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PREVALENCE AND ANTIBIOTIC RESISTANCE OF *E. COLI* IN URINARY TRACT INFECTIONS AMONG PREGNANT WOMEN IN NIGERIA

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ABSTRACT: *Urinary tract infections (UTIs) are a significant health issue for pregnant women, primarily due to physiological and anatomical changes during pregnancy that increase susceptibility. This review investigates the prevalence and antibiotic resistance patterns of Escherichia coli (E. coli), the leading cause of UTIs in pregnant women in Nigeria. Uropathogenic E. coli (UPEC) has been identified as the primary pathogen, with studies indicating high prevalence rates across various regions of Nigeria. The rise in antibiotic-resistant UPEC strains poses a considerable challenge for treatment, often leading to complications. Contributing factors include poor socioeconomic conditions, inadequate healthcare infrastructure, and the misuse of antibiotics, which exacerbate the situation. The review evaluates various diagnostic methods, including urine culture, polymerase chain reaction (PCR), and Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) mass spectrometry, emphasizing the necessity for accurate and timely detection to effectively manage UTIs. The impact of UTIs during pregnancy is significant, potentially resulting in preterm birth, low birth weight, and maternal morbidity if untreated. The importance of routine screening, antibiotic stewardship, and enhanced surveillance is highlighted as essential strategies to mitigate these adverse outcomes and improve maternal and neonatal health. Public health interventions are urgently needed to enhance diagnostic infrastructure, implement effective antibiotic stewardship programs, and strengthen surveillance of antibiotic resistance patterns. Additionally, educating healthcare providers and patients on the prudent use of antibiotics and the importance of early detection and treatment of UTIs is crucial. Addressing these challenges requires a multifaceted approach involving improved healthcare practices, policies, and continuous research, aiming to enhance health outcomes for both mothers and infants in Nigeria.*

KEYWORDS: Urinary Tract Infections (UTIs), Pregnant Women, *Escherichia coli* (*E. coli*), Antibiotic Resistance, Multidrug-Resistant (MDR) Strains, Nigeria.

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INTRODUCTION TO UTI

Numerous human ailments stem from infections induced by bacterial pathogens, whether they are external or internal to the human host. An example of such a bacterial infection is Urinary Tract Infection (UTI), which entails the presence of bacteria in the naturally sterile urinary tract (UT) (Zorc, 2005). UTI stands as a prevalent ailment affecting individuals across all age groups and genders, often resulting from inadequate diagnosis and classified as a common hospital-acquired infection (Koffuor *et al.*, 2012; Kolawole *et al.*, 2009).

UTIs are classified as complicated or uncomplicated. Uncomplicated UTIs usually affect people who are otherwise healthy and do not have structural or neurological urinary tract abnormalities. These infections are divided into lower UTIs (cystitis - bladder infection) and upper UTIs (pyelonephritis - kidney infection). Complicated UTIs are defined as UTIs that are associated with factors that compromise the urinary tract or host defence, including pregnancy, urinary obstruction, immunosuppression, urinary retention caused by neurological disease, etc. (Flores-Mireles *et al*., 2015). Symptoms linked to bladder and kidney infections differ, with cystitis manifesting as painful and frequent urination due to bladder involvement, while pyelonephritis commonly presents with symptoms such as high fever and flank pain (Jamaluddin *et al.*, 2022).

Urinary tract infection (UTI) is a prevalent health issue typically linked with the state of pregnancy (Ali *et al.*, 2022). Expectant mothers face an elevated susceptibility to UTI owing to physiological adjustments and anatomical modifications throughout pregnancy (Ahmed *et al.*, 2019; Michelin *et al.*, 2016). UTIs during pregnancy can manifest as asymptomatic bacteriuria, acute cystitis or pyelonephritis (McCormick *et al.*, 2008). Asymptomatic bacteriuria is evident in approximately 2% to 10% of all pregnancies, and if left untreated, it may progress to acute cystitis and pyelonephritis in up to 30% and 50% of expectant mothers (Smaill & Vazquez, 2007). Neglected bacteriuria has been correlated with a range of adverse health consequences during pregnancy, including low birth weight, preterm birth, sepsis, septic shock, anaemia, and perinatal mortality (Taye *et al.*, 2018).

Urinary Tract Infections (UTIs) are attributed to a variety of microorganisms including Gram-negative and Gram-positive bacteria, as well as certain fungi (Zorc, 2005). The primary causative agent responsible for both simple and complex UTIs is uropathogenic *Escherichia coli* (UPEC). The colonization of the urinary tract by bacteria is mainly instigated by Gram-negative strains like *Escherichia coli*, Klebsiella, Proteus, and Pseudomonas, with occasional involvement of Gram-positive microbes such as hemolytic Streptococci and Staphylococcus saprophyticus. Gram-positive bacteria contribute to 15-20% of UTIs, while Gram-negative bacteria account for 80-85% of cases (Cheesbrough, 2006). *Escherichia coli* stands out as the predominant pathogen among Gram-negative bacteria; however, in complicated UTIs, there is an escalation in the prevalence of other antibiotic-resistant organisms like Klebsiella, Proteus, Serratia, Enterobacter, and Pseudomonas. Within the realm of Gram-positive bacteria, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, *Streptococcus pyogenes*, and *Staphylococcus aureus* are commonly found and exhibit resistance to a spectrum of antibiotics (Dube *et al.,* 2022; Jamaluddin *et al.*, 2022).

Escherichia coli (*E. coli*), a gram-negative bacterium belonging to the order Enterobacterales, has been identified as the predominant pathogen linked to urinary tract infections in pregnant women (Al-Badaii *et al.*, 2023; Cotton *et al.*, 2022; Mohammed *et al.*, 2022; Mishra *et al.*,

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2018). It possesses adhesins that exhibit a high affinity for the uroepithelium, along with various mechanisms that allow it to survive lethal concentrations of antibiotics. These mechanisms include the production of enzymes that degrade aminoglycosides and beta-lactamases, as well as alterations in target proteins and the upregulation of efflux proteins (Yeta *et al.*, 2021; Odongo *et al.*, 2020). Furthermore, *Escherichia coli* has been recognized as a significant contributor to multidrug-resistant urinary tract infections during pregnancy, both in human populations and animal experimental models (Ugwu *et al.*, 2022).

One sort of drug resistance that microorganisms can withstand when exposed to antibiotics is known as antibiotic resistance (Sengupta & Chattopadhyay, 2012). One major factor contributing to the formation of resistance by bacteria is the extensive use of antibiotics both within and outside of the medical field. Nowadays, it is all too frequent to contract an illness from a resistant bacterial strain, and certain pathogens have developed resistance to several classes or types of antibiotics (antimicrobials used to treat bacterial infections) (Goossens *et al.*, 2005).

The treatment of UTI poses greater challenges as a result of the emergence of drug-resistant uropathogens to commonly used antimicrobial agents (Abejew *et al.*, 2014; Ade-Ojo, 2013). Within the Nigerian context, the prevalence of drug abuse and misuse is notably high among untrained practitioners, drug users, and healthcare providers. Additional research indicates the significant impact of drug resistance on the efficacy of managing previously treated infections, thereby potentially leading to heightened levels of morbidity, mortality, and treatment expenses (Nkene *et al.*, 2015; Demilie *et al.*, 2014; Delzell & Lefevre, 2000). Various factors contribute to the increased prevalence of UTI, including poor socioeconomic status, which substantially elevates the risk of UTI infection, with a fivefold increase in risk observed among economically disadvantaged patients (Derese *et al.*, 2016; Alfred *et al.*, 2012; Encarnacion, 2012; Haider *et al.*, 2010).

The management of urinary tract infections (UTI) in pregnant women holds significance in alignment to promoting safe motherhood, aiming to guarantee the well-being of women throughout the gestational period and delivery, as well as the birth of robust infants. The emergence of antibiotic resistance poses a significant challenge in the global management of infectious diseases (Tadesse *et al.*, 2014; Emiru *et al.*, 2013; Alemu *et al.*, 2012).

Epidemiology of *E. coli* UTIs in Pregnant Women

E. coli is implicated in many UTIs in pregnant women all over the world, causing both complicated and uncomplicated UTIs. *E. coli* UTIs, as well as those arising from *Klebsiella pneumoniae, Staphylococcus saprophyticus*, *Proteus mirabilis,* amongst others, are a recognized public health problem (Flores-Mireles *et al*., 2015). A South-African study attested that the gram-negative lactose fermenter was predominant in all urine samples of pregnant women examined for six consecutive years. The organism also co-infected its human hosts alongside *E. faecalis* and *Klebsiella pneumonia*e (Nana *et al*., 2021). Owing to its ubiquity and virulence in both community-acquired and nosocomial infections of pregnant women, research has been conducted in diverse countries to measure the prevalence of *E. coli* UTIs among other UTIs. Much of such research investigated its virulence patterns, antibiogram, or even molecular epidemiology in different clinical settings. Forson *et al*. (2018) characterised and determined the antibiogram, resistance genes, and profiles of virulence of 82 *E. coli* isolates from bacteriuria in pregnant women in Ghana. Ramos *et al*. (2012) similarly investigated the

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virulence features of *E. coli* isolates associated with UTI in Sweden, Vietnam, and Uganda, thus corroborating the cosmopolitan nature of UTI infections due to the uropathogenic *E. coli* (UPEC). A similar epidemiological study has been conducted in Mexico, where *E. coli-associated* maternal and perinatal complications in pregnant women were described (Dautt-Leyva *et al*., 2018). *E. coli* was also the most implicated pathogen causing UTIs among pregnant women attending antenatal clinics at Khartoum North Teaching Hospital, presenting itself in both asymptomatic and symptomatic bacteriuria (Hamdan *et al.,* 2011). A retrospective cohort study conducted in a Danish community between January 2010 and September 2016 in adults (including men, non-pregnant, and pregnant women) with community-acquired *E. coli* Bacteriuria found close to 22000 cases of UTIs (Boel *et al*., 2019). A cross-sectional study was also conducted by Mohamed *et al*. (2024) between August 2022 and December 2022 on prevalence, antimicrobial susceptibility pattern, and associated risk factors of UPEC among pregnant women attending a popular hospital in Somalia.

In Nigeria, there is paucity of studies strictly identifying the prevalence of *E. coli* UTIs. This is not surprising as pathogens often co-infect their host organisms. Studies revealing the prevalence of *E. coli* as the primary causal organism of UTIs in different parts of the country, however, exist. Oladeinde *et al*. (2015) recorded a prevalence rate of 55% for UTIs in their study to identify causative organisms of UTIs in Benin City, Nigeria. A semi-quantitative investigative study screening for asymptomatic bacteriuria conducted during the initial trimester of pregnancy on 500 consecutive pregnant women in Benin City identified bacteriuria due to both single and mixed colonies (Akerele *et al*., 2001). Contrary to findings from recent research, this 2001 study found *E. coli* to be second to *S. aureus* among the UTI causative organisms, although with less than 1% difference. Clean midstream urine samples of 200 pregnant women attending outpatients' clinics in selected hospitals in Ebonyi State, between April and August 2013, were found to contain predominantly *E. coli* (50%), followed by *Staphylococcus aureus* (17.3%) (Onuoha *et al*., 2014). At the Murtala Muhammed Specialist Hospital in Kano, Northern Nigeria, *E. coli* is similarly the most identified causative organism of the UTIs (Ali & Abdallah, 2019), with a higher incidence rate found among pregnant women between 26 and 30 years. A study conducted in southern Nigeria, recording 25.3% as the prevalence rate of UTIs among pregnant women, also identified *E. coli* (40%) as the most commonly isolated organism in all cases that tested positive for UTIs, followed by *Pseudomonas aeruginosa* (Lawani *et al*., 2015). An alarming prevalence rate was found in a 2014 study conducted in Edo State, Nigeria, among pregnant women. Over 80% of the isolated UTI organisms from pregnant women were *E. coli* (Turay *et al*., 2014). *E. coli* was the most predominant pathogen responsible for UTIs in many other studies (Okonko *et al*., 2010; Oladeinde *et al*., 2015; Laili *et al*., 2018; Nwanhukwu *et al*., 2018; Vicar *et al*., 2023). The incidence rate (46.1%) of UTIs in North-central Nigeria was statistically significant, and *E. coli* was 60% prevalent (Akobi *et al*., 2014).

Demographic Characteristics of Affected Pregnant Women in Nigeria

Lawani *et al*. (2015), in their study conducted almost 10 years ago, established that bacteriuria is independent of the age of infected persons. Meanwhile, the incidence of UTIs in pregnant women is strongly associated with certain demographic properties including race, parity, and socioeconomic status in a more recent study (Dautt-Leyva *et al*., 2018). At the Murtala Muhammed Specialist Hospital in Kano, most of the UTI patients were unemployed, rural dwellers, and the majority of UTI patients were also subjects without formal education (Ali & Abdallah, 2019). Maternal sociodemographic features affecting UTIs include age at

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conception, maternal occupation, race or ethnicity, educational attainment at delivery, and household income. UTIs were most prevalent among pregnant women less than or equal to 19 years at conception (Getaneh *et al*., 2021; Johnson *et al*., 2021).

Risk Factors for E. coli UTIs in Pregnant Women

Predominant among predisposing factors of *E. coli* UTIs include physiological change that happens during pregnancy (Ramos *et al*., 2012). Hormonal secretions and mechanical changes which promote urinary stasis, difficulty with hygiene, together with the impact of already short urethra in pregnant women, all promote the incidence or prevalence of UTIs among pregnant women. History of antibiotics use and urinary catheterizations and underlying metabolic disease, such as diabetes mellitus (Majrashi *et al*., 2020), are similarly important risk factors. Vicar *et al*. (2023) submitted that open defecation and use of public defecation facilities are important factors predisposing to UTIs among pregnant women. Other factors include educational level, socioeconomic level, history of UTIs, gestational age, parity, maternal age group, and sexual activity at least once in the past two weeks, with the last two factors being significant statistically (Mohamed *et al*., 2024).

Antibiotic Resistant Patterns of *E. coli*

E. coli has both intrinsic and acquired resistance to some antibiotics. The impermeability of the external cell membrane of *E. coli* to antibiotics and expression of numerous efflux pumps constitute two major ways by which *E. coli* resists the impact of antibiotics intrinsically (Galindo-Méndez, 2020). While the former ensures that the delivery of antibiotics into their site of action is thwarted, the latter dispels the antibiotics from the bacterial cell. Apart from innate resistance to antibiotics, *E. coli* possesses acquired resistance to different drug categories. *E. coli* strains exhibit resistance to β-lactam antibiotics by producing the enzyme extended-spectrum β-lactamase (ESBL), which is a plasmid-mediated β-lactamase that is potent enough to hydrolyse and inactivate β-lactams antibiotics such as cephalosporins and monobactams (Chmielarczyk *et al*., 2014)

In 2018, over 50% of the *E. coli* isolates reported to the European Centre for Disease Prevention and Control exhibited resistance to one or more antimicrobial groups under surveillance, with combined resistance to several antimicrobial groups being frequent (European CDC, 2020). A national surveillance conducted in the United States in 2017 revealed that the prevalence of extended spectrum β-lactamases (ESBL)-producing *E. coli* strains isolated from urinary tract infections (UTI) in the country was 15.7%, whereas levofloxacin and trimethoprim-sulfamethoxazole-resistant rates were ≥24% among all isolates (Critchley *et al*., 2019)

E. coli is also recognized for its acquisition of genes coding for extended-spectrum β-lactamases (conferring resistance to broad-spectrum cephalosporins), carbapenemases (conferring resistance to carbapenems), and 16S rRNA methylases (conferring pan-resistance to aminoglycosides). The gram-negative bacterium has plasmid-mediated quinolone resistance (PMQR) genes and mobilized colistin resistance (mcr) genes, likewise, enabling it to produce proteins that confer resistance to fluoroquinolones and polymyxins, respectively (Poirel *et al*., 2018).

Attempts have been made to cover the antibiotic resistance of *E. coli* in Nigeria. A study by Adekunle *et al*. (2022), which focused on molecular detection of resistance genes in *E. coli* isolates from apparently healthy pregnant women in designated hospitals in Osun State,

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Nigeria, recorded high-level resistance of *E. coli* to amoxicillin. The study reported the presence of multidrug resistance genes in *E. coli* associated with UTI among pregnant women in Osogbo. Specifically, resistance genes in VIM 390bp, bla ctx-M 585bp, and TEM 517bp were detected in the representative *E. coli* isolates tested molecularly. Ayogu *et al*. (2017) obtained a multi-antibiotic resistant index (MARI) of 0.41 for *E. coli* in their study conducted among UTI-positive women from Ebonyi State, Nigeria. The multiple antibiotic resistance (MAR) index is a cost-effective and valid way of tracking the source of a pathogen (Mir *et al*., 2022). MARI value exceeding 0.2 for a pathogen suggests that the pathogen originates from a highly contaminated source, where there is excessive use of antibiotics.

Multidrug-resistant *E. coli* are isolates of the gram-negative bacterium that are resistant to not less than three distinct antibiotic families (Wu *et al*., 2021). About 26% of all *E. coli* isolates analyzed by Wu *et al*. (2021) were multidrug-resistant, with the highest resistance shown to amoxicillin (85%). Amoxicillin, cefuroxime, ceftriaxone, ceftazidime, amoxicillin-clavulanic acid, cefoperazone-sulbactam, and meropenem are all classified as β-lactam antibiotics. The rate of detection for ESBL-producing *E. coli* in the aforementioned study was 55%.

E. coli isolates from pregnant women with UTIs in Enugu, Eastern Nigeria, showed high resistance to routine antibiotics. It showed the greatest resistance to the antibiotics Ampicillin (100%), Tetracycline (78%), and Rocephin (70%) but a low resistance of 16.7% against Nitrofurantoin (Okoani *et al*., 2024).

In Kaduna, Nigeria, a recent study on pregnant women attending antenatal clinics in some selected hospitals discovered that *Escherichia coli* isolates from the urine samples were highly susceptible to Gentamicin (72.9%), Amoxicillin (70.5%), and Streptomycin (70.5%). Contrarily, the isolates showed higher resistance to Perfloxacin (49.4%), Chloramphenicol (38.8%), and Ciprofloxacin (36.5%) (Tijani *et al*., 2020).

There is a constant rise in the number of infections caused by multidrug-resistant *E. coli*, perhaps due to its ease of transmission among humans and from environmental sources. The understanding of the epidemiology of these strains and accurate understanding of their mechanisms of resistance are key components in the fight against these *E. coli* infections (Galindo-Méndez, 2020). Although prevalence rates for multidrug-resistant *E. coli* strains may differ by populations and environments, the impact of resistance to antimicrobials is universal (Von Baum & Marre, 2005). Multidrug-resistant *E. coli* is found everywhere and is a matter of concern to human civilization. About 50% of *E. coli* isolates from drinking water were multidrug resistant (Odonkor & Addo, 2018), in which sixty-three percent (63%) of these strains also recorded a multiple antibiotic resistance (MAR) index value > 0.2.

Data on multidrug-resistant, pan-drug-resistant, and extensively drug-resistant commensal *E. coli* isolates from healthy humans in low- and middle-income countries reported 28% of 14,336 isolates prevalence of multidrug resistance, 24% of 8,686 isolates prevalence of extensive drug resistance, and 5% of 5,670 isolates prevalence of pan resistance (Nkansa-Gyamfi *et al*., 2019). This diverse resistance pattern exhibited by *E. coli* to antibiotics is a public health concern that demands urgent attention, especially in African settings.

Despite the absence of enough studies to represent the status quo of African countries on AMR patterns of *E. coli*, resistance levels recorded in available studies are really high. Tadesse *et al*. (2017) highlight three important findings: the recent AMR data were available for only 40%

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of the countries, the level of resistance to commonly prescribed antibiotics was significant, and the quality of microbiological data is of serious concern.

The burden of AMR can be abated by appropriate actions or programs, including but not limited to antimicrobial stewardship, increased surveillance, and improved diagnoses. Similarly, effort must be geared towards reducing the circulation of multidrug-resistant *E. coli* in the population as its prevalence will ultimately lead to reduced life expectancy. There is also a need to prioritize alternative ways of combating MDR.

Diagnostic Methods

Diagnostic Methods for Detecting E. coli UTIs in Pregnant Women

Diagnosing urinary tract infections (UTIs) in pregnant women can be effectively accomplished through a combination of clinical examination and other techniques. Diagnostic methods for pathogen identification in urine are currently categorized into two types: point-of-care (POC) instruments, such as Dipstick Tests, which provide rapid on-site analysis, and laboratory methods, such as Urine Culture, PCR, and MALDI-TOF, which require sample preparation beforehand (Nicolle, 2008). The primary objective is to accurately detect the presence of a UTI to ensure timely and appropriate treatment, which is crucial during pregnancy to prevent complications that could harm both the mother and the fetus.

Urine Culture

It is considered the gold standard for diagnosing UTIs caused by *E. coli*. This method involves growing urine samples on specialized media to detect and quantify bacterial growth. According to Chandra et al. (2020), this process entails collecting a midstream urine sample or catheter specimen from expectant mothers, followed by microbiological analysis of the urine (urine culture) for pathogen identification, isolation, and antimicrobial susceptibility testing (AST). However, this type of diagnosis often takes two to three days, delaying treatment and allowing the infection to spread. This drawback usually results in empirical decisions and the administration of unnecessary antibiotics (Nicolle, 2008). The advantages of this method are its high specificity and sensitivity, along with the capability to provide quantitative data on bacterial load (Chandra *et al*., 2020). On the downside, it is time-consuming, typically requiring 24-48 hours for results, and necessitates laboratory facilities and skilled personnel (Nicolle, 2008).

Polymerase Chain Reaction (PCR)

It enables rapid and precise detection of bacterial infections by amplifying DNA sequences unique to *E. coli*. These methods significantly reduce detection time and exhibit higher sensitivity and specificity compared to culture-based tests (Santos *et al*., 2022). The combination of PCR with antibiotic susceptibility testing allows for precise assessment and identification of the pathogen's antibiotic resistance. Numerous UTI pathogens, including *Escherichia coli*, have been successfully identified using the Open Array multiplex PCR method due to its remarkable sensitivity, specificity, and accuracy. This technique is potentially useful for the early identification and targeted treatment of UTIs because it can identify various resistance genes (Adekunle *et al*., 2022). However, these processes require a clinical microbiology laboratory, costly supplies and equipment, and highly skilled staff to conduct the testing (Santos *et al*., 2022). Advantages of PCR include high sensitivity and specificity, and

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the ability to deliver quick results within a few hours (Wu *et al*., 2010). However, the disadvantages include the need for specialized equipment and trained personnel, as well as higher costs compared to traditional methods (Liu *et al*., 2018).

Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF)

Mass Spectrometry (MS) is a proteomic diagnostic method that identifies bacteria based on their protein profiles, providing rapid identification of *E. coli* strains. This technology enables early diagnosis of urinary tract infections (UTIs) and guides appropriate antibiotic therapy by quickly detecting clinically relevant urinary tract bacteria directly from urine samples using mass spectrometry (Chen *et al*., 2021). Since 2010, MALDI-TOF MS has been used in clinical microbiology, offering benefits such as ease of use, speed, accuracy, and cost-effectiveness in identifying cultivated colonies and quickly detecting samples, including highly aggressive and drug-resistant pathogens (Calderaro & Chezzi, 2024). Advantages of MALDI-TOF MS include high accuracy and speed, and the ability to identify multiple pathogens simultaneously. Unlike traditional culture methods, which require 24-48 hours to detect bacteria, MALDI-TOF MS can do so in minutes to several hours. The technology's effectiveness against a broad spectrum of bacterial infections increases its use in various therapeutic contexts (Sun *et al*., 2021). However, the disadvantages include expensive equipment and maintenance, and the need for technical expertise (Sun *et al*., 2021).

Automated Urine Analyzer

It uses flow cytometry and other techniques to rapidly analyze urine samples for bacterial presence and white blood cell counts. These analyzers significantly aid in diagnosing urinary tract infections (UTIs) by providing standardized urinalysis data for effective screening and treatment (Szmulik *et al*., 2022). These analyzers measure the number of bacteria and leukocytes in urine samples using advanced technologies like digital imaging, flow cytometry, and reflectometry (Oyaert *et al*., 2019). Studies have shown that automated methods can reliably predict or rule out UTIs based on factors such as the bacterial score, white blood cell count, and clinical symptoms, achieving excellent sensitivity and specificity levels (Foudraine *et al*., 2018). In general, automated urine analyzers improve the effectiveness and precision of diagnosing urinary tract infections (UTIs), potentially reducing the need for unnecessary urine cultures and leading to better patient outcomes (Tessari *et al*., 2015). Advantages of automated urine analyzers include quick results and a reduction in human error (Veron *et al*., 2015). However, the disadvantages include a high initial investment cost and possibly lower sensitivity compared to traditional culture methods (El Kettani *et al*., 2023).

Dipstick Test

It is a popular method for identifying urinary tract infections (UTIs), particularly in resource-limited settings (Maina *et al*., 2023). These tests detect the presence of nitrites and leukocyte esterase, which are indicators of bacterial infection and white blood cells, respectively (Waterfield *et al*., 2022). In cases where there is clinical evidence of a patient having a UTI, urine dipsticks are among the most commonly used diagnostic tools. The detection of nitrite (a metabolic result of common urinary tract infections), leukocyte esterase, protein, and blood (as an indicator of inflammation) is most commonly accomplished with Multistix (Ajayi *et al*., 2010). Advantages of dipstick tests include their quick and easy use, as well as the ability to be performed at the point of care (Devillé *et al*., 2004). However, the disadvantages include lower

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sensitivity compared to urine culture and the possibility of producing false positives or negatives (Maina *et al*., 2023).

Comparison of Traditional Culture Methods vs. Modern Molecular Techniques for UTI Diagnosis

The traditional method for diagnosing urinary tract infections (UTIs) is urine culture, which has long been considered the gold standard (Upadhyay *et al*., 2022). Contemporary molecular techniques such as polymerase chain reaction (PCR), multiplex PCR, and next-generation sequencing (NGS) are becoming effective substitutes because of their enhanced sensitivity in identifying bacteria in urine and the possibility of obtaining faster findings (Damir *et al*., 2023). Studies have demonstrated that molecular methods like RT-PCR and multiplex PCR function similarly to conventional urine cultures. RT-PCR yielded a sensitivity of 0.94 and a specificity of 0.59, whereas multiplex PCR revealed a sensitivity of 0.80 and a specificity of 0.83. These results highlight the potential of molecular techniques to improve UTI diagnosis precision and direct the most suitable course of antibiotic treatment (Guzman *et al*., 2022). While molecular approaches have the potential to decrease unnecessary antibiotic treatments and improve illness identification, traditional culture techniques are still vital. These benefits can enhance antimicrobial stewardship and improve patient outcomes (Szlachta *et al*., 2022).

Traditional culture methods involve growing bacteria from a urine sample on a culture medium to identify and quantify the bacteria present. The advantages of traditional culture methods include high specificity and sensitivity, as they are considered the gold standard due to their ability to accurately identify specific bacteria and determine antibiotic susceptibility. They also provide quantitative results, offering information on bacterial load, which helps assess the severity of the infection. Additionally, cultures can be used to perform antibiotic susceptibility tests, guiding appropriate treatment, and they are cost-effective (Upadhyay *et al*., 2022). However, the disadvantages of traditional culture methods include being time-consuming, with results typically taking 24-48 hours, which delays diagnosis and treatment. They are also labor-intensive, requiring specialized laboratory facilities and trained personnel, and there is a risk of contamination, which can lead to inaccurate results (Damir *et al*., 2023).

Recent advancements in molecular techniques, such as broad-range 16S rDNA PCR and PCR, have revolutionized the diagnosis of urinary tract infections (UTIs). These methods enable rapid and accurate identification of pathogens, facilitating tailored antibiotic therapy (Mathew *et al*., 2017). Innovative immunomodulatory approaches targeting specific immune response regulators have also shown promise in UTI treatment. These therapies bolster the body's defenses against microbes while preventing excessive immune reactions (Butler *et al*., 2022). Overall, these developments not only increase diagnostic precision but also hold potential to reduce healthcare costs and improve patient outcomes in the treatment of UTIs (Mathew *et al*., 2017). The advantages of modern molecular techniques include high sensitivity and specificity, as these methods can detect even low levels of bacterial DNA, providing highly accurate results. They also deliver rapid results, with PCR and other molecular methods able to provide results within a few hours, facilitating prompt treatment. Additionally, these techniques offer multiplex capability, allowing for the detection of multiple pathogens simultaneously in a single test, which is useful for identifying co-infections. They also require only a small volume of urine sample for analysis (Liu *et al*., 2011). However, the disadvantages of molecular techniques include higher costs compared to traditional culture methods due to the need for specialized equipment and reagents. They also require trained personnel to perform and

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interpret the tests, and they often do not provide information on antibiotic resistance, necessitating additional tests (Santos *et al*., 2022).

Evaluation of UTI Diagnostic Accuracy and Reliability in the Nigerian Context

Diagnosing urinary tract infections (UTIs) accurately and reliably is critical for effective treatment, especially in diverse healthcare settings like Nigeria. The Nigerian healthcare context presents unique challenges and opportunities for UTI diagnosis. This evaluation covers traditional culture methods, modern molecular techniques, and point-of-care diagnostics, examining their accuracy, reliability, and applicability in Nigeria (Kwari *et al*., 2022). Several diagnostic methods have been evaluated for their accuracy and reliability in detecting UTIs. Urine culture, despite being the gold standard, relies heavily on adequate laboratory infrastructure and skilled personnel, which poses challenges in resource-limited settings (Nicolle, 2008). Urine culture is known for its high specificity and sensitivity, making it generally accurate in identifying the causative bacteria and determining the bacterial load (Chandra *et al*., 2020). However, the main challenges include resource constraints, as many healthcare facilities lack the necessary laboratory infrastructure and trained personnel, and sample handling issues, such as problems with sample collection, storage, and transportation, which can lead to contamination and false results (Perez *et al*., 2023).

Modern molecular techniques offer high sensitivity and specificity, capable of detecting low levels of bacterial DNA, providing rapid and highly accurate results (Adekunle *et al*., 2022). The primary challenges for these techniques in Nigeria are the high costs and the need for specialized equipment, which limit widespread use, and the requirement for trained personnel for operation and interpretation (Sun *et al*., 2021). Studies have assessed the performance of various diagnostic tests, including urine color examination and microscopic analysis of urine sediment, which play a critical role in predicting and diagnosing UTIs, contributing to timely management and prevention of complications (Nwankwo *et al*., 2020). Point-of-care (POC) methods, such as dipstick tests, provide rapid preliminary results at the site of patient care (Waterfield *et al*., 2022). While POC methods have moderate sensitivity and specificity, making them useful for preliminary screening, they are less accurate than culture and molecular methods. The challenges for POC methods in Nigeria include variability in test quality and interpretation, which can affect reliability, but they are widely available and easy to use even in low-resource settings (Akerele *et al*., 2001).

Impact on Pregnancy Outcomes

Summary of Studies Examining the impact of E. coli UTIs on Pregnancy Outcomes in Nigeria

The impact of *E. coli* UTIs on pregnancy outcomes in Nigeria has been examined in several studies, revealing significant prevalence and risk factors. A study conducted at the antenatal clinic of the Enugu State University of Science and Technology Teaching Hospital aimed to investigate the prevalence of UTIs caused by *E. coli* among pregnant women and the antibiotic susceptibility patterns of the isolated bacteria (Okoani *et al*., 2024). This cross-sectional study involved 200 pregnant women, both symptomatic and asymptomatic for UTI, with mid-stream urine samples collected and cultured on specific media. Criteria for significant bacteriuria included colony counts greater than $10^{\wedge 2}$ colony-forming units per milliliter of urine. The results showed an overall prevalence of UTI among the pregnant women at 15.4%, with E. coli

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being the most frequently isolated organism, accounting for 53.4% of all positive samples. The study also highlighted high levels of resistance in *E. coli* to several antibiotics, including 100% resistance to ampicillin, 78% resistance to tetracycline, and 70% resistance to ceftriaxone. The study concluded with recommendations for routine urine culture to be integrated into antenatal care protocols to guide appropriate antibiotic therapy and mitigate risks associated with UTI complications during pregnancy.

Another study aimed to determine antibiotic sensitivity patterns and identify resistance genes of *E. coli* isolated from mid-stream urine samples of apparently healthy pregnant women in Osogbo, Osun State (Ogundiran *et al*., 2022). This cross-sectional study involved 150 pregnant women, with urine samples cultured on various media and antibiotic susceptibility tested using the standard agar disc diffusion method. The study found high resistance to ampicillin, moderate resistance to penicillin, and lower resistance to ciprofloxacin and levofloxacin, with most *E. coli* isolates showing resistance to meropenem. Molecular analysis revealed the presence of resistance genes, indicating multidrug resistance. The findings highlighted the prevalence of multidrug-resistant *E. coli* in pregnant women and emphasized the importance of antibiotic stewardship and routine surveillance of antibiotic resistance patterns.

Discussion on Complications Such as Preterm Birth, Low Birth Weight, and Maternal Morbidity

UTIs during pregnancy can lead to several serious complications if not properly managed, including preterm birth, low birth weight, and maternal morbidity (Rabiee, M., 2023).

Preterm Birth

This is defined as childbirth occurring before 37 weeks of gestation, which is a leading cause of neonatal morbidity and mortality, associated with long-term health issues such as developmental delays and respiratory problems. UTIs can cause an inflammatory response, leading to the release of cytokines and prostaglandins, which can induce uterine contractions and cervical changes, triggering preterm labor (Sitharam, 2022). Several studies have demonstrated a link between UTIs and an increased risk of preterm birth, with early detection and treatment crucial in preventing this complication (Akerele et al., 2001).

Low Birth Weight (LBW)

This is defined as infants born weighing less than 2,500 grams, which is another significant complication associated with UTIs during pregnancy. Infections like UTIs can impair placental function and nutrient transfer to the fetus, leading to intrauterine growth restriction (IUGR) and resulting in LBW. Studies have shown a correlation between UTIs during pregnancy and an increased incidence of LBW, with regular prenatal care, including UTI screening and treatment, helping mitigate this risk (Olusanya et al., 2010).

Maternal Morbidity

It refers to health complications occurring in the mother due to UTIs, which can range from mild symptoms to severe, life-threatening conditions. UTIs, if untreated, can cause pyelonephritis, which can lead to severe complications such as sepsis, acute renal failure, and chronic kidney disease. Recurrent UTIs can also cause significant discomfort and anxiety, impacting maternal mental health. Research has highlighted the significant morbidity

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associated with UTIs, particularly pyelonephritis, which requires hospitalization and intensive treatment. Timely diagnosis and effective antibiotic treatment are essential in managing UTIs and preventing maternal morbidity, with preventive measures such as proper hydration, urination after intercourse, and good hygiene practices reducing the risk of UTIs (Perez et al., 2023).

Analysis of Factors Contributing to Adverse Outcomes

Several factors contribute to the adverse outcomes of UTIs during pregnancy, including physiological changes, delayed diagnosis and treatment, antibiotic resistance, and socioeconomic and healthcare system challenges.

Pregnancy

It induces physiological changes that increase the risk of UTIs and their complications, such as hormonal changes that slow urine flow and promote bacterial growth, mechanical changes from the growing uterus exerting pressure on the bladder and ureters, and immune modulation making women more susceptible to infections (Nicolle, 2008). These changes make pregnant women more prone to developing UTIs, which can ascend to the kidneys and cause pyelonephritis.

Delayed Diagnosis and Treatment

This is due to inadequate routine screening, non-specific symptoms, and limited access to healthcare facilities, which allows infections to progress, increasing the risk of severe complications (Olusanya et al., 2010).

Antibiotic Resistance

This is driven by overuse and inappropriate prescription of antibiotics, complicating the treatment of UTIs, leading to prolonged infections and higher healthcare costs (Perez et al., 2023).

Socioeconomic and Healthcare System Factors

Low socioeconomic status, lack of education and awareness, and limited healthcare infrastructure, etc, further contribute to adverse outcomes. Addressing these factors requires improved prenatal care, routine screening, effective antibiotic stewardship, and enhanced healthcare access and education to improve the management of UTIs in pregnancy and reduce the associated risks (Nwadioha et al., 2010).

Public Health Implications

Antibiotic resistance in *Escherichia coli* UTIs poses significant public health implications globally. Studies have highlighted the presence of plasmid-mediated quinolone resistance (PMQR) and aminoglycoside resistance genes in *E. coli* strains isolated from rivers in India, emphasizing the ease of horizontal gene transfer and the importance of surveillance to curb the spread of AMR (Singh *et al*., 2022). Furthermore, the excess burden of AMR *E. coli* UTIs has been estimated in countries like the Netherlands and Italy, showcasing the substantial impact on mortality and morbidity, underscoring the necessity of country-specific parameters to assess the burden of resistant infections (Godijk *et al*., 2023). The dissemination of AMR in UPEC,

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particularly against broad-spectrum antibiotics like third-generation cephalosporins and fluoroquinolones, is a severe threat according to the CDC and WHO, necessitating evidence-based interventions and prudent antibiotic use to combat resistance effectively (White, 2021). Additionally, a study in Nigeria revealed a high occurrence of *E. coli* infections with multiple antibiotic resistance patterns, emphasizing the economic and health implications and the importance of judicious antibiotic use under medical guidance to mitigate resistance effectively (Wilkie *et al*., 2024).

Importance of Surveillance and Monitoring Antibiotic-resistant Trends

Surveillance and monitoring of antibiotic resistance trends are crucial in combating the global threat of antimicrobial resistance (AMR). Studies emphasize the significance of local surveillance in understanding resistance profiles, guiding empirical therapy, and implementing timely responsive measures to contain resistance escalation (Wang *et al*., 2018). Furthermore, a comprehensive framework for monitoring emerging resistance to new antibiotics is essential, as highlighted in European research, to support informed antibiotic policies and address surveillance gaps (Arieti *et al*., 2023). The One Health approach underscores the importance of multisectoral surveillance, integrating human, animal, and environmental data to track AMR drivers and patterns, especially in foodborne bacteria, zoonotic pathogens, and during public health crises like the COVID-19 pandemic (Kumar, 2023). Reliable data on resistant infections are vital for evaluating interventions, as seen in global estimates of hospital-associated resistant infections, emphasizing the need for standardized reporting and expanded surveillance criteria to enhance AMR control efforts (Bertagnolio *et al*., 2023).

Role of Public Health Policies and Interventions in Controlling Antibiotic Resistance

Public health policies and interventions play a crucial role in controlling antibiotic resistance, a pressing global health crisis. The overuse and misuse of antibiotics in various sectors contribute significantly to the development of antimicrobial resistance (AMR) (Kaur *et al*., 2024). Implementing tailored public health programs can enhance behaviors associated with antibiotic use in the general population, addressing knowledge, attitudes, and behaviors concerning antibiotics (Pennino *et al*., 2023). Global cooperation and comprehensive policies are essential in combating AMR, recognizing its cross-border nature and the need for coordinated efforts (Kaur *et al*., 2024). Structural interventions focusing on socio-ecological drivers of antibiotic misuse, improving healthcare infrastructure, and aligning disease-specific programs are crucial for addressing prescription behavior and combating AMR effectively (Nair *et al*., 2023). By collectively tackling antibiotic resistance through multifaceted approaches, responsible antibiotic use, and the development of new antibiotics, public health policies can safeguard the effectiveness of antibiotics and public health for current and future generations.

Research Gaps and Future Directions

Current research on *E. coli* UTIs and antibiotic resistance in pregnant women in Nigeria reveals several gaps. Studies from various regions like Calabar, Enugu, Abakaliki, Osogbo, and Bida highlight the prevalence of *E. coli* in UTIs among pregnant women, with resistance to common antibiotics like Ampicillin, Tetracycline, and Rocephin (Ogban *et al*., 2024; Okoani *et al*., 2024; Nair *et al*., 2023). However, there is a lack of significant association between demographic characteristics or risk factors and UTIs caused by carbapenem-resistant

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Enterobacteriaceae (CRE) in pregnant women (Ogban *et al*., 2024). Additionally, the presence of multidrug-resistant ESBL and MBL-producing *E. coli* strains among apparently healthy pregnant women raises concerns about early exposure of fetuses to multidrug resistance, emphasizing the need for proactive measures to address this emerging health risk (Afiukwa *et al*., 2023). Furthermore, the identification of multi-drug resistance genes in *E. coli* associated with UTIs in pregnant women underscores the importance of continuous surveillance and monitoring of antibiotic resistance patterns to guide effective treatment strategies.

CONCLUSION

This review highlights the significant public health challenge posed by urinary tract infections (UTIs) among pregnant women in Nigeria, driven by the high prevalence and increasing antibiotic resistance of *Escherichia coli* (*E. coli*). Uropathogenic *E. coli* (UPEC) is the primary cause of both uncomplicated and complicated UTIs, with multidrug-resistant (MDR) strains complicating treatment and management. Factors such as poor socioeconomic conditions, inadequate healthcare infrastructure, and the misuse of antibiotics exacerbate this issue.

Effective management of UTIs in pregnant women is critical to prevent adverse outcomes, including preterm birth, low birth weight, and maternal morbidity. The review emphasizes the need for accurate and timely diagnostic methods, such as urine culture, polymerase chain reaction (PCR), and Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) mass spectrometry. Routine screening and antibiotic stewardship are essential strategies to mitigate the impact of UTIs and reduce the spread of antibiotic resistance.

Urgent public health interventions are required to improve diagnostic infrastructure, implement effective antibiotic stewardship programs, and enhance surveillance of antibiotic resistance patterns. Educating healthcare providers and patients about the appropriate use of antibiotics and the importance of early detection and treatment of UTIs is also crucial.

Finally, addressing the challenges of UTIs among pregnant women in Nigeria necessitates a multifaceted approach involving improved healthcare practices, policies, and ongoing research. By focusing on these areas, it is possible to enhance maternal and neonatal health outcomes, reduce the burden of antibiotic-resistant infections, and promote the well-being of both mothers and their infants

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