encouragement, enduring me and standing by me.*

Fatma Mostafa Abdel Wahed

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List of Abbreviations

Abbr.	Full term
β-lactam.....	Beta lactam
ASB	Asymptomaic bacteriuria
CAMP	Cyclic adenosine monophosphate
CAUTI	Catheter-associated Urinary tract infection
CDC	Centers for disease control and prevention
CLED	Cystine lactose electrolyte deficient
CLSI.....	Clinical and laboratory standards institute
CTX.....	Cefotaxime
CTX/KV	Cefotaxime /clavulanic acid
DNA	Deoxyribonucleic acid
E.coli	*Escherichia coli*
EPS.....	Extracellular polymeric substances
ESBL.....	Extended spectrum B-lactamas
EXPEC	Extra intestinal pathogenic E.coli
GBS.....	Group-B-Streptococci
HAIS	Health care-associated infections
I	Intermediate

IBC ..... Intracellular bacterial communities

IgA..... Immunoglobulin A

IL-6 ..... Interleukin 6

IL-8 ..... Interleukin 8

K.pneumoniae.. Klebsiella pneumoniae

LTCF ..... Long term care facilities

MDR ..... Multidrug resistant

MSU ..... Mid stream urine

NHSN..... National health care safety network

NIH ..... National institutes of health

P.mirabilis ... Proteus mirabilis

PAP ..... Pyelonephritis Associated Pilli

PCR..... Polymerase chain reaction

QS..... Quorum sensing

R ..... Resistant

S..... Sensitive

S.aureus ..... Staph aureus

SD ..... Standard deviations

Spp ..... Species

SUTI..... Symptomatic urinary tract infection

TLRs ..... Toll-like receptors

UPEC ..... Uropathogenic *Escherichia coli*

USA ..... United State of America

UTIs ..... Urinary tract infections

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ABSTRACT

Background: E.coli is the most common cause of urinary tract infection (UTI) both in the community and hospital settings. Uropathogenic E.coli (UPEC) possesses a number of virulence factors that allow it to colonize and persist in the urinary tract. Of particular interest are the P pili and biofilm formation. The emergence of drug resistant E.coli is a global threat to the public health. **Objectives:** To determine the biofilm producing ability, antimicrobial susceptibility pattern, ESBL production and the presence of the adhesive pap gene (pyelonephritis associated pili) in E-coli strains isolated from Outpatients and Inpatients diagnosed with UTI. **Methodology:** The study was conducted on 40 Inpatients and 40 Outpatients diagnosed with UTI attending Ain Shams University Hospitals. E. coli Isolates were tested for antimicrobial susceptibility using disk diffusion method, ESBL production by ESBL detection discs, in vitro formation of biofilm on Congo red media, and detection of Pap gene using conventional PCR technique**. Results:** The prevalence of antibiotic resistance was significantly higher in E.coli isolates from inpatients group than those from the outpatients group. The prevalence of ESBL production, biofilm formation and pap gene among E. coli isolates was 55%, 82.5% & 40% respectively. ESBL production and biofilm formation were significantly higher in the inpatients with upper UTI than in patients with lower UTI (90- 38.5%) & (100-61.5%) respectively. There was no statistically significant difference between the 2 groups as regards the prevalence of pap gene. **Conclusion:** The prevalence of biofilm producing, ESBL producing and antibiotic resistant E.coli strains is more in the inpatients population particularly those with upper UTI. Special concern should be addressed to the spread of ESBL producing E.coli in the community. Pap gene is expressed equally in the outpatients and inpatients groups which highlights its importance in the establishment of UTI.

Key words: E.coli, UTI, ESBL, pap, gene, congo red medium, virulence factors

INTRODUCTION

Urinary tract infection (UTI) is defined as microbial infiltration of the otherwise sterile urinary tract and is one of the most common bacterial infections world wide. UTIs encompass infections of the urethra (urethritis) ,bladder (cystitis), ureters (ureteritis) and kidney (pyelonephritis) (**Barber etal., 2013)**. They account for ~150–250 million cases globally per year **(Asadi et al., 2014)**. More than 50% of women will have at least one episode of UTI during their lifetime, furthermore, after an initial episode of UTI, women are more likely (20–40%) to get recurrent UTIs **(Grab et al., 2008)**.

UTI patients are classified as either asymptomatic or symptomatic cases. Asymptomatic bacteriuria (ABU) occurs in a small number of healthy individuals and may not need treatment, which makes it different from symptomatic bacteriuria. It often affects pregnant women, with varying prevalence among different populations, depending on factors such as age, sex, sexual activity, and the presence of genitourinary abnormalities **(Grab et al., 2008)**.

Uropathogenic *Escherichia coli* (UPEC) is the most common cause of urinary tract infections (UTIs) both in

community and hospital settings with significant morbidity and mortality worldwide **(Bien et al., 2012)**.

UPEC strains encode widespread virulence factors closely related to colonization, persistence, and pathogenesis of bacteria in the urinary tract, the most important of these factors include adhesins or fimbriae, biofilm formation, and toxins such as hemolysin **(Dhakal et al., 2008)**.

Type I and P are the most common fimbriae found in UPEC strains. They play an important role in binding and invasion to bladder (cystitis) and kidney (pyelonephritis) epithelial cells **(Wullt et al., 2000)**.

Biofilm of UPEC provides a nutrient-rich environment which promotes growth and persistence of microorganisms at the site of infection, and protects bacteria from antimicrobial substances **(Hancock et al., 2010)**. Moreover, UPEC strains often express and secrete a labile pore-forming toxin known as α- hemolysin that is mainly associated with more virulent UPEC strains **(Laura et al., 2012)**.

Emergence of drug resistance to broad-spectrum beta lactams mediated by extended spectrum beta lactamases (ESBLs) and especially multi-drug resistant (MDR) clonal groups among UPEC strains increase the serious threat to global public health **(Hilbert, 2011)**.

AIM OF THE WORK

This study aimed to determine the presence of the adhesive pap gene (pyelonephritis associated pili), the biofilm producing ability, antimicrobial susceptibility pattern and ESBL production in *E-coli* strains isolated from out patients and inpatients diagnosed with UTI in Ain Shams University Hospital.