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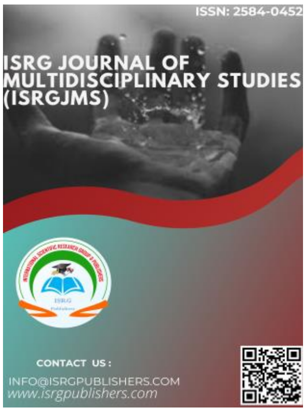

VIRULENCE FACTORS AND ANTIMICROBIAL RESISTANCE PROFILE OF BACTERIAL UROPATHOGENS ISOLATED FROM PRIMARY SCHOOL CHILDREN IN JADA ADAMAWA STATE

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Abstract

This study aimed to assess the incidence, types, and virulence factors of bacterial uropathogens in primary school students in Jada LGA. Analysis of sixty mid-stream urine samples involved culturing on CLED agar and identifying isolates through biochemical tests. Antibiotic susceptibility was determined using Mueller Hinton agar and commercial antibiotic discs. Virulence markers, including biofilm formation and hemolysin presence, were evaluated with Congo red agar and sheep blood agar, respectively. The findings indicated a 31.6% incidence of urinary tract infections in females and 28.6% in males, with the highest prevalence among students aged 6-7 years. The findings indicate that E. coli is the predominant culprit behind bacterial urinary tract infections (UTIs) in the examined population. Antibiotic susceptibility tests reveal that Ciprofloxacin and pefloxacin exhibit the highest efficacy against the isolates, suggesting their potential use in empiric UTI treatment. Additionally, the results highlight that the presence of the toxin, hemolysin (found in 63% of the isolates), and the uropathogenic biofilm-forming ability (84.2% of isolates) might contribute to enhanced pathogenicity. It is recommended that periodic surveillance studies be promoted to promptly identify shifts in uropathogenic prevalence, virulence markers, and antibiotic resistance patterns.

Keywords: *Urinary tract Infection, Uropathogens, Virulence Factors, Susceptibility, Antibiotic resistance*

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Introduction

A urinary tract infection (UTI) affects different parts of the urinary system, such as the urethra, bladder, ureter, or kidneys, each playing a unique role. Infections cause inflammation and disruption of normal function due to pathogen overgrowth (Wu et al., 2022). UTIs are a major public health concern, being one of the most common infectious diseases across all age groups and a significant cause of morbidity and mortality in children (Yang et al., 2022).

Estimating the prevalence of UTIs in children is difficult due to factors such as subclinical infections, non-specific symptoms, errors in collection techniques, and the use of antibiotics for other febrile conditions, which may mask silent infections. Thus, the link between symptomatic UTIs and asymptomatic bacteriuria remains unclear. UTIs are typically diagnosed based on symptoms like fever, vomiting, pyuria, hematuria, and discomfort, which vary by age group (Shaikh et al., 2020). They are classified into lower urinary tract infections (cystitis and urethritis) affecting the bladder and urethra, and upper urinary tract infections involving the ureter, pelvis, and kidney (El-Ghar et al., 2021).

UTI risk factors include anatomical and physiological issues, as well as age, gender, race, underlying health conditions, circumcision status, and sexual activity, particularly in teenage girls (Yang et al., 2021). Delayed urination can increase UTI risk as regular urination helps flush bacteria from the urinary tract (de los Reyes and Koyle, 2023). Inadequate fluid intake, leading to low urine production, can also elevate UTI risk. Chronic constipation, which creates pressure on the bladder and hinders urine flow, may contribute to UTI susceptibility (Axelgaard et al., 2023). Additional factors include inadequate healthcare, poor home treatment practices, and insufficient hygiene (Addis et al., 2021). UTIs are more common in females, partly due to their shorter urethra and its proximity to the anus (Tunç and Özdemir, 2021).

UTIs can be caused by a range of organisms including bacteria, viruses, protozoa, and fungi. Bacteria from the Enterobacteriaceae family, such as *Escherichia coli*, *Enterobacter*, Pseudomonas, *Salmonella*, and *Serratia*, are the most common causes, with *E. coli* responsible for approximately 80% of UTIs. Gram-positive bacteria, such as *Streptococci, Enterococcus*, and *Staphylococcus aureus*, are also frequently involved in UTIs (Chadha et al., 2021).

UTIs result from the interaction between uropathogens and the host, involving various pathogenesis processes. Uropathogens possess virulence factors (VFs) essential for their persistence and colonization in the urinary tract (Arsene et al., 2021). These VFs help the pathogen evade host defenses and may lead to extraintestinal diseases. Key VFs include fimbrial adhesions (P, type 1, S, and F1c fimbriae), flagella, biofilm, hemagglutinin, lipopolysaccharides, toxins (such as hemolysins and cytotoxic necrotizing factors), and siderophores (Sarowska et al., 2019). These factors can be carried on chromosomal DNA, bacteriophage DNA, plasmids, or transposons, which enhance the pathogen's ability to cause disease (Reidl, 1999).

For an infection to establish, uropathogens first attach to the epithelial surface, then colonize and spread through the mucosa, causing damage. They may subsequently ascend to the urinary bladder, leading to either symptomatic or asymptomatic bacteriuria and potentially invading organs involved in urine production (kidneys), transport (ureters and urethra), and storage (bladder) (Larcombe et al., 2011). Recent research has focused on bacterial adhesion, including binding sites on epithelial surfaces, and the exploration of natural anti-adherence mechanisms. Understanding these pathogenic and adherence processes could help physicians develop effective UTI prevention and management strategies (Allamin et al., 2015). This study aims to investigate the virulence factors of uropathogenic bacteria isolated from healthy primary school children and assess their sensitivity to specific antibiotics.

MATERIALS AND METHODS

Study Area

The research was conducted in the Jada I area of Jada Local Government in Adamawa State, Northeastern Nigeria, targeting apparently healthy primary school children aged 6 to 11 years. The study involved three primary schools, with a total of 60 samples collected. Both male and female students were equally represented, and participants were randomly selected. Inclusion was restricted to primary school children, excluding those outside this age range or who had recently taken antibiotics.

Sample Collection

Urine samples were collected from 60 pupils aged 6 to 11 years, specifically from primary grades 4 to 6. A clean catch mid-stream method was used, with pupils instructed on proper collection techniques to avoid contamination. The samples were collected in sterile universal containers, stored in an ice chest, and promptly transported to the laboratory. All analyses were performed within 24 hours to ensure sample integrity.

Culture

CLED (Cystine Lactose Electrolyte Deficient) agar was utilized for isolating uropathogens from urine samples. Before inoculation, the urine sample bottles were thoroughly shaken to ensure an even distribution of microorganisms. A loopful of the urine sample was then streaked onto the CLED agar plates to facilitate the development of discrete colonies. The plates were incubated at 37°C for 24 hours to enable the growth and identification of uropathogens. The identification of individual organisms was carried out using biochemical tests on positive plates, in accordance with the procedures outlined by Abaka et al. (2024). Antimicrobial susceptibility testing was conducted using the disk diffusion method, following the guidelines established by the National Committee for Clinical Laboratory Standards (C.L.S, 2008).

Congo Red Agar (CRA) Method

The Congo red agar method was utilized to detect biofilm-producing bacteria among the isolated strains. The bacteria were cultured on agar plates containing Congo red dye and incubated at 37°C for 24 hours. Biofilm formation was confirmed by the appearance of black crystalline colonies. Colonies that were grey indicated intermediate biofilm production, while red colonies denoted non-biofilm producers.

Detection of Hemolytic Activity

The hemolytic activity of the bacteria was assessed by culturing them on Mueller Hinton agar plates enriched with 5% sheep blood. The plates were incubated at 35°C for 24 hours. Following incubation, the plates were examined for alpha and beta-hemolytic patterns to identify the hemolytic properties of the bacterial isolates.

RESULTS

A total of 60 urine samples were obtained from students in three primary schools in Girei L.G.A. Of the 60 pupils sampled, 16 were

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aged 6-7 (in Primary 4), 32 were aged 8-9 (in Primary 5) and 12 were aged 10-11 (in Primary 6). Of the 60 pupils sampled 28 were males while 32 were females. The result is presented in Table 1.

Table 1: Age and Sex Distribution of the Sample Population

AGE (YRS)	MALE	FEMALE	TOTAL
6-7	7	9	16
8-9	15	17	32
10-11	6	6	12
TOTAL	**28**	**32**	**60**

Of the twenty-eight (28) urine samples obtained from male pupils, 8 (28.6%) yielded growth while in females 11 (34.5%) of the 32 urine samples obtained yielded growth. The infectivity pattern among the sexes is presented in Table 2.

Table 2: Infectivity Pattern among the Sexes

GENDER	Growth	No growth	Total
MALE	78 (28.6%)	19 (70.4%)	27 (45%)
FEMALE	11 (34.5%)	22 (66.7)	33 (55%)
TOTAL	**19**	**41**	**60**

Table 3 shows the infection pattern among the different age groups sampled. The results show that respondents aged 6-7 (primary four pupils) had the highest incidence rate (37.5%) while respondents aged 8-9 (primary 5 pupils) had the lowest infection rate (28.1%).

Table 3: Infectivity Pattern among the Different Age Groups Sampled

AGE (YRS)	Growth	No growth	Total
6-7	6 (37.5 %)	10 (62.5 %)	16 (26.7%)
8-9	9 (28.1 %)	23 (71.9%)	32 (53.3%)
10-11	4 (33.3%)	8 (66.7%)	12 (20%)
TOTAL	**19 (31.7%)**	**41 (68.3%)**	**60 (100%)**

A total of nineteen (19) isolates were obtained from the 60 pupils sampled. The organisms isolated were *Klebsiella* spp., *E. coli, Staphylococcus aureus, and Pseudomonas* spp. Of the four organisms isolated, *E. coli* was the most prevalent organism accounting for 8 (42.1%) of the total isolates while *Klebsiella* spp. had the least incidence with only 1 (5.3%) of the isolates. This is presented in Table 4.

Table 4: Distribution Pattern of Isolates in the Sample Population.

ORGANISM	MALE	FEMALE	TOTAL (%)
E. coli	2	6	**8 (42.1%)**
S. aureus	4	3	**7 (36.8%)**
Pseudomonas sp.	2	1	**3 (15.8%)**
Klebsiella sp.	-	1	**1 (5.3%)**
TOTAL	**8**	**11**	**100%**

The antibiotic susceptibility test of the isolates showed that most were sensitive to the antibiotics used. For Gram-negative organisms, pefloxacin, ciprofloxacin, chloramphenicol, and gentamicin (100%) were the most reactive while nalidixic acid and ampicillin (8.3%) were the least reactive. For Gram-positive organisms, pefloxacin and ciprofloxacin (100%) were the most reactive, and amoxicillin (0.0%) was the least reactive respectively.

Table 5a: Antibiotic Sensitivity Pattern of the Gram Negative Isolates.

BACTERIA	CPX	PEF	OFX	AU	CN	SXT	NA	PM	S	CH
Klebsiella spp. n = 1	1 (100)	1 (100)	1 (100)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	1 (100)
E. coli n=8	8 (100)	8 (100)	5 (62.5)	4 (50)	5 (62.5)	2 (25)	1 (12.5)	0 (0.0)	2 (25)	8 (100)
Pseudomonas sp. n=3	3 (100)	3 (100)	3 (100)	0 (0.0)	3 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0/0)	3 (100)
Total n=12	12 (100)	12 (100)	9 (75)	4 (33.3)	12 (100)	2 (16.7)	1 (8.3)	1 (8.3)	2 (16.7)	12 (100)

KEY: CPX=Ciprofloxacin, SXT= Septrin, CN= Gentamicin PEF=Pefloxacin S= Streptomycin, AU= Augumentin, PEF=Pefloxacin, PM= Ampicillin, NA= Nalidixic acid OFX = Ofloxacin, CH= Chloramphenicol

Table 5b: Antibiotic Sensitivity Pattern of Gram-Positive Isolate

Bacteria (N)	PEF	CN	APX	Z	AM	R	CPX	S	SXT	E
S. aureus n=7	7 (100)	5 (71.4)	5 (71.4)	2 (28.6)	0 (0.0)	1 (14.3)	7 (100)	1 (14.3)	2 (28.6)	2 (28.6)

KEY:

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PEF= Pefloxacin CN= Gentamicin APX= Ampiclox Z= Zinnacef AM= Amoxicillin R= Rifampin CPX= Ciprofloxacin S= Streptomycin SXT= Septrin E= Erythromycin

All the isolates were tested for the presence of two virulence factors: biofilm-forming ability and the presence of the enzyme hemolysin. The results obtained show that 8 isolates were strong biofilm formers, 8 showed weak biofilm formation and 3 showed no biofilm formation. Again, of the 19 isolates obtained, 12 were positive for the presence of the enzyme hemolysin while 7 were negative. The result is presented in Table 6.

Table 6: Virulence Factors of the Isolates.

Bacteria	**Biofilm Production**			**Haemolysin Production**	
	Strong	**Weak**	**None**	**Positive**	**Negative**
E. coli n=8	3	3	2	6	2
S. aureus n=7	3	3	1	4	3
Pseudomonas sp. n=3	1	2	0	2	1
Klebsiella sp. n=1	1	0	0	0	1
Total	**8**	**8**	**3**	**12**	**7**

Discussion

The study found a UTI incidence rate of 31.7%, with bacterial uropathogens identified in 19 out of 60 urine samples. This result aligns with Isa et al. (2013), who reported a similar rate of 31.7% in Borno State, Nigeria. However, it contrasts with findings from Moses et al. (2013) and Ibeneme et al. (2014), who reported incidence rates of 48% and 31.4% in Ebonyi and Enugu States, respectively. Global studies also show varying UTI incidence rates; for example, Moghadas and Irajian (2009) reported a much lower rate of 3.7% in Iran.

The high incidence of UTIs among apparently healthy children in Jada LGA, Adamawa State, may be linked to several factors. Delayed urination increases UTI risk as it prevents the regular flushing of bacteria from the urinary tract. Low urine production due to inadequate fluid intake also heightens UTI risk. Poor toilet and hygiene practices contribute to the problem. Additional factors include the use of irritating bubble baths or soaps, a family history of UTIs, and vesicoureteral reflux (VUR), a condition where urine flows backward from the bladder to the kidneys. VUR, which is present at birth, affects about 30% to 50% of children with UTIs (Thergaonkar and Hari, 2020).

The analysis shows a higher UTI incidence among female pupils, with a rate of 34.5% compared to 28.6% in males. This is consistent with Allamin, (2015), who reported similar findings in Bauchi State, with 46% prevalence in females and 30% in males. The greater susceptibility of females is often attributed to the shorter distance between the female urethra and the anus, which allows easier transfer of gastrointestinal microorganisms, leading to UTIs (Holmes et al., 2021). Males, on the other hand, have a lower UTI rate due to factors such as the longer urethra, a dry environment around the meatus, and the antibacterial properties of prostatic fluid (Vasudevan, 2014).

Analysis of infection rates across different age groups shows that pupils aged 6-7 (Primary 4) had the highest UTI rate at 37.5%, while those aged 8-9 (Primary 5) had the lowest rate at 28.1%. This pattern aligns with findings from Nigeria and elsewhere. Aiyegoro et al. (2007) reported a prevalence of 22.4% in female pupils and 4.56% in male pupils in Ile-Ife, Nigeria. Chulani et al. (2019) noted that children, particularly around ages 7-8 when they start self-care, are more susceptible to UTIs due to difficulties maintaining hygiene and a tendency to "hold it in," which can lead to urine stagnation and bacterial growth. Additionally, girls in this age group often wear nylon underwear, which may promote bacterial growth (Umami et al., 2022).

In this study, four bacterial agents associated with UTIs were identified: *E. coli, Klebsiella* sp., *S. aureus*, and *Pseudomonas* sp. E. coli was the most prevalent, accounting for 42.1% of the isolates, followed by *S. aureus* at 36.8%, *Pseudomonas* sp. at 15.8%, and *Klebsiella* sp. at 5.3%. This finding is consistent with other studies, which also report *E. coli* as the most common pathogen in UTIs among children, with Parajuli et al. (2017) noting an incidence rate of 68.5% and Allamin et al. (2015) reporting 28.9% in Bauchi State. Abdulhadi et al. (2021) observed that the E. coli strains causing UTIs are similar to those found in feces. The results of antibiotic susceptibility tests for Gram-negative isolates revealed sensitivity to pefloxacin, ciprofloxacin, chloramphenicol, and gentamicin, while resistance was observed against nalidixic acid, cotrimoxazole, and ampicillin, commonly used drugs for empirical UTI treatment. Gram-positive isolates, although sensitive to pefloxacin and ciprofloxacin, exhibited resistance to amoxicillin, cotrimoxazole, ampicillin, nalidixic acid, and nitrofurantoin typical antibiotics used in empirical UTI treatment.

Community-based studies on UTIs consistently reveal that uropathogens exhibit varying resistance patterns to commonly used antibiotics, influenced by factors such as geographic location, societal behaviors, and underlying risk factors. In Sub-Saharan African regions, including the study area, a relatively high resistance pattern has been observed, often linked to the irrational and excessive use of antibiotics in the community for treating UTIs (Schmider et al., 2022). This study supports that trend, showing that uropathogens were highly sensitive to chloramphenicol, gentamicin, pefloxacin, and ciprofloxacin, while demonstrating

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significantly reduced sensitivity to ampicillin, penicillin, tetracycline, cotrimoxazole, and cefuroxime. These latter antibiotics are widely available and affordable, often sold in community pharmacies.

Uropathogens derive their ability to cause disease from a wide range of virulence factors that facilitate the colonization of host tissues, spread within the tissues, and hinder phagocyte engulfment (Bien et al., 2012). This study assessed the biofilm-forming ability, a key virulence factor, and found that 16 out of the 19 isolated organisms (84%) were capable of forming biofilms. Similar studies by Amadu et al. (2019) and Osungunna et al. (2018) reported biofilm prevalence rates of 81.8% and 40%, respectively, among uropathogens. Biofilm formation by these pathogens is a major factor contributing to chronic urinary tract infections, as it offers protection against environmental stress, phagocytosis, and enhances antibiotic resistance. Importantly, biofilm production has been linked to recurrent pyelonephritis in children (Mirzaei, 2020). These findings suggest that a significant proportion of children with asymptomatic bacteriuria may be at risk of persistent or recurrent UTIs. Additionally, the study revealed that 63% of the isolates produced the hemolysin toxin. Hemolysins facilitate infection by damaging host tissues or compromising the immune system. Onanuga and Selekere et al. (2016) reported a 12.7% prevalence rate of hemolysin production among bacterial isolates in their study. Hemolysin operates by inserting into the membranes of target eukaryotic cells, forming pores that lead to ion efflux and subsequent cell damage (Cabezas et al., 2017).

Moreover, hemolysin aids in the dissemination of bacteria within the kidneys, which contributes to the onset of pyelonephritis in cases of ascending UTIs (Narang and Narang, 2018). Thus, the presence of hemolysin likely played a significant role in increasing the pathogenicity of the uropathogens identified in this study.

Conclusion

The study revealed a notable incidence of asymptomatic urinary tract infections (UTIs) at 31.6% among seemingly healthy school children in Jada, with a higher prevalence in female pupils (34.5%) compared to males (28.6%). UTIs were more frequently observed in children aged 6-7 years. *E. coli* was identified as the leading cause of bacterial UTIs in this group. Antibiotic susceptibility testing showed that Ciprofloxacin and Pefloxacin were the most effective antibiotics against the isolates, indicating their potential utility in the empirical treatment of UTIs. The study also emphasized that the pathogenicity of the isolates may have been enhanced by the presence of the hemolysin toxin and the ability of the bacteria to form biofilms. These findings highlight the importance of understanding the microbial profile, antibiotic resistance patterns, and virulence factors associated with UTIs in this population.

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