



Research Article

Infections Associated with *Proteus* Species and their Drug Resistance Pattern in Northeastern, Nigeria

Isyaka M. Tom^{1,2*}, Usman A. Dutsinma¹, Aishatu A. Ibrahim¹, Muhammad M. Ibrahim³, Askira M. Umoru², Jidda B. Umar⁴

¹Department of Microbiology, Faculty of Life Sciences, Bayero University Kano, Nigeria

²Department of Medical Laboratory Science, University of Maiduguri, Nigeria

³Department of Microbiology, Faculty of Life Sciences, University of Maiduguri, Nigeria

⁴Department of Medical Microbiology, University of Maiduguri Teaching Hospital, Nigeria

*Corresponding author's Email: isyakatom77@gmail.com, doi.org/10.55639/607.525150

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ABSTRACT

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This study conducted in North-eastern Nigeria aimed to investigate *Proteus* species associated with infections across various anatomical sites and assess their susceptibility to commonly prescribed antimicrobial drugs. A total of 1,500 clinical samples were collected from patients in selected hospitals. Among these samples, 144 (9.60%) showed the growth of *Proteus* species, with a higher prevalence in males (65.25%) compared to females (43.75%). *Proteus mirabilis* was identified as the predominant species (90.97%), followed by *Proteus vulgaris* (8.33%) and *P. Penneri* (0.69%). Wound swab samples exhibited the highest isolation rate at 31.94%, followed by urine (15.28%), while diarrhetic stool samples had the lowest rate (6.25%). Antimicrobial susceptibility tests revealed that the isolates were highly sensitive to Levofloxacin (87.50%), Ciprofloxacin (72.92%), Meropenem (67.36%), and Ofloxacin (65.28%). Conversely, they demonstrated high resistance to Ampicillin (84.72%) and Nalidixic acid (81.94%). Multidrug resistance (MDR) was prevalent, with *P. Penneri* showing the highest MDR phenotype (100.0%), followed by *P. mirabilis* (88.54%) and *P. vulgaris* (66.67%). Although the distribution of MDR *Proteus* strains across various hospitals was not statistically significant, SSH Maiduguri recorded the highest rate of isolation (20.60%). Multiple Antibiotic Resistance (MAR) was present in all isolates, with the MAR index ranging from 0.13 to 0.96. The study concludes that *Proteus* species contribute to nosocomial infections in the region, with *Proteus mirabilis* being the primary etiological agent. Multidrug resistance among *Proteus* species is widespread in the study area, limiting treatment options for critically ill patients.

Corresponding author: Isyaka M. Tom, Email: isyakatom77@gmail.com
Department of Medical Laboratory Science, University of Maiduguri, Nigeria

INTRODUCTION

Proteus is a member of the family *Enterobacteriaceae*. It is a pleomorphic, Gram-negative, rod-shaped bacterium with distinct swarming motility on solid agar. The genus *Proteus* consists of five named species: *P. mirabilis*, *P. vulgaris*, *P. Penneri*, *P. myxofaciens* and *P. hauseri* and three unnamed genomospecies: *Proteus* genomospecies 4, 5, 6 (O'Hara *et al.*, 2000). *Proteus* is widespread in the environment and makes up part of the normal flora of the human gastrointestinal tract. *Proteus* species are a major cause of diseases acquired outside the hospital, where many of these diseases eventually require hospitalization (Jabur *et al.*, 2013). It ranks third as the cause of health care-associated infections and three species: *P. vulgaris*, *P. mirabilis*, and *P. Penneri* are opportunistic human pathogens (Senthamarai *et al.*, 2015). *Proteus* spp have a diverse mode of transmission, some of the incriminating sources of transmission are soil, contaminated water, food, equipment, intravenous solutions, the hands of patients and health-care personnel (Tom *et al.*, 2018). *Proteus* species are ubiquitous in nature albeit due to their diverse nutritional choice, and they are mostly linked with infections in different anatomical sites. *Proteus* species mostly remain sensitive to a range of antibiotics; increasing rates of acquired antibiotic resistance in the *Enterobacteriaceae* are a growing problem (Iredell *et al.*, 2016). They can be naturally resistant to antibiotics; some strains produced penicillinase and almost all possess intrinsic resistance to colistin, tigecycline and tetracycline (Qin *et al.*, 2015). Antibiotic resistance remains a serious public health problem with a continually increasing rate worldwide (Bonnet 2004; Yan *et al.*, 2006; Magiorakos *et al.*, 2011). The accelerated emergence of antibiotic resistance is

attributed to the excessive use of antibiotics and the remarkable genetic plasticity of microorganisms, posing a serious threat to the management of infectious diseases (Robert, 2009). The situation is even more worrisome in a resource constrained country like Nigeria, with weak healthcare facilities and poor drug regulatory/monitory systems, making it easy for the availability of fake and counterfeit drugs. This study aims to describe the prevalence and antibiotic susceptibility profile of *Proteus* spp causing various infections in hospitals in the North-eastern region of Nigeria.

MATERIALS AND METHODS

Study Population

The target population for the study includes inpatients and out-patients attending six healthcare centers within the North-eastern sub-region of Nigeria. These centers serve a population of over 40 million in the North-eastern sub-region of Nigeria, comprising six states (Borno, Bauchi, Yobe, Adamawa, Taraba and Gombe) as well as a sizeable number across the borders of Cameroon, Chad and Niger Republic (Umar *et al.*, 2016).

Sample Collection and Processing

A total of 1500 clinical samples (comprising of wound, sputum, urine, ear swab, catheter tip, genital swab, stool and other body fluids) were randomly collected from consented patients attending selected Hospitals. These hospitals include: Abubakar Tafawa Balewa Teaching Hospital, Bauchi, State Specialist Hospital, Maiduguri, Federal Medical Centre, Yola, State Specialist Hospital, Damaturu, Federal Medical Centre, Gombe and Federal Medical Centre, Jalingo. Patients' demographic data were collected and recorded prior to sample collection.

Bacteriological Analysis

The clinical samples were cultured by plating on to 5% Blood agar, MacConkey agar and Cystine Lactose-Electrolyte-

Deficient (CLED) agar plates and incubated aerobically at 37°C for 18-24 hour (Cheesbrough, 2006; Baker *et al.*, 2007). Suspected colonies that developed were subcultured further to obtain discrete colonies. Gram stain was conducted as a preliminary test. Pure cultures of the isolate were identified using morphological appearance, swarming motility on Blood agar, Gram stain reaction and biochemical tests which include, phenylalanine deamination, urease, Triple Sugar Ion Agar Test (TSI), indole, methyl red, voges proskauer, citrate, maltose fermentation and ornithine decarboxylase test, (Cheesbrough, 2006; Baker *et al.*, 2007).

Antibiotic Susceptibility Test

Preparation and Standardization of Bacterial Inoculum

Pure isolates of *Proteus* spp were inoculated into Nutrient broth and incubated at 37°C for up to 5 hours until turbidity equals to 0.5 Mcfarland turbidity scale. This turbidity scale was prepared by adding 0.6ml ml of 1% aqueous solution of barium chloride in 99.4ml of 1% sulphuric acid giving an approximate bacterial density of 1.2×10^9 cfu/ml (Cheesbrough, 2006).

Sensitivity Pattern of *Proteus* Isolates

The Kirby-Bauer disc diffusion method as described by Akubuenyi *et al.* (2011) was used for this test. Pure isolates of *Proteus* were tested against commonly used antibiotics in the region, containing disc of the following antibiotics; Ceporex (10 µg/ml), Gentamicin (10µg/ml), Amoxicillin (30 µg/ml), Augumentin (30µg/ml), ceftriaxone (30µg), ceftazidime (30µg), cefotaxime (30µg), Meropenem (30µg/ml), Eetapenem (30µg/ml), Aztreonam (30µg/ml), Nalidixic acid (30µg/ml), Streptomycin (30 µg/ml), Norfloxacin (30 µg/ml), Ofloxacin (30 µg/ml), Pefloxacin (10 µg/ml), Ciprofloxacin (10 µg/ml), Levofloxacin (10

µg/ml), Chloramphenicol (10 µg/ml), Rifampicine (10 µg/ml), Erythromycin (10 µg/ml), Ampicillin (30 µg/ml) and Cotrimoxazole (30 µg/ml), by (Fondo laboratories, Nigeria) and (Oxoid Limited, UK).

Prepared *Proteus* inoculums (1.2×10^9 cfu/ml) were seeded by flooding onto a prepared Mueller Hinton agar (MHA) plates under aseptic condition and the surface was allowed to absorb at 37°C for two minutes. Commercially obtained antibiotics disc were carefully placed onto the surface of the seeded plate using a sterile forceps and incubated at 37°C for 24 hours. After 24 hours, the zones of inhibition were measured. Obtained results were compared with the standard performance chart for antimicrobials disc susceptibility testing provided by CLSI (2014), and the frequencies of sensitivity and resistant antibiotics were recorded.

Data Analysis

Data were presented as frequencies and percentages. Chi-square was used, and evaluations were carried out at a 99% confidence level, with $p < 0.01$ considered statistically significant. Confidence interval of $\pm 2.0\%$ was calculated and used to interpret the prevalence rates in this study.

RESULTS

One thousand and five hundred (1500) samples were collected from patients attending selected Hospitals in the North-Eastern states of Nigeria, comprising of State Specialist Hospital (SSH), Maiduguri, SSH, Damaturu, Federal Medical Centre (FMC), Yola, Abubakar Tafawa Balewa Teaching Hospital (ATBU-TH), Bauchi, FMC, Gombe and FMC, Jalingo, and examined for pathogenic *Proteus* infection. The clinical samples collected from patients for the study includes, Wound swab, urine, Ear swab, Catheter tip, Sputum, Stool, Genital swab and Body fluids.

Sex Distribution of Patients with *Proteus* Infection

Out of the 1500 sample collected 144 were positive for *Proteus* infections with a prevalence rate of 9.6%. *Proteus* infection was higher in males (56.25%) than in females (43.75%) ($p>0.01$). Mean prevalence was observed to be 72.0% with a standard deviation of 12.7 and Standard error mean of 8.98. Since the confidence interval is $\pm 2.0\%$, it can be deduced that the prevalence rate of *Proteus* spp infection in northeastern Nigeria falls between the ranges of 7.6% to 11.6% of the population at 99% confidence level (Figure 1).

Pathology of *Proteus* Species

In this study, the most predominant *Proteus* species isolated was *Proteus mirabilis* 131 (90.97%) followed by *Proteus vulgaris* 12 (8.33%) and the least was *Proteus Penneri* 1 (0.69%). The distribution among sample types showed that, Wound swab recorded the highest isolates of 46 (31.94%) followed by Urine with 22 (15.28%), and Stool of patients with chronic diarrhoea the least 9 (6.25%) (Table 1).

Antimicrobial Susceptibility Pattern of *Proteus* Species

The susceptibility pattern showed that the species were most sensitive to Levofloxacin 87.50%, Ciprofloxacin 72.92%, Meropenem 67.36%, Ofloxacin 65.28% and highly

resistant to Ampicillin 122 (84.72%), Nalidixic acid 118 (81.94%), Ceporexin, Amoxicillin, Cefotaxime with 116 (80.56%), Norfloxacin 79.86%, Ceftazidime 106 (73.61%) and Ampiclox 103 (71.53%) (Table 2). Multidrug resistance phenotype was found in 125 of the isolates with a prevalence rate of 86.81%, with the only one isolate of *P. Penneri* recorded the highest frequency of 100.0%, followed by *P. mirabilis* 116 (88.54%) and *P. vulgaris* 8 (66.67%) having each proved resistant to at least three antibiotics from different classes (Table 3). The distribution of MDR strains of the *Proteus* spp in relation to age showed that patients within the age category of 31-40yrs had the highest number of multidrug resistant isolates 27 (18.75%) while patients in the age group of >60yrs had 11 (7.64%) displayed the least (Table 4). The frequency of isolation of multi drug resistant *Proteus* spp from samples collected in the selected Hospitals showed that patients attending SSH, Maiduguri recorded the highest rate of isolation, 26 (20.60%), while FMC, Yola and ATBU-TH, Bauchi the least with 17 (13.60%) respectively (Table 5). Multiple antibiotic resistances (MAR) index revealed the joint resistance of isolates to more than two antibiotics. Two isolates were resistant to 22 antibiotics out of the 23 tested with an index of 0.96 (Table 6).

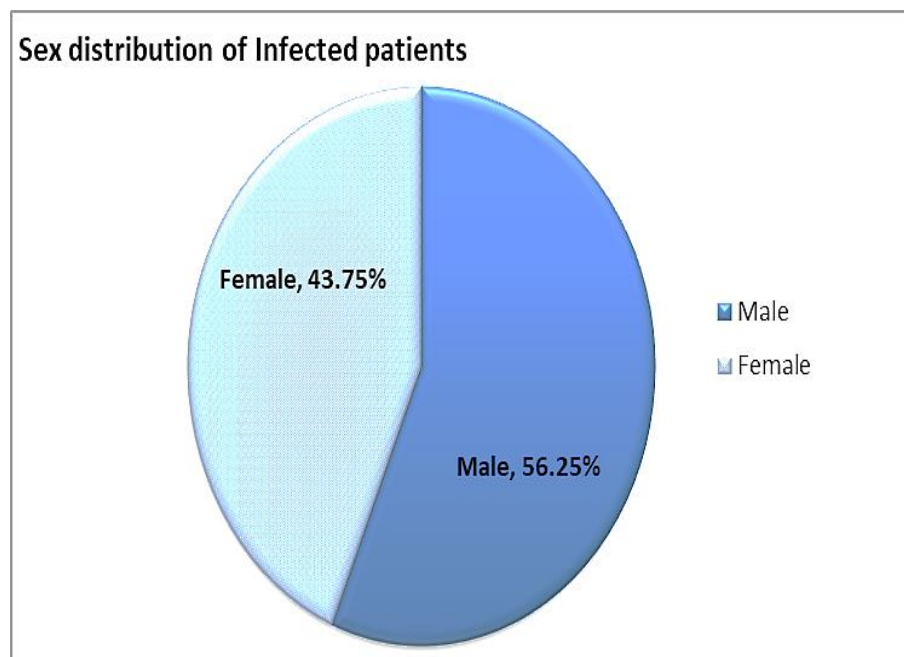


Figure 1: Distribution of *Proteus* spp according to Sex of patients attending hospitals in Northeastern Nigeria ($p > 0.01$)

Table 1: Frequency of *Proteus* spp. Isolated from Various Sample Types in the Study Area.

Specie Type	Sample Type (%)								Total (%)
	Wound	Urine	Ear Swab	Catheter	Sputum	Stool	Genital Swab	Body Fluid	
<i>P. mirabilis</i>	40(27.78)	20(13.89)	19(13.89)	13(9.03)	11(7.64)	9(6.25)	10(6.94)	9(6.25)	131(90.97)
<i>P. vulgaris</i>	6 (4.17)	2 (1.39)	1 (0.69)	0 (0.00)	0 (0.00)	0 (0.00)	2 (1.39)	1 (0.69)	12 (8.33)
<i>P. Penneri</i>	0 (0.00)	0 (0.00)	1 (0.69)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.69)
Total (%)	46(31.94)	22(15.28)	21(14.58)	13(9.03)	11(7.64)	9(6.25)	12(8.33)	10(6.94)	144(100)

Table 2: Antimicrobial Susceptibility Pattern of *Proteus* Spp. Isolated from Patients in the Selected Hospitals.

Antimicrobial Agents tested	Susceptibility pattern	
	Sensitivity (%)	Resistance (%)
<i>Quinolones</i>		
Ciprofloxacin (CPX)	105 (72.92)	39 (27.08)
Ofloxacin (OFX)	94 (65.28)	50 (34.72)
Pefloxacin (PEF)	77 (53.47)	67 (46.52)
Nalidixic acid (NA)	26 (18.06)	118 (81.94)
Norfloxacin (NB)	29 (20.14)	115 (79.86)
Levofloxacin (LEV)	126 (87.50)	18 (12.50)
<i>β-lactam Antibiotics</i>		
Ampicillin (PN)	22 (15.28)	122 (84.72)
Cephalexinin (CEP)	28 (19.44)	116 (80.56)
Amoxicillin (AMX)	28 (19.44)	116 (80.56)
Augmentin (AU)	51 (35.42)	93 (64.58)
Ampiclox (APX)	41 (28.47)	103 (71.53)
Ceftazidime (CAZ)	38 (26.39)	106 (73.61)
Cefotaxime (CTX)	28 (19.44)	116 (80.56)
Ceftriazone (CRO)	55 (38.19)	89 (61.81)
Meropenem (MEM)	97 (67.36)	47 (32.64)
Ertapenem (ETP)	65 (45.14)	79 (54.86)
Aztreonam (ATM)	68 (47.22)	76 (52.78)
<i>Aminoglycosides</i>		
Gentamicin (CN)	68 (47.22)	76 (52.78)
Streptomycin (S)	79 (54.86)	65 (45.14)
<i>Sulphonamide</i>		
Cotrimoxazole (SXT)	74 (51.39)	70 (48.61)
<i>Rifampins</i>		
Rifampicin (RD)	86 (59.72)	58 (40.28)
<i>Chloramphenicols</i>		
Chloramphenicol (CH)	70 (48.61)	74 (51.39)
<i>Macrolides</i>		
Erythromycin (E)	73 (50.69)	71 (49.31)

Table 3: Multidrug Resistance/Antimicrobial Resistance profile of *Proteus* Spp. Isolated in the Study Area

Antimicrobial Drug Resistance	<i>Proteus</i> spp		
	<i>P. mirabilis</i> (%) (n=131)	<i>P. vulgaris</i> (%) (n= 12)	<i>P. Penneri</i> (%) (n=1)
Total MDR	116 (88.54)	8 (66.67)	1 (100.0)
PN	97 (83.62)	7 (87.50)	1 (100.0)
CEP	86 (74.14)	6 (75.00)	1 (100.0)
OFX	52 (44.83)	2 (25.00)	1 (100.0)
NA	93 (80.17)	7 (87.50)	1 (100.0)
PEF	59 (50.86)	4 (50.00)	0 (0.00)
CN	67 (57.76)	6 (50.0)	1 (100.0)
AU	79 (68.10)	5 (62.50)	1 (100.0)
CPX	35 (30.17)	1 (12.50)	0 (0.00)
SXT	62 (53.45)	5 (62.50)	1 (100.0)
S	59 (50.86)	3 (37.50)	0 (0.00)
APX	90 (77.59)	7 (87.50)	1 (100.0)
RD	54 (46.55)	3 (37.50)	0 (0.00)
AMX	96 (82.76)	7 (87.50)	1 (100.0)
NB	99 (85.34)	6 (75.00)	1 (100.0)
CH	68 (58.62)	5 (62.50)	0 (0.00)
E	65 (56.03)	4 (50.00)	1 (100.0)
LEV	14 (12.07)	3 (37.50)	0 (0.00)
CAZ	92 (79.31)	5 (62.50)	1 (100.0)
CTX	98 (84.48)	7 (87.50)	1 (100.0)
CRO	76 (65.52)	5 (62.50)	1 (100.0)
MEM	40 (34.48)	6 (75.00)	1 (100.0)
ETP	72 (62.07)	6 (75.00)	1 (100.0)
ATM	66 (56.90)	7 (87.50)	1 (100.0)

Key: CPX= Ciprofloxacin, OFX= Ofloxacin, PEF= Pefloxacin, NA= Nalidixic acid. NB= Norfloxacin, LEV= Levofloxacin, PN= Ampicillin, CEP= Ceporexlin, AMX= Amoxicillin, AU= Augmentin, CAZ= Ceftazidime,CTX= Cefotaxime, CRO= Ceftriazone, APX= Ampiclox, CN= Gentamicin, S= Streptomycin, SXT= Cotrimoxazole,RD= Rifampicin, CH= Chloramphenicol, E= Erythromycin, MEM= Meropenem, ETP= Etapenem, ATM= Aztreonam

Table 4: Rate of Distribution of MDR *Proteus* Spp. Isolated from Patients Attending Selected Hospitals in the Study Area.

<i>Proteus</i> spp	Hospital (%)						Total (%)
	SSH-M	FMC-Y	SSH-D	ATBUTH	FMC-G	FMC-J	
<i>P. mirabilis</i>	23(18.40)	15(12.0)	22(17.6)	15(12.00)	23(18.40)	18(14.4)	116(92.80)
<i>P. vulgaris</i>	2 (1.60)	2 (1.60)	0(0.00)	2(1.60)	1(0.80)	1 (0.80)	8(6.40)
<i>P. Penneri</i>	1 (0.80)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1(0.80)
Total (%)	26(20.60)	17(13.60)	22(17.6)	17(13.60)	24(19.20)	19(15.20)	125(100)

Key: ATBU-TH= Abubakar Tafawa Balewa Teaching Hospital, Bauchi. SSH-M=State Specialist Hospital, Maiduguri, FMC-Y= Federal Medical Centre, Yola, SSH-D =State Specialist Hospital, Damaturu, FMC-J= Federal Medical Centre, Jalingo, FMC-G= Federal Medical Centre, Gombe.

Table 5: Frequency of the Distribution of Multi-drug Resistance *Proteus* Isolates in Relation to Age of Patients Examined in the Study Area

Age Group (years)	<i>Proteus</i> pp Isolated (%)	MDR <i>Proteus</i> spp (%)
0-10	18 (12.5)	14 (9.72)
11-20	16 (11.11)	13 (9.03)
21-30	27 (18.75)	25 (17.36)
31-40	30 (20.83)	27 (18.75)
41-50	26 (18.06)	22 (15.28)
51-60	14 (9.72)	13 (9.03)
>60	13 (9.03)	11 (7.64)
Total (%)	144 (100)	125 (86.81)

Table 6: Distribution Rate of Multiple Antibiotic Resistance (MAR) and Multiple Resistance Indices of *Proteus* Spp

Number of Antimicrobial Agent to which Isolates are Resistance.	Number of Isolates with MAR	MAR Indices
Three	2	0.13
Four	2	0.17
Five	3	0.22
Six	5	0.26
Seven	6	0.30
Eight	6	0.35
Nine	6	0.39
Ten	10	0.43
Eleven	7	0.48
Twelve	13	0.52
Thirteen	10	0.52
Fourteen	12	0.61
Fifteen	6	0.65
Sixteen	3	0.70
Seventeen	12	0.74
Eighteen	8	0.78
Nineteen	10	0.83
Twenty	5	0.87
Twenty-one	4	0.90
Twenty-two	2	0.96
Twenty-three	0.0	0.0

$$\text{MAR Index} = \frac{\text{Number of Antimicrobial Agent Isolates is Resistant to}}{\text{Number of Antimicrobial Agents Tested (ie. 23)}}$$

DISCUSSION

Proteus spp. is ranked third among gram negative bacteria isolated in hospital environment, and a leading cause of nosocomial infections responsible for high morbidity and mortality worldwide. In this study, 1500 clinical samples were examined for pathogenic *Proteus* spp., where 144 yielded bacterial growth, which translates to a prevalence rate of 9.6%. This is similar to the results reported by Feglo *et al.* (2010), and Tom *et al.* (2018). A much higher prevalence of 18.42% and 28.75% was reported by Yusha'u *et al.* (2010) and Jabur *et al.* (2013) respectively.

In this study, higher *Proteus* infections was observed among male patients (56.25%) compared to female patients (43.75%). However, the difference in gender in relation to the distribution of *Proteus* infections was statistically not significant ($p > 0.01$). Bashwan and Shafey, (2013) and Tom *et al.* (2018) affirmed that males are more vulnerable than females in acquiring *Proteus* infections. This is most likely due to the fact that male exposure to predisposing risk factors such as poor sanitations, weak immune system due to stress, delayed demand for medical attention and high tendency of drugs misuse and abuse is greater.

Proteus species are highly ubiquitous and are mostly associated with infections in different anatomical sites. This is likely attributed to its intrinsic resistance nature, ability to acquire resistance from environment and diverse nutritional choices. In this study, the most predominant *Proteus* species observed was *Proteus mirabilis* with (90.97%) followed by *Proteus vulgaris* (8.33%) and the least was *Proteus Penneri* (0.69%). This is in agreement with the results of Feglo *et al.* (2010), who affirmed that *P. mirabilis* was the most common species isolated, accounting for 61.5 % of all the infections and hence responsible for the majority of *Proteus* infections. Additionally, Gillespie

and Hawkey, (2006), reported that *Proteus vulgaris* and *P. Penneri* cause a wide range of infections similar to *P. mirabilis* but are by far not very common in occurrence (Gillespie and Hawkey, 2006).

The distribution of *Proteus* spp based on sample type revealed that Wounds recorded highest yield followed by Urine and the least was Diarrheic stool samples. The observation that highest yield of *Proteus* spp. was among patients with wound infection is in agreement with the findings of Yah *et al.* (2007) in Nigeria, Newman *et al.* (2006) and Feglo *et al.* (2010) in Ghana, Bashwan and Shafey (2013) in Saudi Arabia, Pandey *et al.* 2013 in India but differ with that of Reslinski *et al.* (2005). Most wounds occurring impromptu, that is sudden unplanned for which promotes multiple invasions by pathogenic bacteria due to damage to the skin and bleeding, and can induce immune suppression (Nayak *et al.*, 2014; Glasser *et al.*, 2010). This makes the wounds a perfect avenue for the colonization and proliferation of opportunistic *Proteus* spp. In this study, Urinary tract infection (UTI) was the second most widespread infection accounting for 15.28% of *Proteus* spp. High prevalence of *Proteus* spp, as an agent of Urinary tract infection (UTI) was also acknowledged by Okon *et al.* (2014) and Chedi *et al.* (2009) in a study conducted in Nigeria and they concluded that, UTI is a common clinical episode seen within the hospital and community setting but the rate of occurrence varies from one community to other and one hospital settings to another.

Proteus spp. also recorded a high degree of isolation from Ear swab samples in this study. This is similar to the report of Feglo *et al.*, (2010) from Ghana. *Proteus* spp. are among the most common microorganisms found in Chronic suppurative otitis media (CSOM) alongside *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Aspergillus spp* and *Candida spp*. The pathology involves a perforation on the tympanic membrane and

active bacterial infection within the middle ear space for several weeks or more, but these organisms vary across different geographical areas (Umar *et al.*, 2016). Other samples with lesser degree of occurrence of pathogenic *Proteus* spp includes, Catheter tip, Genital swab, Sputum, and Body fluid. Common properties of *Proteus* spp involved in the infection process include adhesion to epithelial surfaces, invasion (penetration) of host cells, intracellular multiplication of the pathogen, colonization of the cell tissue or transmission to a new susceptible host. Other features are production of enzymes which damage the host defence system, and synthesis of toxins (hemolysins and endotoxin) (Johnson, 1991; Hacker and Goebel 1987), which act individually or in concert during infection.

The antimicrobial susceptibility tests generally revealed that Levofloxacin and Ciprofloxacin was the most effective antibiotic against *Proteus* spp. This is followed by Meropenem and Ofloxacin. Similar observation was made by Tom *et al.* (2018), but contrary finding was reported by Senthamarai *et al.* (2015), who reported moderate sensitivity to Quinolones although their isolates were highly sensitive to Carbapenems. Those that gave moderate or intermediate antimicrobial sensitivity include Rifampicin, Streptomycin and Pefloxacin. The *Proteus* species isolated were found to have higher antimicrobial resistance against Ampicillin, Nalidixic acid, Cefotaxime, Ceporex and Amoxicillin, Norfloxacin, Ceftazidime, Ampiclox, Augumentin and Ceftriazone. Others that were moderately resistant include: Ertapenem, Aztreonam, Gentamicin, Chloramphenical, Erythromycin and Cotrimoxazole. The difference in the *Proteus* species resistant rates may be related to the selective pressure due to misuse of antimicrobials and their distribution in the various environments, from which the infection could be acquired.

In this study, the analysis of multidrug resistance among the three species of *Proteus* isolated showed that *P. Penneri* exhibited the maximum MDR followed by *P. mirabilis* and *P. vulgaris* the least. Multidrug resistant *Proteus Penneri* isolates displayed resistance to all the beta-lactam antibiotics tested (100%). There have been several reports of production of extended spectrum beta-lactamases (ESBLs) by *Proteus* spp. (Bradford, 2001; Dhillon and Clark, 2011). The ESBLs can confer resistance to Penicillins, third generation Cephalosporins such as Cefotaxime, Ceftriaxone and Ceftazidime, as well as the Monobactam, Aztreonam (Bhattacharya *et al.*, 2013; Philippon *et al.*, 2002). Tumbarello *et al.* (2012) established that recent history of contact with the health care system and/or therapy with fluoroquinolones or oxyiminocephalosporins by patients infected with *P. mirabilis* increases the possibility that the isolate will prove to be MDR trait. The distribution of MDR strains of *Proteus* spp among the selected Hospitals shows that SSH, Maiduguri had the highest percentage of MDR strains followed by FMC, Gombe and SSH, Damaturu. Distribution of MDR strains across the various Hospitals was statistically not significant ($p < 0.01$). Patients within the age group of 31-40yrs had the highest number of multidrug resistant isolates followed by those within 21-30yrs, while the least was observed among patients in the age group of >60yrs. Adolescents and active adults form the bulk of labour force with limited time to visit health care centres, and have a higher tendency of patronizing over the counter drug and in some cases from roadside hawkers which can results to abuse and misuse of drugs which invariably can leads to multidrug resistance (Yusha'u *et al.*, 2009).

In this study, Multiple Antibiotic Resistance (MAR) index was used to determine the combined resistance shown by isolates to more than two antibiotics (Ngwai *et al.*,

2011; Ajayi *et al.*, 2011; Isibor and Uwabor, 2015). It can be seen that MAR was present in almost all the isolates, with the MAR index ranging from 0.13 to 0.96. Two isolates were resistant to 22 of the 23 antibiotics tested. These isolates can be described as Pandrug resistant isolates. Krumperman, (1983) observed, that isolates that demonstrate a MAR index above 0.2 indicate that such isolates originate from an environment where antimicrobial agents are freely available and accessible with high potential for abuse. In developed countries antibiotic stewardship programs are becoming more commonplace in hospital settings and have been correlated in many cases to significant reductions in the emergence of resistant bacteria (Yong *et al.*, 2010; Fishman, 2006; Carling *et al.*, 2003). This is largely a problem in majority of developing countries like Nigeria.

CONCLUSION

The study establishes the dissemination of *Proteus* associated nosocomial infections in the region, as *Proteus* infections occurring in all the Hospitals studied, and the specie most

implicated in the etiology of *Proteus*-implicated nosocomial infection is *Proteus mirabilis* (92.80%). The study also revealed a high prevalence of multidrug resistance among *Proteus* species in the region as MDR ranges from 66.67-100%. Species identification, surveillance and study of the epidemiology of antimicrobial resistance to monitor the pattern and dynamics of spread is important, this will assist in the effective therapeutic management of patients by reducing the prescription of large spectrum of antibiotics for the treatment and control of infections.

CONSENT

All authors declare that informed consent was obtained from the patients (or other approved parties) for sample and data collection.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX

Biochemical Test that Differentiate between Human Pathogenic *Proteus* Species

Test	Proteus Specie		
	<i>P. mirabilis</i>	<i>P. vulgaris</i>	<i>P. penneri</i>
Indole	-ve	+ve	-ve
Methyl red	+ve	+ve	+ve
Citrate	Slow +ve	-ve	Slow +ve
Voges-Proskauer	d	-ve	-ve
Maltose	-ve	+ve	+ve
ODC	+ve	-ve	-ve

Key: +VE =Present; -VE =Absent, ODC = Ornithine Decarboxylase, D = Different Strains Give Different Results.