Prevalenceand Antibiotic Susceptibility Profileof UropathogenicESBL-Producing *Klebsiella pneumonia* in Keffi Metropolis.

ABSTRACT

Antibiotic resistance is a rising dilemma of significant implications on global public health. Few data exist for the prevalence and trends of *Klebsiella pneumonia* antibiotic resistance in Keffi metropolis.

Aim: This study was carried out to determine the prevalence and antibiotic susceptibility pattern of uropathogenic*K.pneumonia* in Keffi.

Study Design: The study was a cross-sectional study by collecting random urine samples from concenting participants

Place and Duration of Study: The study was carried out in Keffi local Government located 128 km from Lafia, the capital of Nasarawa Stateand about 50 km from abuja the Federal Capital of Nigeria. The study was conducted from July to October 2024.

Methodology: A total of 160 early morning urine samples were randomly collected from consenting participants in the six selected hospitals. Isolation and identification of *K. pneumoniae* was done using standard microbiological methods. The antibiotic susceptibility profile of isolates was carried out using the Kirby-Bauer disc diffusion method and interpretation was done following the Clinical and Laboratory Standards Institute protocol. Results obtained in this study were analysed using Smith's Statistical Package (version 2.8, California, USA) and *P*value of ≤ 0.05 was considered statistically significant.

Results: The result of this study revealed an overall prevalence of 20/160 (12.5%). The highest prevalence of the isolate was seen in females 14(8.75)compared to males 6 (3.75%), while the highest prevance regarding age was recorded among the 15-34 age group 12(7.5%) while the

least was recorded among those greater than 65 years 0 (0%). Furthermore, the highest number of isolate was recorded at FMCK 7 (4.4%) followed jointly by GHK and PHCTK 4 (2.5%) with PHC, KP and PHC AJ 1 (0.63%) beign the least respectively. There was a high level of resistance to ceftazidime 20 (100%), followed jointly by ceftriaxone, cefurexime and treptomycin 19 (95%) and augmentin 18 (90%) but low to amoxicillin 6 (30%) and ofloxacin 6 (30%) respectively. Mostof the isolates tested were multidrug resistant and all were extended spectrum beta lactamase (ESBL) producing

Conclusion: The relatively high detection rate of multidrug resistant uropathogenic*K. pneumonia* in this study is worrisom. More worrisom is the isolation from primary health care centers(PHCs) signifying the importance of universal health coverage and the place of PHCs in antimicrobial stewardship (AMS) programs as one of the strategies to control the spread of antimocrobial resistance.

Key Words: Urinary tract infection; *K. pneumoniae*; Antibiotic susceptibility; Primary health care; Keffi.

1.0 INTRODUCTION

The human gastrointestinal tract harbours Enterobacteriaceae which are a group of bacteria also referred to as commensals. Their presence renders few benefits to the host as long as they do not acquire virulent traits from invading pathogens in the environment**[1]**.When they are found at different anatomical sites however, they can become virulent causing varying serious infections which include urinary tract infections (UTIs), sepsis, meningitis, and soft tissue infections depending on their loads and host´s immune system [2].*Klebsiella pneumoniae* is one of such opportunistic bacterial pathogens that is mostly implicated in nosocomial and community-acquired infections such as meningitis, septicaemia, wound infection, pneumonia, and urinary tract infections (UTIs). Millions of people of all ages and gender across the world are affected by

urinary tract infections and constitute one of the most common encountered conditions in the emergency unit in hospitals [3,4].Urinary tract infection especially hospital acquired, are common and contribute to severe morbidity and high fatality rate in patients if not properly diagnosed and treated promptly. Patients who undergo instrumentation of the urinary tract including passing of catheter are more at risk [5,6]. The proximity and physiology of the female urethra to the opening of the intestinal tract contributes to the fact that UTIs are more frequently reported in women than in men [7]. Antibiotic resistance in health care facilities and indeed the general population is an increasingly worrying public health trend. One of the mechanisms by which Gram-negative bacteria acquire resistance to beta-lactam antibiotics is the production of beta-lactamase enzymes[8]. Plasmid-mediated enzymes known as the extended-spectrum β-lactamases (ESBLs) are able to hydrolyze and inactivate broad spectrum β-lactam antimicrobials namely: third-generation cephalosporins, penicillins and aztreonam but are inhibited by clavulanic acid.

Extended spectrum beta-lactamases are commonly found in *Klebsiella* species and *E. coli*, but have been described in other members of the Enterobacteriaceae such as Enterobacter, Serratia, Citrobacter, Proteus and Salmonella. Urinary tract infection is one of the commonest infections globally and is responsible for frequent hospital visits especially among females with an incidence of 50 to 60%. This is especially common among young sexually active females [9]. Patients who are admitted in the hospital are predisposed to UTI caused by Gram-negative bacteria such as *Klebsiella*, *E. coli*, *Proteus* and *Pseudomonas* [10]. In Nasarawa State, a prevalence ranging from 10% to 12.78% have been reported [11,12,13], while a prevalence of 8.0% to 37.0% have been reported in other parts of the country [14,15, 16, 17,18,19]. Antibiotic resistance is on the rise globally due to inappropriate use and the emergence of resistant bacteria,

this among other factors complicates the treatment of UTIs [20]. The access to health or universal health coverage as defined by the World Health Organization is the access by all people to the health services they need, when and where they need them of sufficient quality to be effective, without financial hardship. This covers essential health services, from health promotion to prevention, treatment, rehabilitation, and palliative care across the life course [21]. Primary health care (PHC) refers to a broad range of health services provided by medical professionals in the community. This means universal health care is accessible to all individuals and families in a community [22].The primary health care (PHC) facilities are domicilled in all the LGAs as the point of entry into the health care system for the community, rendering preventive, curative, promotive, and pre-referral care services. Laboratory services are however restricted to certain test which does not include culture and sesitivity [23]. Overprescribing by health care professionals, rising incomes, high background rates of infectious diseases and easy, over-the-counter access to antibiotics, driven in part by lack of access to good-quality primary care, are exacerbating the problem of resistance in low-and middle-income countries. Low-income countries are particularly vulnerable because the second-line antibiotics needed to combat the most resistant infections are often unaffordable [24]. The the importance of primary care in the war against antimicrobial resistance can not be overemphasized, given the growing threat of antimicrobial resistance [25]. Literatures have shown that optimising antimicrobial use through functional hospital antimicrobial stewardship (AMS) programs is one of the strategies to control the spread of AMR [26,27]. This study seeks to contribute to the understanding of thethe prevalence ofantibiotic resistance associated with*K. pneumoniae* isolated from patients with UTIs in the study area. Furthermore, data obtained in this study will inform the development of

effective diagnostic and therapeutic strategies for managing*K. pneumoniae* infectionsin Keffi, ultimately improving patient outcomes and reducing the global burden of antibiotic resistance.

2. Materials and Methods

2.1 Study Design and Population

The investigation was a cross-sectional study which utilized random sampling of patients from four hospitals in Keffi from July to October 2024.

2.2 Study Area

Keffi is located approximately 50 km from Abuja, the Federal Capital Territory and 128 km from Lafia, the capital of Nasarawa State. It is located geographically between latitude $8^0$3'N of the equator and longitude $7^0$50'E and situated at an altitude of 850m above sea level [28]

2.3 Sample Size Determination

A total of 160 samples was estimated using the formula described by Sapra [29]

$$N = \frac{Z^2pq}{D^2}$$

Where; N=sample size,

Z= standard normal distribution at 95% confidence interval=1.96,

P= prevalence rate of *K. pneumoniae* infection from previous studies = 10.13%[11].

d = level of significance (allowable error) = 5% or 0.05

q= 1-p

Thus, N= $(1.96)^2 \times 0.1013 \times (1-0.1013)/ (0.05)^2 = 3.8416 \times 0.1013 \times 0.8987 /0.0025 =$ 139.893109≈ 140

N= 140

However, actual sample size= Calculated sample size + 10% Attrition rate. But 10% Attrition rate = 14

Therefore, actual sample size = 140 + 14= 154

However, to increase chances of isolation, it was rounded up to 160 samples.

2.4 Inclusion and Exclusion Criteria

Patients of all age group and gender with suspected UTI assessing healthcare in the selected health facilities were included in this study. While those with suspected UTIs but on antibiotics attending the selected health facilities were excluded from this study.

2. 5 Ethical Consideration

Ethical clearance for this research was obtained from the Nasarawa State Ministry of Health (NHREC Protocol number: 18/06/2017) in line with the Declaration of Helsinki on the conduct of biomedical research involving human subjects. All participants gave their consent to participate in the study.

2.6 Sample Collection

A total of 160 early morning mid-stream urine samples of patients with suspected cases of UTI were collected from six hospitals in the study area designated: Federal Medical Centre Keffi (FMCK), General Hospital Keffi (GHK), Primary Health Centre Angwan Waje (PHC AW), Primary Health Centre Kofar Pada (PHC KP), Primary Health Centre TsohonKasuwa (PHC TK), Primary Health Centre Angwan Jaba (PHC AJ) using sterile sample containers and transported to the Microbiology Laboratory of Federal Medical Centre Keffi for analysis. The socio-demographic and clinical data for each patient were obtained through a structured questionnaire.

2.6.1 Isolation of *Klebsiella pneumonia*

Urine samples were mixed gently by inverting the containers several times. Using a sterile wire loop, the samples were streaked on Cysteine Lactose electrolyte-deficient agar (CLED) agar and incubated at 37˚C for 24 hours. Yellowish colonies from the 24 hours plates were selected as presumptive K. pneumoniae [30,31].

2.6.2 Identification of *Klebsiella pneumonia*

Identification of *K. pneumonia* isolates was done by cultural, morphological, biochemical and motility testingfollowing standard procedures [32,33]

2.7 Antibiotic Susceptibility Testing

The susceptibility profile of antibiotics commonly prescribed for *K. pneumoniae*infections was determined using Kirby-Bauer disc diffusion method in accordance with CLSI guidelines [34].The antimicrobial agents tested included: Ofloxacin (10µg), Augmentin (30 µg), Ceftazidime (30 µg), Gentamycin (10 µg), Ciprofloxacin (10 µg), Chloramphenicol (30 µg), Ceftriaxone (30 µg), Streptomycin (30 µg), Cefurexime(30 µg), and Amoxicillin (30 µg).

2. 7 Data Analysis

The data obtained were analyzed using Smith's Statistical Package (version 2.8, California, USA). Chi-square test was conducted at 95% confidence interval and P values ≤ 0.05 were considered statistically significant.

3.0 Results

3.1 Distribution of *K. pneumoniae* Isolates Regarding Some Sociodemographic Variables

In the current study, 20 (12.5%) out of the 160 urine samples collected were positive for *K. Pneumonia.* The distribution of infection on the basis of gender revealed that females had higher 14(8.75%) compared to males6(3.75%) P=0.789. On the basis of age group, the highest prevalence was recorded among those within 15-34 age group 12 (7.5%), followed by 35-64 age group 5(3.13%)and those aged less than 14 years 3 (1.87%) with the least seen among those greater than 60 years 0 (%) P=0.100. The prevalence regarding marital status was found to be higher among the singles 12 (7.5%), followed by married 5 (3.12%)while the least was among those divorced 2 (1.25%) and widowed 1 (1.25%) P= 0.035.Furthermore, the prevalence regarding occupation was found to be higher among the unemployed 7 (4.37%)followed by students 5 (3.13%), and the self employed 4 (2.5%) while it was lower among the civil servants and privately employed 2 (1.25%) respectively P= 0.021 as shown in Table 1.

Table 1 Distribution of *K. pneumoniae* Isolates Regarding Some Sociodemographic Variables

Age	Number examined (%)	Number of Isolates (%)	*P* value
< 14	26(16.25)	3(1.87)	
15-34	113(70.62)	12(7.5)	0.100
35-64	16(10.00)	5(3.13)	
≥ 65	5 (3.13)	0(0)	
Total	160(100)	20(12.5)	
Gender			
Male	44(27.5)	6(3.75)	
Female	116(72.5)	14(8.75)	0.789
Total	160(100)	20(12.5)	
Marital staus			

Married	48(30)	5(3.12)	
Divorced	37(23.1)	2(1.25)	0.035
Widowed	23(14.4)	1(0.63)	
Single	52(32.5)	12(7.5)	
Total	160(100)	20(12.5)	
Ocupation			
Student	54(33.75)	5(3.13)	
Self employed	41(25.63)	4(2.5)	0.021
Civil servant	33(20.62)	2(1.25)	
Unemployed	20(12.5)	7(4.37)	
Private employed	12(7.5)	2(1.25)	
	160(100)	20(12.5)	

3.2 Prevalence of *K. pneumoniae* Isolates Regarding Some Clinical Signs and Symptoms

Of the 160 participants, 25(15.6%) experienced painful urination, 12(7.5%) experienced frequent urination, 31(19.37%) experienced burning sensation, 16(10.0%) experienced itching, 23(14.4%) had lower abdominal pain, 13(8.13%) had dicharge, 18(11.3%) urine had fishy smell, and 22(13.7%) had fever. Those that experienced painfull urination and those that had discharge jointly had a prevalence of 4(2.5%) respectively, followed by those who experienced burning sensation while urinating, lower abdominal pain and those who had fever 3(1.87%) respectively, 2(1.25%) for those who urinated frequently, while the least was recorded among those whose urine had a fishy smell 1(0.63%). *K. pneumonia* was not isolated in the urine of those that experienced itching 0(0.0%) P= 0.353 as shown in Table 2.

Table 2Prevalence of *K. pneumoniae* Isolates Regarding Some Clinical Signs and Symptoms

Variable	Number examined (%)	Number positive (%)	*P* value
Painful urination	25(15.6)	4(2.5)	
Frequent urination	12(7.5)	2(1.25)	0.353
Burning sensation	31(19.37)	3(1.87)	
Itching	16(10.0)	0(0)	
Lower abdominal pain	23(14.4)	3(1.87)	
Discharge	13(8.13)	4(2.5)	
Fishy smell	18(11.3)	1(0.63)	
Fever	22(13.7)	3(1.87)	
Total	160(100)	20(12.5)	

3.3. Antimicrobial Resistance Profile of the Urinary *Klebsiella pneumoniae* Isolated in Selected Hospitals of Keffi.

The antibiotic resistance profile of the *K. pneumoniae* isolates is represented in Table 5, where a significantly high 20(100%) resistance to ceftazidime was recorded, closely followed by ceftriaxone 19(95%), streptomycin 19(95%), cefurexime 19(95%) and augmentin 18(90%),

chloramphenicol 17(85%). While the least resistance was recorded for ciprofloxacin 8(20%), amoxicillin 6(30%) and ofloxacin 6(30%) P=0.000.

Table 3. Antimicrobial Resistance Profile of the Urinary Klebsiella pneumoniae Isolated in Selected Hospitals of Keffi, Nasarawa State, Nigeria.

Antimicrobial Agent	Disc Content (µg)	Number of tested isolates	Sensitive Number (%)	Resistance Number (%)	*P*. value
Ofloxacin(OFX)	10	20	14(70)	6(30)	
Augmentin (AU)	30	20	2(10)	18(90)	0.000
Ceftazidime (CTZ)	30	20	0()	20(100)	
Gentamycin (CN)	10	20	9(45)	11(55)	
Ciprofloxacin (CPX)	10	20	12(60)	8(20)	
Chloramphenicol (CH)	30	20	3(15)	17(85)	
Ceftriaxone (TRX)	30	20	1(5)	19(95)	
Streptomycin (S)	30	20	1(5)	19(95)	
Cefuroxime (CEF)	30	20	1(5)	19(95)	
Amoxicillin (AM)	30	20	14(70)	6(30)	

3.4. Multidrug Resistance Pattern of the Urinary *Klebsiella pnuemoniae* Isolated from Selected Hospitals of Keffi.

Different antimicrobial resistance combinations (Multidrug) by the isolate were recorded as represented in Table 4. The highest multidrug profile was AM, AU, CEF, CH, CN, CPX, CTZ, OFX, S, TRX 6(30%), followed by AU, CEF, CH, CTZ, S, TRX 5(25%), AU, CEF, CH, CTZ, S, TRX 4(20%) and AU, CEF ,CTZ, S, TRX 2(10%), while the least was CTZ 1(5%) AU, CEF, CH,CTZ, OFX, S, TRX 1(5%) and AU, CEF, CH, CN, CPX, CTZ, S, TRX 1(5%) respectively (P=0.89).

Table 4. Multidrug Resistance Pattern of the Urinary *Klebsiella pnuemoniae* Isolated from Selected Hospitals of Keffi, Nasarawa State, Nigeria.

Antibiotic resistance types	*K .pnuemoniae* isolates Number (%)	P value
CTZ	1(5)	$X^2 = 10.967$

AU, CEF ,CTZ, S, TRX	2(10)	P = 0.89
AU, CEF, CH, CTZ, S, TRX	4(20)	
AU, CEF, CH, CN, CTZ, S, TRX	5(25)	
AU, CEF, CH,CTZ, OFX, S, TRX	1(5)	
AU, CEF, CH, CN, CPX, CTZ, S, TRX	1(5)	
AM, AU, CEF, CH, CN, CPX, CTZ, OFX, S, TRX	6(30)	
Total	20(100)	

Key: AM= Aoxycillin, AU= Augmentin, CEF= Cefurexime, CH= Chloramphenicol, CN= Gentamycin, CPX= Ciprofloxacin, CTZ= Ceftazidime, OFX= Ofloxacin, S= Streptomycin, TRX= Cefriaxone

3.5 Phenotypic Detection of ESBL-Producing *K. pneumonia*

Out of the 20 positive isolates, 16 were found to be ESBL producing after screening using the phenotypic confirmatory disc difusion test,P=0.000, while 15 turned out to be ESBL producing *K.pneumoniae* after the double disc synergy test as seen in Table 5. FMCK recorded the highest ESBL producers 7(46.6%) followed by GHK 3(20.0%), PHC AW 2(13.3%) while the least was recorded from PHC KP, PHC AJ and PHC TK 1(6.7%) respectively P= 0.464.

Table 5 Phenotypic Detection of ESBL-Producing *K. pneumonia*

Facility	No. Resistant	PCDDT			DDST		
		ESBL Pos. (%)	ESBL Neg.	*P* value	ESBL Pos (%)	ESBL Neg	*P* value
FMCK	7	7(43.75)	0		7(46.6)	0	
GHK	3	3(18.75)	0	0.000	3(20.0)	0	0.464
PHC AW	3	3(18.75)	0		2(13.3)	1	
PHC KP	1	1(6.25)	0		1(6.7)	0	
PHC AJ	1	1(6.25)	0		1(6.7)	0	
PHC TK	1	1(6.25)	0		1(6.7)	0	
Total	16	16(100)	0		15(100)	1	

Key: FMCK= Federal Medical Centre Keffi, GHK= General Hospital Keffi, PHC AW= Primary Healthcare Clinic Angwan Waje, PHC KP= Primary Healthcare Clinic Kofar Pada, PHC AJ= Primary Healthcare Clinic Angwan Jamaa, PHC TK= Primary Healthcare Clinic TsohonKasuwa, ESBL= Extended spectrum betaLactamase, PCDDT= Phenotypic Confirmatory disc difusion test,DDST= Double disc synergy test.

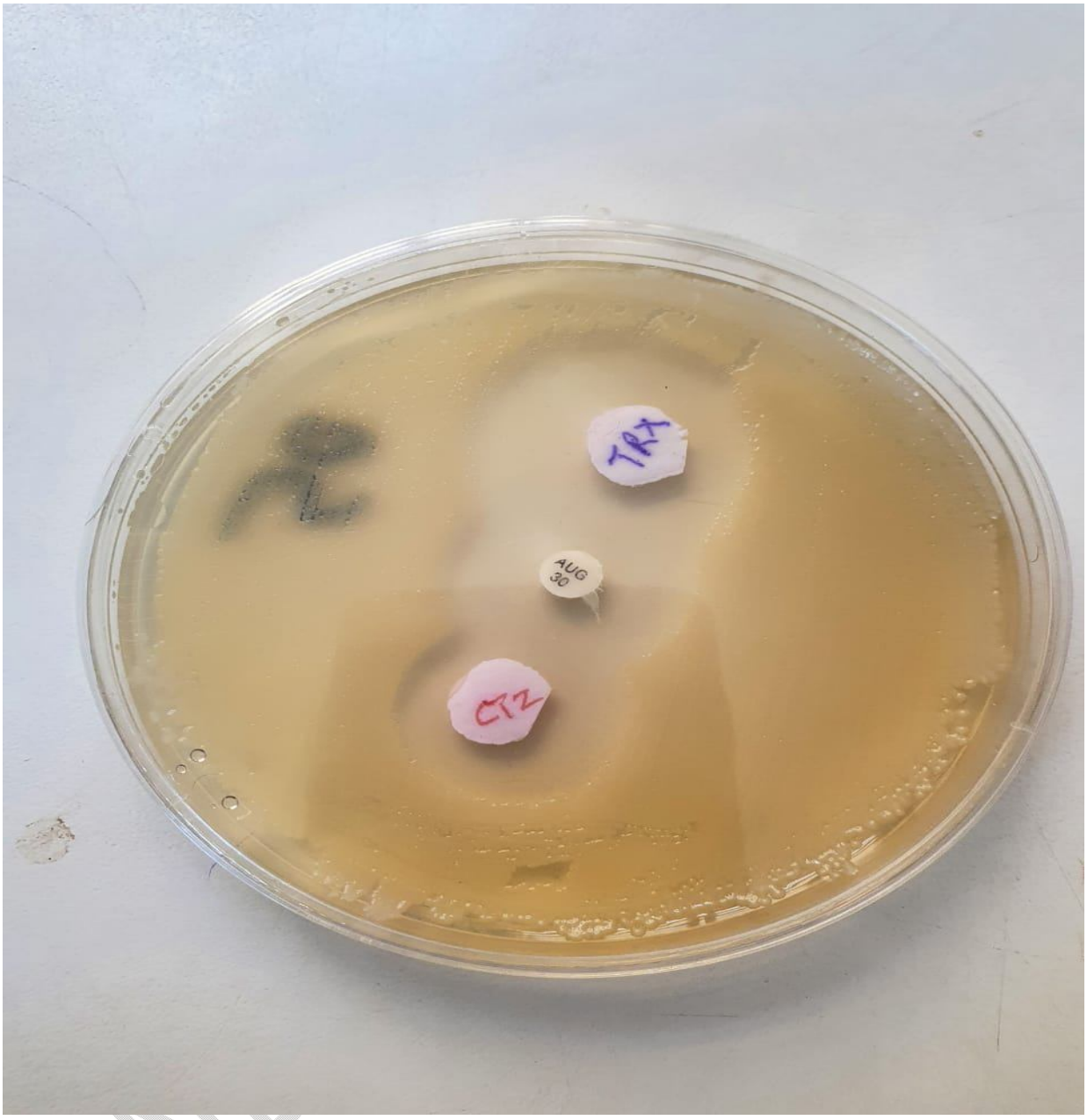

Plate 1 Showing Positive Disc Difusion Synergy Test

4.0 Discussion

Urinary tract infections (UTIs) are among the most encountered bacterial in fection of humans that affect both gender of all age groups. If not managed properly, it can result in high mortality of infected patients [36]. *K pneumonia* has been reported to be an important pathogen commonly associated with UTI [37]. Historically, *K. pneumoniae* have been associated with infections in patients that have compromised immuninity. With the recent appearance and dissemination of hypervirulent strains however, healthy individuals have also become susceptible to infection [2, 45]. In this study, out of 160 urine samples collected from patients with UTI in the selected hospitals in Keffi metropolis for the detection and molecular characterization of *K. pneumoniae*, an overall prevalence of 12.5% was recorded. FMCK recorded the highest 7(4.4%) followed jointly by GHK and PHC TK 4(2.5%) and PHC AW 3(1.9%), whereas the least was detected in PHC KP and PHC TK 1(0.63%) respectively though there was no statistical significance (P = 0.509).

The prevalence of 12.5% obtained in this study is higher than 10.13% reported by [11] in Nasarawa South senatorial district. Similarly, it was higher than 8.0% reported by [38] among HIV clients in Ethiopia, 8.5% reported in the Gambia by [38], 8.7% reported by [40] in Somaliland, 11.6% reported in Uganda by [41]. In Gabon, a low prevalence of 11.6% was reported by [42] while 10.3% was reported by [43] in Bahrain. Interestingly, similar prevalence of 12.78% was previously reported in Lafia the capital city of Nasarawa state [43] and [46] in Ethiopia even though this study focused on children. Conversely, higher prevalence have been reported in various parts of Nigeria such as 60% by [47], 16% by [15], 15.8% by [48], 16.4% by [49], 14.0% by [18], 34% by [19], 20.0% by [50], 14.78% by [51], 18.1 % by [52], 23.1% by

[35] and 23.53 % by [53]. Simillary, higher prevalence have been recorded in other parts of Africa and accross other continents [54,55,56,57].

The difference in the prevalence could be attributed to gender, age, duration of hospitalization,the methods employed, sample size, geographic location and level of personal and environmental hygiene [58,59,60].

In this study, the prevalence regarding some sociodemographis was highlighted. Out of the 160 urine samples collected in the selected hospitals, the prevalence of UTI was higher among females 116(72.5%) compared to males 44(27.5%) with no statistical significance P=0.789. Similar prevalence regarding gender have been reported within and outside Nigeria such as [15,39,41,43,47,61,62]. Also, [63] reported a higher prevalence among females compared to males. These diferrences could be as a result of the shorter distance from the urethral opening to the bladder, and the closer proximity of the urethral opening to the bacteria-rich vagina and rectum. For healthy premenopausal females, the risk of both acute cystitis and recurrent UTI is increased with recent or frequent sexual activity, the use of contraceptives and pregnancy [64,65,66].

Regarding the age of the participants, a significant relatinship was observed (P=0.100). Those aged between 15-36 had the highest 113(70.62) prevalence followed by those less than 14 years 26(16.25%) and thse aged between 35-64 years 16(10.0%) while it was least prevalent among those greater than 65 years 5(3.13%). A similar high prevalence was reported by [43,62]. Interestingly, urinary tract infection and asymptomatic bacteriuria are common in older adults. Distinguishing symptomatic urinary tract infection from asymptomatic bacteriuria is problematic unlike in younger adults [67,68].

There was no statistical relationship regarding marital staus even though those who are single had the highest 52(32.5%) followed by those that are married 48(30.0%), those that are divorced 37(23.1%) and the least from those that are widowed 23(14.4%) (P=0.035). Report by [15] is in agreement with our findings as singles presented higher prevalence followed by married, widowed although in their study the least was seen among the divorced. [38] and [49] both reported a diverging prevalence from ours with a higher prevalence among married participants followed by those who were single while [35] and [41] in their respective studies reported higher prevalence among the married participants.

Regarding the participant's occupation, a significant relationship was established in this study where students recorded the highest 54(33.75%) closely followed by the self employed 41(25.63%), civil servants 33(20.62%), the unemployed 20(12.5%) while the least was recorded among those that are private employed 12(7.5%) P=0.021. In a similar study, [15] reported a prevalence of 98% among students, while [35] and [69] reported higher prevalence among students. Overcrowding in hostels, lack of adequate hygiene in latrines necessitated by absence of water could predispose students to easily pick up infection [69].

There was no statistical relationship with regard to clinical symptoms (P= 0.353). Of the 160 participants, 31(19.37%) experienced burning sensation, 25(15.6%) experienced painful urination, 3(14.4%) had lower abdominal pain 12(7.5%) experienced frequent urination, 16(10.0%) experienced itching, , 13(8.13%) had dicharge, 18(11.3%) urine had fishy smell, and 22(13.7%) had fever. Those that experienced painfull urination and those that had discharge jointly had a prevalence of 4(2.5%) respectively, followed by those who experienced burning sensation while urinating, lower abdominal pain and those who had fever 3(1.87%) respectively, 2(1.25%) for those who urinated frequently, while the least was recorded among those whose

urine had a fishy smell 1(0.63%). *K. pneumonia* was not isolated in the urine of those that experienced itching 0(0.0%). [15] reported frequent urination as the most prevalent symtom while the least was abdominal pain, while [35] recorded the highest among clients that had increased frequency of urination. On the contrary, [70] reported dysuria as the common symptom.

The antibiotic resistance was substantially linked with the rate of the *K. pneumoniae* infection (P=0.000). A 20(100%) resistance to ceftazidime was recorded, closely followed by ceftriaxone 19(95%), streptomycin 19(95%), cefurexime 19(95%) augmentin 18(90%) and chloramphenicol 17(85%). While the least resistance was recorded for ciprofloxacin 8(20%), amoxicillin 6(30%) and ofloxacin 6(30%). This is in agreement with the report by [43] where there was high resistance to ceftazidime (38.46%), ceftriaxone (22.73%) and cefurexime (28.57%).In contrast however, [58 reported high susceptibility to ceftazidime 90.3 % and cefotaxime 95.1%. Intrestingly, in other related studies carbapenems exhibit the broadest spectrum of β-lactam antibiotics, and have been shown to present the highest potency against Gram-negative bacteria. Also, they are characterized by stability to hydrolysis by the majority of β-lactamases. Their use in treatment of severe ESBL-producing *K. pneumoniae* infections is associated with improved outcomes in patients and remains the 'gold standard' especially in critically ill patients [71,72,73].

The occurence of multidrug resistant ESBL- producing *K. Pneumonia* was determined using phenotypic and molecular methods. There was no statistical significance with respect to multidrug resistant *K. Pneumonia* isolated in the study area P= 0.89. The occurence6(30%) of multidrug resistant ESBL- producing *K. Pneumonia* in the study area is however worrisome.

Several reports are available on the prevalence of multidrug resistant *K. Pneumoniae* within and outside Nigeria[13,18,19,41,74,7576,77].

4.0 Conclusion

The relatively high prevalence (12.5%) of multidrug resistant uropathogenic*K. pneumonia* isolated in this study is worrisom. More worrisom is the isolation from primary health care centers signifying the importance of universal health coverage and the place of PHCs in antimicrobial stewardship (AMS) programs as one of the strategies to control the spread of antimocrobial resistance.Amoxicillin–Clavulanic acidalong sideceftriaxone and ceftazidime use in the double-disk synergy test for phenotypic confirmatory test for checking carbapenemasesproduction.was a potent and strong predictor for the reliability of phenotypic confirmatory results in Keffi. Overprescribing of antimicrobials by health care professionals, rising incomes, high background rates of infectious diseases and easy over-the-counter access to antibiotics, driven in part by lack of access to good-quality primary care, are exacerbating the problem of resistance in low-and middle-income countries. Low-income countries are particularly vulnerable because the second-line antibiotics needed to combat the most resistant infections are often unaffordable

5.2 Recommendations

1. Carrying out antibiotic susceptibility test before prescription of drugs is highly recommended

2.Continuous monitoring for mechanisms of resistance to a new generation of β-lactam using combined disk test is recommended.

3. Further studies on phenotypic and genotypic detection of of ESBL-producing *K. pneumoniae* and sequencing is recmmended.

CONSENT

Written informed consent was taken from each participant.

ETHICAL APPROVAL

Ethical clearance for this research was obtained from the Nasarawa State Ministry of Health (NHREC Protocol number: 18/06/2017) in line with the Declaration of Helsinki on the conduct of biomedical research involving human subjects.

REFERENCE

[1]. Moreira de Gouveia, M. I., Bernalier-Donadille, A., &Jubelin, G. (2024). *Enterobacteriaceae* in the Human Gut: Dynamics and Ecological Roles in Health and Disease. *Biology*, *13*(3), 142. https://doi.org/10.3390/biology13030142

[2]. Abbas, R., Chakkour, M., Zein El Dine, H., Obaseki, E.F., Obeid, S.T., Jezzini, A., Ghssein, G., & Ezzeddine, Z. (2024). General Overview of *Klebsiella pneumonia*: Epidemiology and the Role of Siderophores in Its Pathogenicity. *Biology*. *13*, 78. https://doi.org/10.3390/biology13020078

[3]. Rønning, T. G., Aas, C. G., Støen, R., Bergh, K., Afset, J. E., Holte, M. S., & Radtke, A. (2019). Investigation of an outbreak caused by antibiotic-susceptible Klebsiella oxytoca in a

neonatal intensive care unit in Norway. *Acta paediatrica (Oslo, Norway : 1992)*, *108*(1), 76–82. https://doi.org/10.1111/apa.14584

[4]. Alrashid, S., Ashoor, R., Alruhaimi, S., Hamed, A., Alzahrani, S., & Al Sayyari, A. (2022). Urinary Tract Infection as the Diagnosis for Admission Through the Emergency Department: Its Prevalence, Seasonality, Diagnostic Methods, and Diagnostic Decisions. *Cureus*, *14*(8), e27808. https://doi.org/10.7759/cureus.27808

[5]. Gorrie, C.L., Mirčeta, M., Wick, R.R., Judd, L.M., Lam, M., Gomi, R., Abbott, I.J., Thomson, N.R., Strugnell, R.A., Pratt, N.F., &Garlick, J.S. (2022). Genomic dissection of *Klebsiella pneumoniae* infections in hospital patients reveals insights into an opportunistic pathogen. *Nature Communications* 13:1–7. https://doi.org/10.1038/s41467-022-30717-6

[6]. Narimisa, N., Goodarzi, F., &Bavari, S. (2022). Prevalence of colistin resistance of *Klebsiella pneumoniae* isolates in Iran: a systematic review and meta-analysis. *Annals of* Clinical Microbiology *and Antimicrobials*21:1–9. https://doi.org/10.1186/s12941-022-00520-8

[7]. Sakamoto, S., Miyazawa, K., Yasui, T., Iguchi, T., Fujita, M., Nishimatsu, H., Masaki, T., Hasegawa, T., Hibi, H., Arakawa, T., Ando, R., Kato, Y., Ishito, N., Yamaguchi, S., Takazawa, R., Tsujihata, M., Taguchi, M., Akakura, K., Hata, A., & Ichikawa, T. (2019). Chronological changes in epidemiological characteristics of lower urinary tract urolithiasis in Japan. *International Journal of Urology: Official Journal of the Japanese Urological Association*, *26*(1), 96–101. https://doi.org/10.1111/iju.13817

[8]. Butt, T., Raza, S., & Butt, E. (2017). Predicament in Detection and Reporting of Extended Spectrum Beta Lactamase Production in Routine Antibiotic Susceptibility Testing. *Journal of the College of Physicians and Surgeons--Pakistan : JCPSP*, *27*(12), 788–790.

[9]. Medina, M., & Castillo-Pino, E. (2019). An introduction to the epidemiology and burden of urinary tract infections. *Therapeutic Advances in Urology*, *11*, 1756287219832172. https://doi.org/10.1177/1756287219832172

[10]. Muhammad, A., Khan, S. N., Ali, N., Rehman, M. U., & Ali, I. (2020). Prevalence and antibiotic susceptibility pattern of uropathogens in outpatients at a tertiary care hospital. *New microbes and new infections*, *36*, 100716. https://doi.org/10.1016/j.nmni.2020.100716

[11]. Ashefo, D. P., Ngwai, Y. B., &Ishaleku, D. (2023) Isolation and Antimicrobial Resistance Phenotype of Klebsiella pneumonia from the Urine of Suspected UTI Patients Attending Public Hospitals in Nasarawa South Senatorial District, Nasarawa State, Nigeria. FUDMA Journal of Sciences. 7 (1), 119 – 125. DOI: https://doi.org/10.33003/fjs-2023-0701-1258

[12]. Ngwai, Y.B., Onehi, L.M., and Tsahyel J. (2023). Molecular detection of carbapenemase resistance in Klebsiella pneumoniae isolated from urine of patients assessing General Hospital in Keffi, Nasarawa state, Nigeria. AROC in Pharmaceutical and Biotechnology. 3(1);01-07, https://doi.org/10.53858/arocpb03010107

[13]. Ashefo, D. P., Ngwai, Y. B., Ishaleku, D., Nkene, I. H., Abimiku, R. H., & Tama, S. C. (2023). Detection of Antimicrobial Susceptibility Pattern and Molecular Detection of Resistance Genes in Klebsiella pneumoniae Isolated from Urine Samples of Suspected UTI Patients Attending Public Hospitals in Nasarawa South Senatorial District, Nasarawa State, Nigeria. *South Asian Journal of Research in Microbiology*, *17*(1), 15–26. https://doi.org/10.9734/sajrm/2023/v17i1319

[14]. Hamza S., Abdulhadi, S. and Kumurya, S. (2016). The Prevalence of Klebsiella Species Causing Urinary Tract Infections in Murtala Muhammad Specialist Hospital, Kano, Nigeria.

American Journal of Biomedical and Life Sciences. 4(2): 11-15. doi: 10.11648/j.ajbls.20160402.11

[15]. Mike-Ogburia, M., Monsi, T. &Nwokah, E. (2023) Prevalence and Associated Risk Factors of Uropathogenic *Klebsiella* Species in Port Harcourt. *Advances in Infectious Diseases*, 13, 333-353. doi: 10.4236/aid.2023.132030

[16]. Chinyere, E. L., Nura, S. M., Ahmad, G. M., Kemi, A. F., & Sani, M. N. (2020). Prevalence and molecular analyses of extended spectrum β-lactamase producing uropathogens among pregnant women, Jigawa state, Nigeria. *J Clin Microbiol Biochem Technol*, *6*(1), 033-038.

[17]. Onanuga, A., & Selekere, T. L. (2016). Virulence and antimicrobial resistance of common urinary bacteria from asymptomatic students of Niger Delta University, Amassoma, Bayelsa State, Nigeria. *Journal of pharmacy & bioallied sciences*, *8*(1), 29–33. https://doi.org/10.4103/0975-7406.171684

[18]. Mofolorunsho, K. C., Ocheni, H. O., Aminu, R. F., Omatola, C. A., & Olowonibi, O. O. (2021). Prevalence and antimicrobial susceptibility of extended-spectrum beta lactamases-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated in selected hospitals of Anyigba, Nigeria. *African health sciences*, *21*(2), 505–512. https://doi.org/10.4314/ahs.v21i2.4

[19]. Akinyemi, K. O., Abegunrin, R. O., Iwalokun, B. A., Fakorede, C. O., Makarewicz, O., Neubauer, H., Pletz, M. W., & Wareth, G. (2021). The Emergence of *Klebsiella pneumoniae* with ReducedSusceptibility Against Third Generation Cephalosporins and Carbapenems in Lagos Hospitals, Nigeria. *Antibiotics (Basel, Switzerland)*, *10*(2), 142. https://doi.org/10.3390/antibiotics10020142

[20]. Antimicrobial Resistance Collaborators (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet (London, England)*, *399*(10325), 629–655. https://doi.org/10.1016/S0140-6736(21)02724-0

[21]. WHO (2023). Universal Health Coverage (UHC).https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc)

[22]. Behera, B. K., Prasad, R., &Shyambhavee (2022). Primary health-care goal and principles. *Healthcare Strategies and Planning for Social Inclusion and Development*, 221–239. https://doi.org/10.1016/B978-0-323-90446-9.00008-3

[23].Obasanya, J. O., Ogunbode, O., & Landu-Adams, V. (2022). An appraisal of the contextual drivers of successful antimicrobial stewardship implementation in Nigerian health care facilities. *Journal of global antimicrobial resistance*, *31*, 141–148. https://doi.org/10.1016/j.jgar.2022.08.007

[24]. World Bank (2017).Drug-resistant infections: a threat to our economic future. Washington DC:https://documents1.worldbank.org/curated/pt/323311493396993758/pdf/final-report.pdf

[25]. WHO.(2018).Technical Series on Primary Healthcare. https://www.who.int/docs/default-source/primary-health-care-conference/amr.pdf

[26]. Garau, J., & Bassetti, M. (2018). Role of pharmacists in antimicrobial stewardship programmes. *International journal of clinical pharmacy*, *40*(5), 948–952. https://doi.org/10.1007/s11096-018-0675-z

[27]. Majumder, M. A. A., Rahman, S., Cohall, D., Bharatha, A., Singh, K., Haque, M., & Gittens-St Hilaire, M. (2020). Antimicrobial Stewardship: Fighting Antimicrobial Resistance and

Protecting Global Public Health. *Infection and drug resistance*, *13*, 4713–4738. https://doi.org/10.2147/IDR.S290835

[28]. Akwa, V.L., Binbol, N.L. Samaila, K.L., Marcus, N.D. (2007). Geographical perspective of Nasarawa State, Onaive Printing and Publishing Company Ltd, Keffi, 503

[29]. Sapra, R.L. (2022). How to Calculate an Adequate Sample Size? In: How to Practice Academic Medicine and Publish from Developing Countries? *Springer, Singapore*. https://doi.org/10.1007/978-981-16-5248-6_9

[30]. Public Health England. UK Standards for Microbiology Investigations. Investigation of urine. B 41 Issue 8.7.https://www.rcpath.org/static/de4a6639-b118-46ea-9d3b8a0be4014944/UK-SMI-B-41i87-January-2019-Investigation-of-urine.pdf

[31]. Karah, N., Rafei, R., Elamin, W., Ghazy, A., Abbara, A., Hamze, M., &Uhlin, B. E. (2020). Guideline for Urine Culture and Biochemical Identification of Bacterial Urinary Pathogens in Low-Resource Settings. *Diagnostics (Basel, Switzerland)*, *10*(10), 832. https://doi.org/10.3390/diagnostics10100832

[32]. Osman, E. A., El-Amin, N., Adrees, E. A. E., Al-Hassan, L., & Mukhtar, M. (2020). Comparing conventional, biochemical and genotypic methods for accurate identification of *Klebsiella pneumoniae* in Sudan. *Access microbiology*, *2*(3),acmi000096. https://doi.org/10.1099/acmi.0.000096

[33]. Sagar, A. (2022). Biochemical test and identification of *Klebsiella pnuemoniae*. https//: www.microbiologyinfo.com/biochemical-test-and-identification-of-klebsiella-pneumoniae/

[34]. Clinical Laboratory Standards Institute (CLSI) (2021) Performance standards for antimicrobial susceptibility testing, 31st ed. https://clsi.org/about/press-releases/clsi-publishes-m100-performance-standards-for-antimicrobial-susceptibility-testing-31st-edition/

[35]. Bassey, E. E., Mbah, M., Akpan, S. S., Ikpi, E. E., &Alaribe, A. A. A. (2024). Prevalence of Symptomatic Significant Bacteriuria and Associated Risk Factors Among Patients Attending Major Hospitals in Calabar, Nigeria. African Journal of Clinical and Experimental Microbiology. 25 (1): 48 – 59 https://dx.doi.org/10.4314/ajcem.v25i1.6

[36].Mancuso, G., Midiri, A., Gerace, E., Marra, M., Zummo, S., & Biondo, C. (2023). Urinary Tract Infections: The Current Scenario and Future Prospects. *Pathogens (Basel, Switzerland)*, *12*(4), 623. https://doi.org/10.3390/pathogens12040623

[37]. Maldonado-Barragán, A., Mshana, S. E., Keenan, K., Ke, X., Gillespie, S. H., Stelling, J., Maina, J., Bazira, J., Muhwezi, I., Mushi, M. F., Green, D. L., Kesby, M., Lynch, A. G., Sabiiti, W., Sloan, D. J., Sandeman, A., Kiiru, J., Asiimwe, B., & Holden, M. T. G. (2024). Predominance of multidrug-resistant bacteria causing urinary tract infections among symptomatic patients in East Africa: a call for action. *JAC-antimicrobial resistance*, *6*(1), dlae019. https://doi.org/10.1093/jacamr/dlae019

[38]. Tessema, N. N., Ali, M. M., & Zenebe, M. H. (2020). Bacterial associated urinary tract infection, risk factors, and drug susceptibility profile among adult people living with HIV at Haswassa University Comprehensive Specialized Hospital, Hawassa, Southern Esthiopia. Scientific reports, 10(1), 10790. https://doi.org/10.1038/s41598-020-67840-7

[39]. Kebbeh, A., Dsane-Aidoo, P., Sanyang, K., Darboe, S. M. K., Fofana, N., Ameme, D., Sanyang, A. M., Darboe, K. S., Darboe, S., Sanneh, B., Kenu, E., & Anto, F. (2023). Antibiotics

susceptibility patterns of uropathogenic bacteria: a cross-sectional analytic study at Kanifing General Hospital, The Gambia. *BMC infectious diseases, 23*(1), 723. https://doi.org/10.1186/s12879-023-08373-y

[40]. Ali, A. H., Reda, D. Y., &Ormago, M. D. (2022). Prevalence and antimicrobial susceptibility pattern of urinary tract infection among pregnant women attending Hargeisa Group Hospital, Hargeisa, Somaliland. *Scientific reports, 12*(1), 1419. https://doi.org/10.1038/s41598-022-05452-z

[41].Odoki, M., AlmustaphaAliero, A., Tibyangye, J., Nyabayo Maniga, J., Wampande, E., Drago Kato, C., Agwu, E., &Bazira, J. (2019). Prevalence of Bacterial Urinary Tract Infections and Associated Factors among Patients Attending Hospitals in Bushenyi District, Uganda. *International journal of microbiology, 2019*, 4246780. https://doi.org/10.1155/2019/4246780

[42]. Prastiyanto, M. E., Iswara, A., Khairunnisa, A., Sofyantoro, F., Siregar, A. R., Mafiroh, W. U., Setiawan, J., Nadifah, F., Wibowo, A. T., & Putri, W. A. (2024). Prevalence and antimicrobial resistance profiles of multidrug-resistant bacterial isolates from urinary tract infections in Indonesian patients: A cross-sectional study. Clinical Infection in Practice, 22, Article 100359. https://doi.org/10.1016/j.clinpr.2024.100359

[43]. Shaaban, O. A., Mahmoud, N. A., Zeidan, A. A., Kumar, N., & Finan, A. C. (2021). Prevalence and Resistance Patterns of Pediatric Urinary Tract Infections in Bahrain. *Cureus, 13*(12), e20859. https://doi.org/10.7759/cureus.20859

[44]. Paul, A. D., & Habibu, T. (2024). Incidence And Antibiotic Resistance Profile of Klebsiella Pneumoniae Isolated from Urine of Patients Attending Primary Health Care Centers in Lafia

Metropolis and its Environs, Nasarawa State, Nigeria. *Journal of Health Systems Research*, *3*(3). https://ssaapublications.com/sjhsr/article/view/144

[45]. World Health Organization (2024).Antimicrobial Resistance, Hypervirulent Klebsiella pneumoniae - Global situation. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON527

[46]. Mekonnen, S., Tesfa, T., Shume, T., Tebeje, F., Urgesa, K., & Weldegebreal, F. (2023). Bacterial profile, their antibiotic susceptibility pattern, and associated factors of urinary tract infections in children at Hiwot Fana Specialized University Hospital, Eastern Ethiopia. *PloS one*, *18*(4), e0283637. https://doi.org/10.1371/journal.pone.0283637

[47]. Innocent , I. G., Gowon, A. G., Ademah, C., Agbese, J. B., Kuleve, M. I., & Jonah , O. I. (2023). Isolation and Antibiotic Sensitivity of Klebsiella pneumoniae among Urinary Tract Infected Patients in Dalhatu Araf Specialist Hospital Lafia, Nasarawa State Nigeria. *Journal of Advances in Microbiology*, *23*(7), 1–6. https://doi.org/10.9734/jamb/2023/v23i7731

[48]. Haruna, U. L., Abdulmumin, I. S., Halilu, H., & Qasim, M. (2024). Prevalence and antibiotic susceptibility pattern of Uro-pathogens isolated from urine in a tertiary care hospital in Nigeria. *GSC Biological and Pharmaceutical Sciences*, 28(03), 253–260. :https://doi.org/10.30574/gscbps.2024.28.3.0321

[49].Ugwu, M. C., Shariff, M., Nnajide, C. M., Beri, K., Okezie, U. M., Iroha, I. R., &Esimone, C. O. (2020). Phenotypic and Molecular Characterization of β-Lactamases among

Enterobacterial Uropathogens in Southeastern Nigeria. *The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologiemedicale, 2020*, 5843904. https://doi.org/10.1155/2020/5843904

[50]. Abhadionmhen, O.A., & Imarenezor, E.P.K. (2024). Antibiogram of *Klebsiella pneumoniae* isolates from Urine Samples of patients attending Hospital in Wukari, North-East Nigeria. Covenant Journal of Health and Life Sciences, 2(1). https://journals.covenantuniversity.edu.ng/index.php/cjhl/article/view/4329

[51]. Abdulfatai, K., Sanusi, S.B., Usman, A., Lawal, S.M., & Idris, H. (2023) Prevalence and Antimicrobial Susceptibility Pattern of Klebsiella Pneumoniae and Pseudomonas Aeruginosa among Women With Urinary Tract Infections Attending Antenatal Care In Kaduna, Nigeria. Science World Journal 18 (1) 114-119

[52].NdakoJames, A., OwolabiAkinyomade, O., OranusiSolomon, U., FajobiVictor, O., Charles, O.O., Jeremiah, A., &OhioborGladys, O. (2019). Incidence of Urinary Tract Infection in a Rural Community of South-West, Nigeria. Saudi Journal of Biomedical Research. 4(9): 306-311. DOI:10.36348/sjbr.2019.v04i09.002

[53]. Echendu M. N., Ekuma U. O., Ihenetu F. C., Chikwendu C. I., & Nwabueze R. N. (2024). Prevalence of Klebsiella pneumoniae and Acinetobacter baumannii in Urine Samples of Pregnant Women in South-East, Nigeria. Microbiology Research Journal International, 34(5), 48–58. https://doi.org/10.9734/mrji/2024/v34i51446

[54]. MouangaNdzime, Y., Onanga, R., Kassa Kassa, R. F., Bignoumba, M., Mbehang Nguema, P. P., Gafou, A., Lendamba, R. W., MbombeMoghoa, K., &Bisseye, C. (2021). Epidemiology of

Community Origin *Escherichia coli* and *Klebsiella pneumoniae* Uropathogenic Strains Resistant to Antibiotics in Franceville, Gabon. *Infection and drug resistance*, *14*, 585–594. https://doi.org/10.2147/IDR.S296054

[55]. Haque, Q.T., Alam, M.S., Sazzad, J., Ali, M.T., Haque, M.A., Rahman, M.M., & Nadi, S.R. (2023). Antimicrobial Susceptibility Patterns of Klebsiella Species Causing Urinary Tract Infections in Pregnant Women. TAJ: Journal of Teachers Association. DOI:10.3329/taj.v36i1.68280

[56]. Lin, Z., Yu, J., Liu, S., & Zhu, M. (2022). Prevalence and antibiotic resistance of *Klebsiella pneumoniae* in a tertiary hospital in Hangzhou, China, 2006-2020. *The Journal of international medical research*, *50*(2), 3000605221079761. https://doi.org/10.1177/03000605221079761

[57]. Kaye, K.S., Gupta, V., Mulgirigama, A., Ashish, V. J., Gang,Ye., Nicole, E., Scangarella-Oman, Kalvin, Y., & Fanny, S. M. (2024). Prevalence, regional distribution, and trends of antimicrobial resistance among female outpatients with urine *Klebsiella* spp. isolates: a multicenter evaluation in the United States between 2011 and 2019. *Antimicrobial Resistance and Infection Control*. 13, 21 https://doi.org/10.1186/s13756-024-01372-x

[58]. Miftode, I. L., Nastase, E. V., Miftode, R. Ș., Miftode, E. G., Iancu, L. S., Luncă, C., Anton Păduraru, D. T., Costache, I. I., Stafie, C. S., &Dorneanu, O. S. (2021). Insights into multidrug-resistant *K. pneumoniae* urinary tract infections: From susceptibility to mortality. *Experimental and therapeutic medicine*, *22*(4), 1086. https://doi.org/10.3892/etm.2021.10520

[59]. Jelly, P., Verma, R., Kumawat, R., Choudhary, S., Chadha, L., & Sharma, R. (2022). Occurrence of urinary tract infection and preventive strategies practiced by female students at a

tertiary care teaching institution. *Journal of education and health promotion*, *11*, 122. https://doi.org/10.4103/jehp.jehp_750_21

[60]. Mtenga, A., Fimbo, Adam., Shewiyo, D., Makonope, R., Mwambene, S., Hebron, Y., Mwamitwa, K., &Sangeda, R. (2024). Assessment of Antibiotics Resistance from Isolates Responsible for UTI in Four Regional Referral Hospitals in Tanzania.. 10.1099/acmi.0.000905.v1.

[61]. Yabwa, K.G., Ajobiewe, H.F., Ajobiewe, J.O., Ogundeji, A. &Umeji, L.C. (2020). Prevalence of Klebsiella pneumoniae Infection in Adults Attending National Hospital, Abuja, Nigeria. Scholars Journal of Applied Medical Sciences. 8. 1667-1672. 10.36347/sjams.2020.v08i07.006.

[62]. Mehta, A., Gupta, H. K., & Tripathi, K. (2023). Antimicrobial Susceptibility Pattern of Uropathogens at a Tertiary Care Hospital in Central India During Covid Era. International Journal of Pharmacy and Pharmaceutical Sciences, 15(5), 28–33. Https://Doi.Org/10.22159/Ijpps.2023v15i5.47533

[63]. Polse, R.F., Qarani, S.M., Assafi, M.S., Sabaly, N. and Ali, F. (2020) Incidence and Antibiotic Sensitivity of Klebsiella Pneumonia Isolated from Urinary Tract Infection Patients in Zakho Emergency Hospital/Iraq. Journal of Education and Science, 29, 257-268.https://doi.org/10.33899/edusj.2020.126827.1056

[64]. Lacerda Mariano, L., & Ingersoll, M. A. (2020). The immune response to infection in the bladder. *Nature reviews. Urology*, *17*(8), 439–458. https://doi.org/10.1038/s41585-020-0350-8

[65]. Rosenthal, Y. S., Rosenthal, A., Shalev Ram, H., Ram, S., Chodick, G., & Koren, G. (2021). Association between oral contraceptives and serious infections: A population-based cohort study. *British journal of clinical pharmacology*, *87*(11), 4241–4251. https://doi.org/10.1111/bcp.14840

[66]. Vicar, E. K., Acquah, S. E. K., Wallana, W., Kuugbee, E. D., Osbutey, E. K., Aidoo, A., Acheampong, E., & Mensah, G. I. (2023). Urinary Tract Infection and Associated Factors among Pregnant Women Receiving Antenatal Care at a Primary Health Care Facility in the Northern Region of Ghana. *International journal of microbiology*, *2023*, 3727265. https://doi.org/10.1155/2023/3727265

[67]. Cortes-Penfield, N. W., Trautner, B. W., & Jump, R. L. P. (2017). Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. Infectious disease clinics of North America, 31(4), 673–688. https://doi.org/10.1016/j.idc.2017.07.002

[68]. Akhtar, A., Ahmad Hassali, M. A., Zainal, H., Ali, I., & Khan, A. H. (2021). A Cross-Sectional Assessment of Urinary Tract Infections Among Geriatric Patients: Prevalence, Medication Regimen Complexity, and Factors Associated With Treatment Outcomes. *Frontiers in public health*, *9*, 657199. https://doi.org/10.3389/fpubh.2021.657199

[69]. Barwa, J. & Bishop, H. G. (2022). Prevalence and antibiotic susceptibility profiles of Escherichia coli and Klebsiella pneumoniae in urine of students of Ahmadu Bello University. 10.13140/rg.2.2.11476.78723.

[70]. Ghosh, Susanta Kumar & Santosh, Kumar & Saha, Santosh & Islam, Milia & Susanta, Dr & Ghosh, Kumar. (2020). Etioclinical Profile of Urinary Tract Infection in Children.

[71]. Pana, Z. D., &Zaoutis, T. (2018). Treatment of extended-spectrum β-lactamase-producing *Enterobacteriaceae* (ESBLs) infections: what have we learned until now?. *F1000Research*, *7*, F1000 Faculty Rev-1347. https://doi.org/10.12688/f1000research.14822.1

[72]. Hammoudi, H. D., &Ayoub, M. C. (2020) The Current Burden of Carbapenemases: Review of Significant Properties and Dissemination among Gram-Negative Bacteria. *Antibiotics*. 9(4):186. https://doi.org/10.3390/antibiotics9040186

[73]. Armstrong, T., Fenn, S. J., & Hardie, K. R. (2021). JMM Profile: Carbapenems: a broad-spectrum antibiotic. *Journal of medical microbiology*, *70*(12), 001462. https://doi.org/10.1099/jmm.0.001462

[74]. Jalal, N. A., Al-Ghamdi, A. M., Momenah, A. M., Ashgar, S. S., Bantun, F., Bahwerth, F. S., Hariri, S. H., Johargy, A. K., Barhameen, A. A., Al-Said, H. M., & Faidah, H. (2023). Prevalence and Antibiogram Pattern of *Klebsiella pneumoniae* in a Tertiary Care Hospital in Makkah, Saudi Arabia: An 11-Year Experience. *Antibiotics (Basel, Switzerland)*, *12*(1), 164. https://doi.org/10.3390/antibiotics12010164

[75]. Kijineh, B., Alemeyhu, T., Mengistu, M., & Ali, M. M. (2024). Prevalence of phenotypic multi-drug resistant Klebsiella species recovered from different human specimens in Ethiopia: A systematic review and meta-analysis. *PloS one*, *19*(2), e0297407. https://doi.org/10.1371/journal.pone.0297407

[76]. Sahoo, S., Mohanty, J., Routray, S., Sarangi, A., Nayak, D., Shah, S., Das, J., Subudhi, E., & Swarnkar, T. (2024). Prevalence of multidrug-resistant *Klebsiella pneumoniae* in urinary tract

infections: A retrospective observational study in eastern India. *Microbes and Infectious Diseases*, (), -. doi: 10.21608/mid.2024.276619.1844

[77]. Santella, B., Boccella, M., Folliero, V., Iervolino, D., Pagliano, P., Fortino, L., Serio, B., Vozzella, E. A., Schiavo, L., Galdiero, M., Capunzo, M., Boccia, G., & Franci, G. (2024). Antimicrobial Susceptibility Profiles of *Klebsiella pneumoniae* Strains Collected from Clinical Samples in a Hospital in Southern Italy. *The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologiemedicale*, *2024*, 5548434. https://doi.org/10.1155/2024/5548434