

**THE ANTIBIOTIC PROFILE OF BACTERIA ISOLATED FROM CASES OF
URINARY TRACT INFECTIONS IN ILE-IFE AND THE
CHARACTERISATION OF THE PREDOMINANT *Escherichia coli***

By

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CERTIFICATION

I certify that this project was carried out by OLORUNMOLA, Felix Oluwasola in the Department of Microbiology, Obafemi Awolowo University, Ile-Ife.

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ABSTRACT

The primary objective of this study was to determine the antibiotic resistance profile of the various uropathogenic isolates from both in-patient and out-patient cases, and to investigate the virulence factors exhibited by the predominant *E. coli* isolates in order to determine their level of pathogenicity.

Clean voided midstream urine samples were collected daily from patients at the Obafemi Awolowo University Teaching Hospital Complex (OAUTHC), and the Seventh Day Adventist Hospital (SDAH), Ile-Ife, between May 2002 and December 2004. Urine samples were obtained from 215 in-patients and 181 outpatients. There were 168 male (42.42%) and 228 female (57.58%) patients. The samples were cultured on McConkey Agar (Oxoid) or Cysteine Lactose Erythrocyte Deficient (CLED) medium for isolation of the organism with bacterial counts of 10^5 colony forming unit per milliliter (CFU/ml.) and above were considered as being indicative of urinary tract infection (UTI). Bacterial isolates were identified based on cultural, morphological and biochemical characteristics. Their antibiotic susceptibility pattern was determined by the agar disc diffusion method, using standard antibiotic discs. Production of virulence factors such as haemagglutinin, haemolysin, colicin and capsule by the *E. coli* isolates were also determined using standard methods.

. The samples yielded a total of 412 isolates, made up of 33.25% *E. coli*, 19.42% *Klebsiella pneumoniae*, 9.47% *Staphylococcus aureus*, 8.50% *Pseudomonas aeruginosa* and, *Proteus* species (7.04%). Other organisms occurred to less than 5% of the total and these are: *Serratia marcescens* (4.13%), Coagulase negative staphylococci (3.88%), *Providencia* species (3.15%), unspiciated cocci (3.64%), *Enterobacter aerogenes* (2.66%), *Salmonella* species (1.46%), *Pantoea agglomerans* (1.21%), *Morganella morganii* (0.98%) and *Citrobacter* species (1.21%).

The major organisms were more than 50% resistant to amoxicillin, trimethoprim/sulphamethaxole, gentamycin, nalidixic acid, augmentin, tetracycline and erythromycin. The result also highlighted a high level of resistance to the fluoroquinolones; norfloxacin, (76.3% and 86.9%), ciprofloxacin (50.0%, and 65.7) and ofloxacin (42.5% and 51.1%) by the predominant *E. coli* and *Klebsiella pneumoniae* respectively. There was not much difference in the antibiotic resistance patterns of inpatient and outpatient isolates. Gram-positive isolates generally demonstrated lower antibiotic resistance than the Gram-negative ones. Nitrofurantoin was highly effective against all the Gram-negative isolates except *Pseudomonas aeruginosa*. Twenty-one (63.64%) of the 33 trimethoprim resistant *E. coli* were able to transfer their resistance traits into plasmidless *E. coli* K12 C600. Furthermore, the results revealed for the first time in this environment, that most of these multiple and highly antibiotic resistant *E. coli* isolates possess virulence factors such as haemolysin (7.3%), mannose resistant haemagglutinin (13.87%), colicin (9.49%) and capsule (37.23%), thus confirming that they are truly uropathogenic *E. coli* (UPEC) strains.

In conclusion, this study shows that the resistance of isolates from both the inpatient and outpatient cases of UTI is high and widespread in this environment.

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Bacterial infection of the urinary tract, commonly known as urinary tract infection (UTIs), is a condition where one or more structures in the urinary tract become infected after bacteria have overcome its strong natural defenses. In spite of these defenses, UTIs are the most common and serious health problems that affect millions of people all over the world (Nidus Information Services, 2001). While it may be asymptomatic in some patients i.e. having significant bacteriuria without symptoms (Sobel and Kaye, 1995), in some others it may be accompanied by dysuria, cystitis and pyelonephritis (Karaoune and Hanna, 1981; Delzell and Lefferre, 2000), in which case it is said to be symptomatic. Significant bacteriuria has been historically defined as the presence of 10^5 colony forming units or more per milliliter (cfu/ml.) of mid stream urine (Kass, 1957). Urinary tract infections have been reported in all age groups, and in both sexes. They can be divided into seven epidemiologically defined groups (Brumfitt and Hamilton-Miller, 1991) (i) Children < 1 year of age; (ii) girls; (iii) pre-menopausal women; (iv) men with prostatic or other causes of urinary tract obstruction; (v) post-menopausal women; (vi) individual with neurogenic bladders and (vii) patients with in-dwelling urinary catheters. Although the pathophysiology of infections in each of these groups is different owing to a variety of host factors, a common denominator is the ability of the pathogen responsible for the infection to grow and multiply in urine. Russo *et. al.*, 1996 has suggested that the low level of arginine present in human urine is responsible for the survival and proliferation of the pathogens. UTIs are known to cause morbidity (Savage *et. al.*, 1973; Jacobson *et. al.* 1992; Jacobson *et. al.*, 1994) and mortality (Neumann and Pryless, 1962), particularly in children when poor or delayed management may result in renal damage, which in later life may lead to hypertension and renal failure (Smellie and Normand, 1986; Jacobson *et. al.* 1992).

1.2 Classification of Urinary Tract Infections

Urinary Tract Infections have been classified into the following categories (Nidus Information Services, 2001; Brettle, 2005)

1.2.1 Primary and recurrent UTIs, depending on whether they are the first infection or whether they are repeat events. Primary or isolated infections are either initial episodes of infection or are separated by six months from other episodes of infections. Between 25 to 40% of women, ranging from 30-40 years of age and, most men present with isolated infections (Coln and Schaeffer, 2001)

Recurrence is often categorized as either re-infection or relapse (also known as unresolved) infection. Relapse is a less common form of recurrent UTI than re-infection. It is diagnosed when a UTI recurs within two weeks of treatment of the first episode and is usually due to treatment failure. Relapse usually occur in kidney infection (pyelonephritis) or is associated with obstructions such as kidney stones, structural abnormalities or in men's chronic prostatitis. A re-infection occurs several weeks after antibiotics treatment has cleared up the initial episode and can be caused by the same bacteria strain that caused the original episode or a different one from outside the urinary tract. Re-infection represents about 80 to 95% of recurrent UTIs in women.

1.2.2 Community- or Hospital- acquired infection: Although the mechanisms of occurrence or the mode of spread of most UTIs remain unclear, they are thought to develop in the community at large. Most community-acquired infections are not serious and probably develop when the intestines become colonized with bacteria that are also pre-disposed to infecting the urinary tract. Hospital acquired (Nosocomial) UTI are the urinary tract

infections that are commonly acquired in the hospital, often due to contaminated catheters. Hospital acquired infections tend to be more serious because the bacteria that cause them are often resistant to drug treatment and the patients are often in poor general health.

1.2.3 Uncomplicated and Complicated UTIs: UTIs are sometimes further defined as either being uncomplicated or complicated depending on the factors that trigger the infections. Uncomplicated infections are only associated with bacterial infection most often *Escherichia coli*. They affect women much more than men because the women urethra is short and, the urethral opening is near the sources of bacteria from the anus and vagina, thereby allowing bacteria quick access to the bladder (Strom et. al., 1987). Uncomplicated urinary tract infections can be any of the following types:

Cystitis - this is sometimes referred to as acute uncomplicated UTI, and is the most common urinary tract infection (NIS, 2001). It occurs in the lower urinary tract (the bladder and urethra) and nearly always in women. In most cases, the infection is brief and acute and only the surface of the bladder is infected.