

ORIGINAL RESEARCH ARTICLE

Determinants of virulence and antimicrobial resistance in *Proteus* species from women with urinary tract infections in Lafia, NigeriaMaryam Hassan Muhammad¹, Joseph F. Nfongeh², Stella Ladi Ageba²,
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Abstract

Urinary tract infections (UTI) are a recurring issue in women's health as a result of the associated high economic burden. Our study profiled antibiotic resistance and virulence factors in *Proteus* species isolated from women with UTI from the University Teaching Hospital, Lafia, Nigeria. A total of 368 women aged 18 and above participated in the study. Urine samples were collected from volunteers and screened for significant bacteriuria using the pour plate technique. The isolates were identified using biochemical tests, and *Proteus* species were characterized for antibiotic susceptibility using the Kirby–Bauer disk diffusion method. The plasmids of the isolates were extracted and identified using agarose gel electrophoresis. Only 21 participants had significant bacteriuria, and 9 bacterial genera were isolated from their urine samples. *Escherichia coli* (52.4%), *Klebsiella* sp. (57.1%), and *Proteus* sp. (42.9%) were the most occurring species, while *Corynebacterium* sp. (4.8%) was found in only one patient. The demographic profile revealed that women aged 31–40 with a 40% incidence of *Proteus* sp. were the most susceptible group, and women who use a water system for sewage disposal and a borehole water source each had an incidence of 80%, respectively. Four *Proteus* isolates, P3, P5, P6, and P9, were resistant to nine antibiotics, and streptomycin had the best inhibition against the 10 *Proteus* isolates. Adhesion and hemolysin plasmids were the most commonly identified virulence plasmids, while resistance plasmids included conjugative R-plasmid, extended-spectrum beta-lactamase plasmids, and multi-conjugative plasmids of 50 kb, 40 kb, 80 kb, and 200 kb, respectively. The findings underscore the need for improved surveillance of antibiotic resistance promoters in the community. The co-occurrence of multiple plasmids is of concern as it promotes antibiotic resistance through horizontal gene transfer.

Keywords: Antibiotic resistance; Virulence; Plasmids; Demographic profile; Bacteriuria

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1. Introduction

Urinary tract infections (UTIs) are mostly bacterial infections that place a heavy burden on healthcare facilities and patients, both clinically and economically.¹ Women's predisposition to the infection is determined by their anatomical characteristics,

hormonal fluctuations, and sexual activity. *Escherichia coli* is the predominant causal organism; other organisms, such as *Proteus* species, complicate infections and cause recurrent UTIs.² *Proteus* UT infections are often underreported because laboratories do not routinely differentiate among the uropathogenic species, except for *E. coli*.³ The *Proteus* genus belongs to the Morganellaceae family. *Proteus* species are Gram-negative, facultative anaerobes. These bacteria are widely distributed in the environment and are commonly found in the human gastrointestinal tract. They are implicated in nosocomial infections, especially in immunocompromised patients. *Proteus* species cause UTIs and account for about 10% of community-acquired cases and a higher proportion of catheter-associated infections.³ They are also implicated in wound infections, septicemia, and, in some cases, respiratory infections in hospitalized patients. They form biofilms on medical devices, thereby contributing to their persistence in healthcare settings.

Proteus vulgaris and *Proteus penneri* are sometimes identified in hospitalized patients or those with structural abnormalities of the urinary tract.⁴ The pathogenesis of *Proteus* species is multifactorial. They exhibit swarming motility, which facilitates colonization and surface penetration. They also produce urease, which elevates urine pH, and form struvite and apatite crystals, which can lead to kidney stones. *Proteus* cells adhere to host tissues via fimbriae that attach to uroepithelial cells. The bacteria also produce hemolysins, proteases, and lipopolysaccharide as virulence determinants that damage tissues, aid in immune evasion, and cause inflammation. These virulence traits enable the bacteria to colonize and persist on uroepithelial cells, leading to recurrent infections despite treatment.⁵

Antimicrobial resistance (AMR) in *Proteus* isolates is presently a concern.⁶ The first-line β -lactams, aminoglycosides, and fluoroquinolones that were once potent against these bacteria are now ineffective due to β -lactamases.⁷ The scenario is compounded by the horizontal dissemination of encoding resistance genes via conjugative plasmids, integrons, and transposons within and across bacterial species.⁸ *Proteus* isolates also carry resistance to trimethoprim-sulfamethoxazole, tetracyclines, and fluoroquinolones that result from mutations or acquisition of plasmid-borne determinants. AMR has been projected to cause about 10 million deaths per year by 2050 if unchecked, with the third world bearing the most significant burden.⁹

Nigeria, with poor regulation, antibiotic abuse, poor infection management, and inadequate laboratory monitoring, contributes to the increase in AMR. Nasarawa State, located in the North-Central region of Nigeria, has recently experienced rapid urbanization and the expansion

of healthcare facilities. Women of reproductive age frequently present with UTIs in primary and secondary healthcare centers across the State. Given the limited number of studies, there is a need to characterize the etiologic agents beyond routine culture and biochemical identification. An understanding of the resistance mechanisms and virulence gene repertoire of *Proteus* isolates in the State is essential. This can guide treatment administration, prevent complications, and curb the spread of multidrug-resistant (MDR) uropathogens within the State.

2. Materials and methods

2.1. Study location

The study was conducted in Nasarawa, Nigeria. Samples were collected from the University Teaching Hospital, Lafia.

2.2. Study population and participation criteria

Women aged 18 to 65 years were recruited for the study. Women who had confirmed UTI and voluntarily consented were included in the sampling, while those on antibiotic treatment, with underlying chronic infections, or who did not provide consent were excluded. The women were administered questionnaires to collect their demographic information.

2.3. Ethical clearance

The permission (referenced ERC/MHNS/1342) to conduct the study was obtained from the Ethical and Research Committee of the Ministry of Health, Nasarawa State.

2.4. Sample size and collection of urine samples

Midstream clean-catch urine was collected from women into clean sterile containers and labeled. Samples were obtained from 368 women using Daniel's¹⁰ sample size determination method. The sample size was determined using the formula proposed (Equation 1):

$$n = \frac{Z^2 P(1-P)}{d^2} \quad (1)$$

where Z represents the standard normal variate at a 95% confidence level (1.96), P is the estimated prevalence of 39.8% obtained from a previous study by Nwankwo *et al.*¹¹, and d is the allowable margin of error set at 5% (0.05) with a type I error rate of 5%.

2.5. Isolation and identification of bacterial species

Bacterial isolation was conducted using cystine-lactose electrolyte-deficient agar (ReadyMED®, Chaitanya Agro Biotech Pvt., India) and chocolate agar (ReadyMED®,

Chaitanya Agro Biotech Pvt., India). The cultures were incubated at 37 °C for 24 h, and the chocolate agar was incubated in a CO₂-enriched enclosure using a candle jar. Significant growth was defined as bacterial growth $\geq 1.0 \times 10^5$ colony-forming unit (CFU)/mL of the midstream urine. The isolates were described based on their colonial and microscopic characteristics, after which Gram staining and biochemical tests (citrate, urease, hydrogen sulfide production, indole, motility) were performed.

2.6. Molecular identification of *Proteus* species

The DNA was extracted from an overnight broth culture. About 1 mL of the isolate in Luria–Bertani broth was spun at 14,000 rpm for three minutes. The supernatant was decanted, and the pellet was suspended in 1 mL of distilled water in a 1.5 mL centrifuge tube and centrifuged again at 14,000 rpm for 10 mins. The process was repeated after suspending the pellet in 100 µL of sterile distilled water. The pellet was again suspended in 500 µL normal saline and heated at 95 °C for 20 min. The suspension was then cooled on ice for 10 min and spun at 14,000 rpm for three min. The supernatant with DNA fragments was transferred to a 1.5 mL tube and stored at –20 °C. The polymerase chain reaction (PCR) mixture was then prepared: 4 µL master mix, 2 µL forward primer, 2 µL reverse primer, 2 µL DNA template, and 15 µL DNase-free water (Zymo Research, United States of America). For the identification of *Proteus*, universal primers 16S rRNA (ReadyMED®, Chaitanya Agro Biotech Pvt., India) were used, while primers targeting the *ureR*, *ureaseC*, and *pureR* genes were used to identify *Proteus* at the species level (Table 1). Amplification was performed according to the protocol: initial denaturation at 95 °C for five min, 30 cycles of denaturation, annealing, and extension at 94 °C, 52 °C, and 72 °C for 30 sec, 30 sec, and 85 sec, respectively, followed by a final extension at 72 °C for 10 min.

2.7. Antibiotic susceptibility test for *Proteus* species

Isolates presumptively identified as the genus *Proteus* were tested against 10 regimens of antibiotics using the Kirby–Bauer disk diffusion method. Isolates were inoculated by streaking on Mueller–Hinton agar and incubating at 37 °C for 24 hours.¹² The antibiotics tested included ceftazidime (30 µg), gentamicin (10 µg), ciprofloxacin (5 µg), ceporex (30 µg), ceftriaxone (30 µg), streptomycin (10 µg), cefuroxime (30 µg), ofloxacin (5 µg), augmentin (20 µg), and pefloxacin (5 µg). The zones of inhibition were measured in mL, and the MDR index was recorded.

2.8. Plasmid extraction: Alkaline lysis and large-plasmid preparation

Proteus isolates were cultured in 5 mL of Luria–Bertani broth and incubated overnight at 37 °C with agitation at 180 rpm. Approximately 1.5 mL of the culture was pelleted by centrifugation at $12,000 \times g$ for one minute in a 1.5 mL microfuge tube, and the supernatant was discarded. The step was repeated till all cultures were processed. The pellets were resuspended in 200 µL resuspension buffer and vortexed until homogeneous. Lysis buffer (200 µL) was then added and mixed by inversion, followed by incubation on ice for five minutes until the solution turned clear. A volume of 300 µL neutralization buffer was then added, and the mixture was inverted to ensure thorough mixing. It was incubated again on ice for 10 minutes, centrifuged at $12,000 \times g$ for 10 minutes at 4 °C, and transferred to a 500 µL tube. Isopropanol (300 µL) was added to the mixture, which was then incubated for 10 min and inverted to precipitate the DNA. The solution was centrifuged again at $12,000 \times g$ for 10 min, and the supernatant was discarded. The pellets were then washed in 500 µL ice-cold 70% ethanol, centrifuged at $12,000 \times g$ for two minutes, and air-dried for 5 to 10 min.

Table 1. Specific primer for *Proteus* species identification

Target	Primer	Sequence (5'–3')	bp	Species
16S rRNA	27F	AGAGTTTGATCCTGGCTCAG		
	1492R	GGTTACCTTGTTACGACTT		
<i>ureR</i>	PM-F	GCAAATTGAGTGACTTTGGCTGGACC	225	<i>Proteus mirabilis</i>
	PM-R	GGTGAGATTTGTATTAATGG		
<i>ureaseC</i>	PV-F	CGCTTTGCGATGGCAAGTACAAGTAAG	263	<i>Proteus vulgaris</i>
	PV-R	GCAAATTGAGTGACTTTGGCTGGACC		
<i>pureR</i>	PP-F	GCGTGGAGTGATTGTGGTTA	317	<i>Proteus penneri</i>
	PP-R	TTGAGGAGCCGTAGAGTGAA		

Abbreviation: bp: Base pair.

Large plasmid extraction was conducted using High Purity Plasmid DNA Miniprep Kit (Wuhan Servicebio Technology Co., Ltd, China) according to the manufacturer's protocol. The pulse-field gel electrophoresis (PFGE; CHEF-DR III, Bio-Rad, United States of America) was performed as follows: (i) gel concentration: 1% PFGE-grade agarose in $0.5 \times$ tris-borate-EDTA buffer; (ii) pre-run: 6 V/cm, 14 °C, 30 min; (iii) run parameters: voltage: 6 V/cm; switch time: one second initial, 25 seconds final, with a run time of 18 h; (iv) angle: 120°; and (v) temperature: 14 °C. The gel was stained with 0.5 µg/mL ethidium bromide for 30 min and destained in water for 30 min, after which it was visualized under an ultraviolet transilluminator.

For the PCR run, the master mix consisted of: 2× PCR master mix: 12.5 µL, forward primer (10 µM): 1.0 µL (final 0.4 µM), reverse primer (10 µM): 1.0 µL, template DNA (plasmid prep): 1.0 µL (10–50 ng plasmid DNA), and nuclease-free water: 9.5 µL. The thermocycler program was as follows: initial denaturation at 95 °C for three minutes, 35 cycles of denaturation at 95 °C for 30 sec, annealing at 52–60 °C for 30 sec, and extension at 72 °C for one minute. The final extension was at 72 °C for five minutes, followed by a hold at 4 °C. The amplicon was detected by running 5 µL of the PCR product on a 1.5% agarose gel with a 1 kb ladder, and the bands were visualized. The genes screened were extended-spectrum beta-lactamases (ESBLs): *bla*_{CTX-M}, *bla*_{TEM}, and *bla*_{SHV}; and virulence genes: *hlyA* (hemolysin) and *fimH* or *pap* operon genes (adhesins).

3. Results

Of the 368 women who participated in the study (Table 2), only 21 had bacterial counts greater than 1.0×10^5 CFU/mL in their urine (significant bacteriuria). These values ranged from 3.7×10^5 CFU/mL to 28.8×10^5 CFU/mL. *E. coli*, *Klebsiella* sp., *Proteus* sp., *Enterobacter* sp., *Pseudomonas auruginosa*, *Enterococcus faecalis*, *Staphylococcus aureus*,

Corynebacterium sp., and *Streptococcus agalactiae* were among the bacteria isolated from their urine samples. *E. coli* was isolated in the urine of 14 women, while *Corynebacterium* sp. was isolated in only one woman in the study group. *Proteus* spp. was present in 10 urine samples with a 42.9% occurrence rate. The identity of the *Proteus* and their species were confirmed, as shown in Figure 1.

Table 3 shows that the patients with the highest significant bacteriuria (38.1%) and *Proteus* spp. counts (40%) were among the 31–40 age group. By occupation, housewives had a 42.9% significant rate of bacteriuria and a 60% *Proteus* count, while civil servants had a 33.3% significant rate of bacteriuria and a 30% *Proteus* count. Students in the study group recorded no cases. The demographic study also showed that women who use the water system for sewage disposal had 80.0% *Proteus* counts and 71.4% bacteriuria, compared to 20.0% *Proteus* counts and 28.6% bacteriuria for women who use pit latrines. In the study, those who consumed water from boreholes had 61.9% bacteriuria and 80% *Proteus* infection. Across all parameters studied, only sewage disposal showed a statistically significant association with *Proteus* infection ($p = 0.011$). None of the other groups showed significant associations at $p < 0.05$.

The antibiotic susceptibility profile of the *Proteus* isolates showed a high level of resistance to commonly used antibiotics. Most isolates were resistant to β-lactam antibiotics, with only ceftazidime showing susceptibility in isolates P4 and P9, and ceftriaxone in P2 (Table 4). Gentamicin showed poor activity, inhibiting only isolate P8. Streptomycin showed the best antibacterial activity, with zones of inhibition of 15 mm, 19 mm, 17 mm, 18 mm, 15 mm, 13 mm, and 20 mm against *Proteus* isolates P1, P2, P3, P4, P6, P7, and P10, respectively. Fluoroquinolones showed variable activity against the isolates. Ciprofloxacin was effective against four isolates (P1, P5, P7, and P8), while ofloxacin and pefloxacin inhibited three isolates

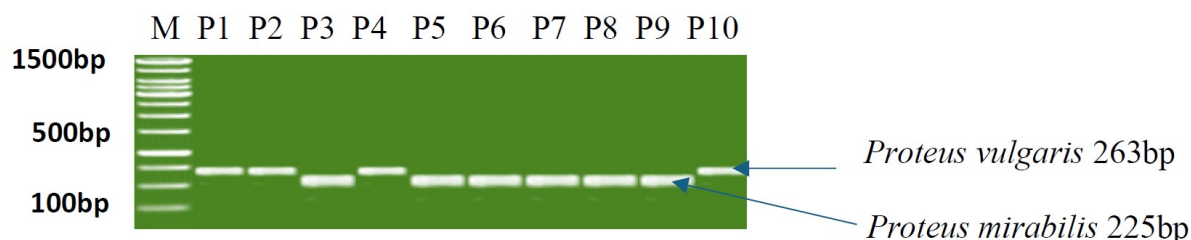


Figure 1. Agarose gel electrophoresis of the amplified DNA of *Proteus vulgaris* and *Proteus mirabilis*

Note: Lane M: 1,500 bp DNA molecular ladder; lanes P1, P2, P8, and P10: expression of the *ureaseC* (263 bp) gene in *Proteus*; lanes P3, P5–P9: Expression of the *ureR* (225 bp) gene in *Proteus*.

Table 2. Patients with bacteriuria and associated bacterial species in women with suspected urinary tract infection in Nasarawa State

Patient ID	Mean (× 10 ⁵ CFU/mL)	Escherichia coli	<i>Klebsiella</i> sp.	<i>Proteus</i> sp.	<i>Enterobacter</i> sp	<i>Pseudomonas aeruginosa</i>	<i>Enterococcus faecalis</i>	<i>Staphylococcus aureus</i>	<i>Corynebacterium</i> sp	<i>Streptococcus agalactiae</i>
M2	20.4	+	+	-	-	+	+	-	-	-
B11	3.7	+	-	-	-	+	+	-	-	-
T1	7.2	+	+	-	-	-	-	-	-	-
K12	26.4	+	+	+	+	-	-	-	-	-
A7	9.2	+	-	+	+	-	-	+	-	-
L14	13.9	+	-	+	+	-	-	-	-	+
T3	20.8	+	-	+	+	-	-	-	-	-
C3	11.9	+	+	-	-	+	+	-	-	-
M4	21.8	+	+	-	-	-	-	+	+	-
D3	5.8	+	-	+	+	-	-	-	-	-
M7	11.3	-	+	-	-	+	+	+	-	-
U9	17.4	-	-	+	-	+	-	-	-	-
A4	6.7	+	-	-	-	-	-	+	-	-
O6	28.8	-	+	+	-	-	-	-	-	-
I5	21.1	+	-	+	-	-	-	-	-	-
A1	13.6	-	+	+	-	-	-	-	-	-
S3	7.2	-	+	-	+	+	-	-	-	-
D6	10.2	-	+	-	+	+	-	-	-	-
I2	21.2	-	+	-	-	+	-	+	-	-
D2	5.6	+	-	+	-	-	-	-	-	-
P2	24.1	+	+	-	-	+	-	-	-	+
Percentage incidence (%)	52.4	57.1	42.9	28.6	38.1	23.8	23.8	4.8	14.3	

Abbreviation: CFU: Colony-forming unit.

Table 3. Demographic characteristics of the women with urinary tract infections

Parameters	Category	Total sampled, n (%)	Significant bacteriuria positive, n (%)	<i>Proteus</i> positive, n (%)	χ^2	df	p-value
Age group (years)	11–20	95 (25.8)	3 (14.3)	1 (10.0)	9.84	6	0.13
	21–30	110 (29.9)	5 (23.8)	2 (20.0)			
	31–40	57 (15.5)	8 (38.1)	4 (40.0)			
	41–50	51 (13.9)	3 (14.3)	2 (20.0)			
	51–60	33 (9.0)	1 (4.8)	1 (10.0)			
	61–70	14 (3.8)	1 (4.8)	0			
	≥ 71	8 (2.2)	0	0			
Occupation	Farmers	53 (14.4)	3 (14.3)	1 (10.0)	9.10	4	0.06
	Business	34 (9.2)	2 (9.5)	0			
	Civil servants	67 (18.2)	7 (33.3)	3 (30.0)			
	Students	81 (22.0)	0	0			
	Housewives	133 (36.1)	9 (42.9)	6 (60.0)			
Sewage disposal	Water system	133 (36.1)	15 (71.4)	8 (80.0)	9.09*	2	0.011
	Pit latrine	218 (59.2)	6 (28.6)	2 (20.0)			
	Open defecation	17 (4.6)	0	0			
	Borehole	188 (51.1)	13 (61.9)	8 (80.0)			
Water source	Well	84 (22.8)	5 (23.8)	1 (10.0)	3.14	3	0.37
	Stream	41 (11.1)	2 (9.5)	1 (10.0)			
	Others	55 (14.9)	1 (4.8)	0			

Note: * $p < 0.05$.

Abbreviation: df: Degree of freedom.

each. *Proteus* in P8 had zones of inhibition of 13 mm with gentamicin, 22 mm with ciprofloxacin, and 26 mm with both ofloxacin and pefloxacin.

The antibiotic resistance pattern showed that the *Proteus* species were mostly resistant to augmentin and ceftazidime (Table 5). *Proteus* species in P5 and P6 were susceptible to one antibiotic each. Isolate P8 was the least resistant to the antibiotic classes cephalosporin, aminoglycosides, and penicillin, while the other isolates were all resistant to fluoroquinolone.

The virulence plasmids identified in the isolated *Proteus* species were the hemolysin and adhesion plasmids (Table 6). The adhesion plasmid, with a molecular weight of 20 kb, was found in eight of the isolates. Isolate P4 (*P. vulgaris*) had both the adhesion and hemolysin plasmid (30 and 50 kb, respectively). The other isolates had either the 30-kb or the 50-kb hemolysin. The ESBL plasmid was the most isolated resistance plasmid present in nine of the isolates, while the conjugative R-plasmid and multidrug conjugative plasmid were found in isolates P1 and P5 (*Proteus mirabilis*), respectively. The resistance plasmids had molecular sizes of 40, 80, and 200 kb, respectively.

4. Discussion

Bacterial counts were generally high, ranging from 3.7×10^5 CFU/mL to 28.8×10^5 CFU/mL among women recruited at the University Teaching Hospital in Lafia, Nasarawa State. These counts indicate the severity of infection

in each patient. High counts are generally associated with susceptibility in some women, the virulence of the isolated pathogens, and the time of infection.^{13,14} Urine contamination was ruled out because the counts were too high, indicating that the infection was progressing to a severe condition. Enterobacteriaceae are reportedly associated with UTIs in women globally.¹⁵ *E. coli* and *Klebsiella* species, which are part of the gut microflora, also colonize the urinary tract to cause infection.¹⁶

Age, pregnancy, and suppressed immunity from comorbidities increase the severity of infection and complications in women.¹³ The 57.1% incidence of *Klebsiella* species in the study differed from that reported in a previous study.¹⁷ Polymicrobial bacteriuria observed among the women suggests that some of them have compromised immunity or live in an environment with antibiotic pressure and abuse.^{18,19} The presence of Gram-positive and Gram-negative bacteria in the women's urine is concerning. This could have contributed to the high bacteriuria observed among participants in the study.²⁰ *S. agalactiae*, detected in some pregnant women, poses an obstetric concern due to its potential to cause neonatal complications.²¹ These pathogens contribute to MDR, a public health issue that warrants attention.

Women aged 31–40 years had high bacteriuria, possibly due to regular sexual activity, the type of occupation, and susceptibility to UTI pathogens.^{22,23} This finding aligns with Kumwenda and Semu,²⁴ who reported similar findings. A high *Proteus* count in urine may be age-specific in

Table 4. Antibiotic susceptibility profile of *Proteus* isolates against common antibiotics

Antibiotic	CLSI cut-off (mm)	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Zone of inhibition diameters (mm)											
Ceftazidime	≤14	8 (R)	12 (R)	12 (R)	17 (S)	12 (R)	9 (R)	9 (R)	11 (R)	16 (S)	12 (R)
Gentamicin	≤12	8 (R)	9 (R)	8 (R)	8 (R)	8 (R)	9 (R)	11 (R)	13 (S)	10 (R)	9 (R)
Ciprofloxacin	≤15	20 (S)	11 (R)	13 (R)	13 (R)	16 (S)	12 (R)	20 (S)	22 (S)	10 (R)	9 (R)
Ceporex	≤14	10 (R)	9 (R)	9 (R)	15 (S)	13 (R)	8 (R)	13 (R)	12 (R)	7 (R)	13 (R)
Ceftriaxone	≤13	13 (R)	14 (S)	12 (R)	9 (R)	13 (R)	13 (R)	8 (R)	12 (R)	9 (R)	9 (R)
Streptomycin	≤11	15 (S)	19 (S)	17 (S)	18 (S)	9 (R)	15 (S)	13 (S)	7 (R)	8 (R)	20 (S)
Cefuroxime	≤14	7 (R)	8 (R)	12 (R)	13 (R)	8 (R)	11 (R)	11 (R)	12 (R)	16 (S)	13 (R)
Ofloxacin	≤24	18 (R)	21 (R)	27 (S)	22 (R)	8 (R)	16 (R)	15 (R)	26 (S)	20 (R)	25 (S)
Augmentin	≤19	13 (R)	13 (R)	18 (R)	16 (R)	17 (R)	18 (R)	12 (R)	9 (R)	21 (S)	17 (R)
Pefloxacin	≤15	14 (R)	22 (S)	16 (R)	10 (R)	14 (R)	12 (R)	18 (S)	26 (S)	11 (R)	15 (R)

Notes: R: Resistant (zone diameter ≤ CLSI cut-off); S: Susceptible (zone diameter > CLSI cut-off); *Proteus* isolate codes: P1–T1A, P2–K12B, P3–L14C, P4–T3D, P5–D3E, P6–U9F, P7–O6G, P8–I5H, P9–A1I, and P10–D2J.

Abbreviation: CLSI: Clinical and Laboratory Standards Institute.

Table 5. Antibiotic and multidrug resistance pattern of the isolated *Proteus* species

<i>Proteus</i> ID	Antibiotics resisted	Antibiotic class	Number resisted	MDR index
P1	Au, Cfa, Cti, Cep, Cef, Gen, Ofi, Pef	P, C, F, A	8	0.8
P2	Au, Cfa, Cep, Cef, Cip, Gen, Ofi	P, C, F, A	7	0.7
P3	Au, Cfa, Cti, Cep, Cef, Cip, Gen	P, C, F, A	7	0.7
P4	Au, Cti, Cef, Cip, Gen, Ofi, Pef	P, C, F, A	7	0.7
P5	Au, Cfa, Cti, Cep, Cef, Gen, Ofi, Per, Stp	P, C, F, A	9	0.9
P6	Au, Cfa, Cti, Cep, Cef, Cip, Gen, Ofi, Pef	P, C, F, A	9	0.9
P7	Au, Cfa, Cti, Cep, Cef, Gen, Ofi	P, C, F, A	7	0.7
P8	Au, Cfa, Cti, Cep, Cef, Stp	P, C, A	6	0.6
P9	Cti, Cep, Cip, Gen, Ofi, Pef, Stp	P, C, F, A	7	0.7
P10	Au, Cfa, Cti, Cep, Cef, Cip, Gen, Pef	P, C, F, A	8	0.8

Notes: A: Amyloglycoside; C: Chlorosporin; F: Fluoroquinolone; P: Penicillin.

Abbreviations: Au: Augmentin; Cef: Cefuroxime; Cep: Ceporex; Cfa: Ceftazidime; Cti: Ceftriaxone; Gen: Gentamycin; MDR: Multidrug resistance; Ofi: Ofloxacin; Pef: Pefloxacin; Stp: Streptomycin.

women,^{5,25} while counts in housewives may be associated with contaminated water sources or poor sanitation.²⁶ The use of water system toilets did not reduce the incidence of infection among women, as reported in the study, which aligns with findings by Akaishi.²⁷ The observed incidence may reflect that most of the women were residents of Lafia, a metropolitan commercial center in North Central Nigeria with a high population density, where women share various facilities.²⁸ The results showed that the sewage system may not predict infection risk, but crowding, shared toilets, or urban exposure could be responsible for the incidence. A high incidence was also associated with the use of borehole water, likely due to exposure to contaminated water.

The study posits that the production of ESBLs was responsible for the resistance recorded against third-generation cephalosporins (ceftazidime, ceftriaxone, cefuroxime, and ceporex) in *Proteus* species. The

fluoroquinolones showed promising inhibition against the isolates, making them effective options. However, reliance on fluoroquinolones over time could lead to resistance due to potential overuse. The high (0.6 to 0.9) MDR index suggests that the *Proteus* isolates likely emanated from settings where antibiotic abuse is frequent or from hospital settings. Resistance to augmentin, cephalosporins, and aminoglycosides among the isolates leaves limited treatment options for UTIs in the study area. The antibiotic susceptibility patterns in this study revealed an alarming resistance among the *Proteus* isolates. Similar MDR patterns have been reported in a Nigerian hospital, where a large proportion of enteric bacteria from UTI cases were resistant to amoxicillin-clavulanate, cephalosporins, and other routine antibiotics.²⁹

The presence of virulence and resistance plasmids in the

Table 6. Plasmid characteristics of multidrug-resistant *Proteus* species from women with urinary tract infections in the University Teaching Hospital, Lafia

<i>Proteus</i> ID	Name of isolate	Virulence plasmid	Molecular size (kb)	Resistance plasmid	Molecular size (kb)
P1	<i>Proteus vulgaris</i>	Adhesion	20	ESBL plasmid	40
P2	<i>P. vulgaris</i>	Adhesion	20	ESBL plasmid	80
P3	<i>Proteus mirabilis</i>	Adhesion	20	ESBL plasmid	80
P4	<i>P. vulgaris</i>	Adhesion Hemolysin Hemolysin	20 30 50	ESBL plasmid	80
P5	<i>P. mirabilis</i>	Hemolysin	30	Multidrug conjugative plasmid	200
P6	<i>P. mirabilis</i>	Adhesion	20	Conjugative R-plasmid ESBL plasmid	50 40
P7	<i>P. mirabilis</i>	Hemolysin	50	ESBL plasmid	80
P8	<i>P. mirabilis</i>	Adhesion	20	ESBL plasmid	80
P9	<i>P. mirabilis</i>	Adhesion	20	ESBL plasmid	40
P10	<i>P. vulgaris</i>	Adhesion	20	ESBL plasmid	80

Abbreviation: ESBL: Extended-spectrum beta-lactamases.

isolated *Proteus* species generally means infections would be more potent and difficult to treat. While the adhesion plasmid (20 kb) aids attachment to uroepithelial cells, thereby contributing to colonization and persistence in the urinary tract, the hemolysin plasmids (30 and 50 kb) cause cell lysis and damage through cytotoxic activity, leading to complicated or recurrent infections.^{1,2} The presence of different types of resistance plasmids, especially ESBL plasmids, in the *Proteus* isolates highlights a concerning antibiotic selection pressure from the abuse of β -lactams in Lafia metropolis. The 200 kb multidrug plasmid, which facilitates horizontal transfer of resistance across species and promotes AMR to different antibiotic classes, is a public health concern.^{30,31} The detection of ESBL and other resistance plasmids in the *Proteus* isolates complements the evidence of transmissible resistance determinants among uropathogens in the region. This suggests that plasmid-mediated resistance is a critical concern across Nigeria.³² These findings reinforce the need for routine culture-associated treatment approaches, robust antimicrobial stewardship, and continuous surveillance of cases to mitigate the spread of MDR uropathogens in Nigeria.

5. Conclusion

This study found a high prevalence of significant bacteriuria among women with UTIs. Women of reproductive age and housewives were the most affected groups, with *Proteus* species contributing significantly to the observed infections. This pattern agrees with reports from other parts

of Nigeria, where UTIs are more common among sexually active women. In addition, the strong association between sewage disposal systems and infection rates highlights the role of poor sanitation and fecal contamination in the spread of UTIs. UTIs caused by *Proteus* species remain a significant concern, especially in regions with limited diagnostic capacity and rising AMR. The combination of virulence factors and plasmid-mediated MDR reported in the study can complicate effective patient management. It is a public health risk through the potential for horizontal gene transfer to healthy people. In Nasarawa State, this study provides epidemiological, phenotypic, and genotypic data on *Proteus* isolates from women with UTIs. These findings can inform appropriate antimicrobial therapy in hospitals and serve as a foundation for future genomic and ecological studies on the spread of AMR and virulence determinants among uropathogenic bacteria in Nigeria.

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Conflict of interest

The authors declare that they have no competing interests.

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Ethics approval and consent to participate

The permission (referenced ERC/MHNS/1342) to conduct the study was obtained from the Ethical and Research Committee of the Ministry of Health, Nasarawa State. Verbal consent to participate in the study was obtained from all patients recruited.

Consent for publication

Not applicable.

Availability of data

Data are available from the corresponding author upon reasonable request.

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