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Prevalence and antimicrobial susceptibility of *Klebsiella pneumoniae* isolated from hospitalized patients at General Hospital, Etim Ekpo, Akwa Ibom State, Nigeria

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ABSTRACT

Klebsiella pneumoniae (KP) was investigated in respondents presenting signs and symptoms of urinary tract infection (UTI) in a rural community. Using simple random sampling, a total of 360 respondents (144 males and 216 females) were recruited into the study following informed consent and ethical approval. Mid-stream urine samples were collected from all the respondents aseptically using standard protocol. Isolation of *K. pneumoniae* was done using morphological characteristics and various biochemical tests while antibiotic sensitivity testing using various antibiotics was done using guidelines of Clinical and Laboratory Standard Institute. A total of 16 samples gave positive culture representing an overall prevalence of 4.4%. Furthermore, prevalence rates of 2.8%, 5.6%, 47.82%, 4.9%, 3.50%, and 8.60% for males, females, diabetics, in-patients, out-patients, and respondents above 60 years of age respectively were obtained. Resistance to antibiotics ranged from 37.50 to 56.25% for gentamycin and nalidixic, and tarivid, respectively. There is need for preventive measures aimed at sensitization of dwellers in community settings.

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Keywords: *Klebsiella pneumonia*, Nosocomial, Prevalence, Antibiotic susceptibility, Resistance

1. INTRODUCTION

Klebsiella pneumoniae (KP) is a Gram negative bacterium which belongs to the Enterobacteriaceae family [1]. They are normal flora of the human intestine and important human pathogens implicated as the causative agents of several infections including pneumonia, septicaemia, wound infections, surgical site infections, meningitis and urinary tract infections (UTI) [1-3] and are second to *Escherichia coli* in causing a wide spectrum of infections [3]. *Klebsiella pneumoniae* have been reported to cause increase in the colonization rate of *Klebsiella* in patients two weeks after hospital admission, up to two- to four-fold due to their capacity to spread in clinical settings [4]. Being the most medically important *Klebsiella* species, *Klebsiella pneumoniae*, is responsible for a significant amount of nosocomial urinary tract infections [5-7]. As an opportunistic pathogen, it causes disease easily in immunocompromised individuals with underlying medical conditions such as diabetes mellitus and chronic pulmonary obstruction [2].

Klebsiella pneumoniae is the second most frequently isolated species from UTI, after *Escherichia coli* [8, 9]. UTI is usually classified according to the infection sites such as kidney (in case of pyelonephritis), bladder (in case of cystitis), or urine, and also can be symptomatic or asymptomatic. The infection rate varies depending on the age, sex, catheterization and hospitalization [10]. Females usually acquire UTI more often than males due to the anatomical structure and position of the female external genitalia [5, 11]. Symptoms of UTI include frequent urination, fowl-smelling cloudy urine, bloody urine, painful urination with a burning sensation, muscle aches, abdominal pains, nausea and vomiting. People with catheters are more prone to UTI. However, they only experience fever as a symptom, which makes diagnosis more difficult [5, 11-13].

KP has been described as a "successful" pathogen as a result of its ability to transfer resistant genes to other strains vertically or horizontally via plasmids and transposons [14, 15]. In the last two decades, KP have been shown to accumulate antibiotics resistant genes (ARGs) via various means including *de novo* mutations and in the process harbouring super resistome thus, positing itself as an extremely drug resistant pathogen (XDR) [15]. Furthermore, it has been shown to have the ability to develop multi-drug resistance (MDR) and have been placed with other MDR pathogens as ESKAPE. The other pathogens include *Enterobacter* spp, *Staphylococcus aureus, Enterococcus faecium, Pseudomonas aeruginosa* and *Acinetobacter baumanni*. ESKAPE is as group of six pathogens that exhibit multidrug resistance, virulence and are commonly associated with nosocomial infections [16, 17].

Antibiotics have been in clinical use for over seven decades now. During this period, pathogens have evolved as a significant public health concern globally [18-20]. The pace at which pathogens develop resistance is faster than the rate of development of newer antibiotics; despite advances in sciences [19, 21]. This has lead to an increasing reports of infection due to these multidrug resistant pathogens even among the Enterobacteriaceae taxa which *K. pneumoniae* is a member [20]. KP has also been shown to develop resistance to the carbapenems and other routinely used antibiotics such as quinolones in the management of KP infection spectrum [2, 20, 22].

Several studies exist that have shown that *Klebsiella pneumoniae* causes UTIs clinical setting in cities [3, 20, 26, 34, 36]. However, studies aimed at MDR KP implicated in UTIs are lacking or non-existent in rural areas with poor health facilities in developing countries like Nigeria.

Furthermore, KP have been shown to have the capacity to become hyper virulent thereby increasing the net of susceptible persons to its spectrum of diseases [23]. Thus, this study was aim to establish the MDR profile of KP isolates implicated in UTI infections in rural community in Akwa Ibom State, South-South, Nigeria amongst hospitalized patients attending a community general hospital.

2. MATERIAL AND METHODS

2. 1. Study site

This study was conducted at Etim Ekpo General Hospital located in Etim Ekpo Local Government Area (LGA) of Akwa Ibom State. The LGA is located on 4º51' - 5º03' North of Equator and Longitude 7º 44' East of the Greenwich Meridian. It occupies a total area of 183.3 Km^2 [24] and as at the 2006 Census, it had male and female populations of 105, 418 people and 55,771, respectively [24]. The General Hospital is managed by both the Local and State Governments. It provides health care services to the people of the LGA and adjoining communities and villages. The major occupation of the inhabitants remains agriculture [24].

2. 2. Experimental design and ethical approval

The study design employed in this study was a cross-sectional study design, a type of observational study that measures outcomes and exposures at the same time using a section of the population [25]. Ethical approval was obtained from the Hospital Management Ethical Approval Board, and as well as Obong University Research Directorate.

2. 3. Inclusion and exclusion criteria

Participants were only included in the study if they were admitted in the hospital, consent to fill our questionnaire, and presenting with signs and symptoms of UTIs. Those that could not meet these criteria were excluded from the study.

2. 4. Design and administration of questionnaires

Open ended questionnaires were designed to obtain sociodemographic and risk factors of the respondents. The questionnaires were administered to the respondents following their informed consent and assurance of the confidentiality of their data.

2. 5. Collection of samples

The study was conducted from February to August, 2019. Following informed consent, simple random sampling was used to recruit respondents. From all the 360 respondents early morning mid-stream urine samples were collected (144 males and 216 females) aseptically and at room temperature.

All samples were appropriately labelled and transported to Obong University microbiology laboratory in an ice pack for microbiological analysis.

2. 6. Inoculation and identification of the isolates

The samples were aseptically inoculated on MacConkey agar using sterile wire loop and incubated at 37 ºC for 24 hours. Discrete, mucoid, rose pink colonies (lactose fermenters) seen on MacConkey agar were picked with a sterile wire loop and sub-cultured onto another freshly prepared MacConkey agar plates to obtain pure cultures. *K. pneumoniae* isolates were identified using cultural characteristics, Gram reaction, microscopic appearance and biochemical tests as previously described [26-28].

2. 7. Antibiotic susceptibility test

Using disc diffusion method, antimicrobial susceptibility test was performed following the guidelines established by the Clinical and Laboratory Standard Institute (CLSI) [29]. Colonies of *Klebsiella pneumonia* isolates were inoculated aseptically in nutrient broth in test tubes and adjusted to 0.5 McFarland standard which corresponds to 1.5×10^8 CFU/ml. This was inoculated on sterile Mueller-Hinton agar by spread plate method. After 3-5 minutes, antibiotic discs were placed and the plates incubated at 37 ºC for 24 hours. The antibiotics used were Ciprofloxacin (10 µg/disc), Streptomycin (30 µg/disc), Peflacine (10 µg/disc), Septrin (30 µg/disc), Ampicilin (30 µg/disc), Tarivid (10 µg/disc), Ceporex (10 µg/disc), Gentamycin (10 µg/disc), Augmentin (30 µg/disc) and Nalidixic acid (30 µg/disc).

After incubation, inhibition zone diameters (IZD) around the discs were measured and recorded to the nearest millimeters. Each isolate was prepared in duplicates and the mean values were recorded. The values obtained were compared with interpretative criteria of CLSI [29] as isolates were identified as susceptible, intermediate and resistant. Isolates that showed resistance to at least one agent in at least three classes of antimicrobial agents were recorded as multidrug resistant bacteria [30, 31].

2. 8. Statistical analysis

Simple descriptive statistics (%) and Chi-square was used to carry out analysis of data obtained in this study test using the Vassarsstat tool. Level of significance was set at 95% (0.05).

3. RESULT

From the 360 urine samples collected and subjected to culture, only 16 samples were positive for *Klebsiella pneumoniae* (Table 1). In other words, the overall prevalence of *K. pneumoniae* was 4.4%. Distribution of the prevalence according to sex revealed that out of the 144 samples collected from male respondents, 4 were positive giving a prevalence of 2.8%. On the other hand, from the 216 samples collected from the female respondents, 12 of them tested positive, giving a prevalence of 5.6%. Furthermore, from the 245 samples obtained from patients in the ward (in-patients), 12 of them were positive giving a prevalence rate of 4.9% while for out-patients, only 4 out of the 115 samples collected were positive with 3.5% prevalence (Table 1). Chi-square analysis gave no significant association between the pathogen and gender and hospital units.

The presence of *K. pneumoniae* in the samples was also evaluated based on the age groups of the patients (Table 2). There was a stepwise increase in the number of *Klebsiella pneumoniae* isolates across the age groups. Of the 91 samples collected from patients within the ages of 10

– 20 years, only two samples were positive for *K. pneumoniae* giving a prevalence of 2.2%. In the group of 21 – 40 years, only 4 were positive giving a prevalence of 3.20% (n = 125). For the age bracket of 41 – 60 years, the prevalence was 5.80% as 5 were positive (n = 86). For the respondents > 60 years of age, the prevalence was 8.60% as 5 were positive amongst the 58 samples that were collected. Chi-square analysis gave no significant association between the pathogen and the various age groups.

Table 3 shows the risk factors predisposing the respondents to *K. pneumonia.* From the result, the respondents that regularly washed their hands were 121, that is, 33.61%. Those with diabetes were 6.39%. The respondents that were married were 44.44% while those that had education levels up to secondary school were 15.56%. The prevalence of *K. pneumonia* according to risk factors indicates that respondents with diabetes had the highest prevalence of 47.82% of *K. pneumoniae* (n = 11/23) followed by education level up to secondary school with 7.14% (n = 4/56). Compared to those that had no diabetes, the prevalence of KP was 3.56% (n = 12/337). Those that wash their hands less than 6 times a day had a higher KP prevalence of 8.63 compared to 3.30 amongst those wash their hands atleast 6 times daily. According to marital status, those not married had a higher prevalence of KP which stood at 6.50% compared to respondents that were still married whose prevalence stood at 1.88. Chi-square analysis gave significant association ($p < 0.0001$).

Table 4 shows the susceptibility pattern of the 16 isolates of KP to the antibiotics tested. K4 was resistant to 8 antibiotics. K5 and K9 were resistant to 5 antibiotics. K1, K3, K12, K13, K14 and K16 showed resistance to 4 antibiotics. K8, K10, K11 and K15 were resistant to 3 antibiotics. K2 and K6 were resistant to 2 antibiotics while K7 was resistant to one antibiotic.
Table 5 shows the percentage susceptibility of the isolates to the antibiotics. 100% of the organisms were susceptible to peflacine, 81.3% to ciprofloxacin, 43.75% to streptomycin and gentamycin, 50% to septrin and nalidixic acid, 56.25% to ampicillin and ceporex, 37.5% to tarivid, and 62.5% to augmentin. Also, 56.25% of the isolates were resistant to tarivid, 50% to septrin, 43.75% to streptomycin, ampicillin and ceporex, and 37.5% to gentamycin and nalidixic acid. Intermediate resistance was found against streptomycin and nalidixic acid (12.5%), tarivid and augmentin (6.25%), and gentamycin (18.75%).

Table 1. Prevalence of *Klebsiella pneumoniae* according to gender and hospital units.

Parameters	**Positive**	**Negative**	**Total**	**X^2 and *p* value**
1. Gender				
Male	4(2.8%)	140	144	
Female	12(5.6%)	204	216	
Total	16(4.4%)	344	360	0.98 and 0.322
2. Hospital Unit				
In-Patient (Ward)	12(4.9%)	233	245	
Out-Patient	4(3.5%)	111	115	
Total	16(4.4%)	344	360	0.11 and 0.740

Table 2. Prevalence of *Klebsiella pneumoniae* according to age groups

Age group (years)	Positive	Negative	Total	C.I, X^2 and *p* value
10 – 20	2(2.2%)	89	91	0.0-0.105, 2.91 and 0.406
21 – 40	4(3.2%)	121	125	
40 – 60	5(5.8%)	81	86	
>60	5(8.6%)	53	58	
Total	16(4.4%)	344	360	

Table 3. Prevalence and risk factors to colonization of respondents to *K. pneumoniae.*

Risk factors	Yes (n, %)	No (n, %)	C.I, X^2 and *p* value
Regular washing of hands up to 6 times daily (Prevalence of ***K. pneumoniae*****)**	121 (4, 3.30)	139 (12, 8.63)	0.106-0.05, 176.85 and <0.0001
Diabetes (Prevalence of ***K. pneumoniae*****)**	23 (11, 47.82)	337 (12, 3.56)	
Marital status (Prevalence of ***K. pneumoniae*****)**	160 (3, 1.88)	200 (13, 6.50)	
Education level up to secondary and above (Prevalence of ***K. pneumoniae*****)**	56 (4, 7.14)	304 (12, 3.95)	

Table 4. The Antibiotic susceptibility pattern of *K. pneumonia* isolates.

Isolate	CIP	STR	PEF	SEP	AMP	TAR	CEP	GEN	AUG	NA
K1	S	S	S	R	R	R	S	I	S	R
K2	S	I	S	S	S	R	S	R	S	I
K3	S	R	S	S	R	S	R	S	S	R
K4	R	R	S	R	R	R	R	R	S	R
K5	S	R	S	R	R	R	S	S	R	S
K6	S	S	S	S	S	S	R	R	I	S

K7	S	S	S	S	S	S	S	I	R	S
K8	R	S	S	S	S	R	S	R	S	S
K9	S	R	S	S	R	S	R	R	S	R
K10	S	I	S	R	S	R	S	S	R	S
K11	S	R	S	R	S	S	S	R	S	S
K12	S	S	S	S	R	R	R	S	S	R
K13	R	S	S	R	S	R	S	I	R	I
K14	S	R	S	S	S	S	R	R	R	S
K15	S	S	S	R	S	I	R	S	S	R
K16	S	R	S	R	R	R	S	S	S	S

K1-16 = *K. pneumonia* isolates; CIP = Ciprofloxacin, STR = Streptomycin, SEP = Septrin, AMP = Ampicilin, TAR = Tarivid, CEP = Ceporex, GEN = Gentamycin, AUG = Augmentin, NA= Nalidixic acid. S = Susceptible, R = Resistant, I = Intermediate.

Table 5. Percentage Susceptibility of the *K. pneumonia* isolates to commonly used antibiotics.

Antibiotics	**Sensitive**	**Intermediate**	**Resistance**
Ciprofloxacin (10µg)	13(81.3%)	-	3(18.7%)
Streptomycin (30µg)	7(43.75%)	2(12.5%)	7(43.75%)
Peflacine (10µg)	16(100%)	-	-
Septrin (30µg)	8(50.0%)	-	8(50%)
Ampicillin (30µg)	9(56.25%)	-	7(43.75%)
Tarivid (10µg)	6(37.5%)	1(6.25%)	9(56.25%)
Ceporex (10µg)	9(56.25%)	-	7(43.75%)
Gentamycin (10µg)	7(43.75%)	3(18.75%)	6(37.5%)
Augmentin (30µg)	10(62.5%)	1(6.25%)	5(31.25%)
Nalidixic acid (30µg)	8(50.0%)	2(12.5%)	6(37.5%)

4. DISCUSSION

The result of this study shows that *Klebsiella pneumonia* infection was seen more in females than the males. This suggests that women have a higher tendency to acquire urinary tract infections than men. Felson *et al*. (2005) [10] explained this to be a result of the relative anatomical position of the external genitalia with respect to the anus. Considering the nature and proximity of the female external genitalia to the anus, faecal materials easily contaminate the female genitourinary system with a resultant increase in urinary tract infections. Gastrointestinal tract and hands of hospital personnel are the main sources of transmission of pathogenic *Klebsiella*. Cases of UTI are frequent in diarrheic patients because faeces is the most significant source of patient infection, followed by contact with contaminated instruments. In Pakistan, from 162 urine samples, 6 were positive representing a total prevalence of 3.96%, which was within range of our reported 4.4%. Amongst the positive in their study, the ratio of males to females was the same (1:1). However, in our study more females than males were positive (3:1) [26]. A 10.70% prevalence (n = 455/4260) for year 2000 to 2006 and 18.10% (n = 965/5331) from 2007 to 2013 of *K. pneumoniae* from blood stream infections in a retrospective study was reported in Brazil [32]. The high prevalence of KP in these studies confirms that it is a versatile pathogen that is of great public health concern.

Furthermore, our result shows that 4.9% and 3.5% of the in-patients and out-patients respectively gave positive cultures. The higher rate of occurrence amongst the in-patients is an indication that the hospitalized immunocompromised patients are more vulnerable to KP. It is also possible that the rate of infection could also lead to a corresponding increase in hospital stay. Longer periods of hospitalization increase the chances of acquiring nosocomial infections. Its infections occur mostly in people with weak immune system. In other words, the infections are mostly seen in old people and those with debilitating diseases. Our result shows that people above 60 years of age are the most infected. The majority of people in this group are believed to have impaired immunity with conditions such as diabetes mellitus, chronic obstructive pulmonary diseases and other health conditions. This infection can also be obtained when a person is in the hospital for some other reasons. Parisi *et al* [33] reported a prevalence of 3.28% (n = 496/15104) from *K. pneumoniae* producing carbapenemases isolates from 15,104 rectal samples in an intensive care unit. Cristea *et al* [34] obtained 32.60% prevalence in *K. pneumoniae* in patients with UTI in Romania. Furthermore, they observed that their MDR isolates correlated with kidney failure, advanced age, male gender, and diabetes mellitus. In our study, those with diabetes had a higher KP prevalence of 47.82%.

Our study also shows that almost all the *Klebsiella pneumonia* isolates were multidrug resistant strains. About 50% of the isolates showed resistance to antibiotics such as tarivid and septrin while 43.75% of the isolates were resistant to streptomycin ampicillin and ceporex among others. However, peflacine was 100% effective. Other antibiotics that were reasonably effective are ciprofloxacin (81.3%) and augmentin (62.5%). As stated earlier, indiscriminate use of antimicrobials has often been held responsible for the occurrence of multidrug resistant *Klebsiella* strains in hospitals [13]. In a study, a two to fourfold increase in colonization rate with *Klebsiella* by the hospital patients receiving antibiotics two weeks after admission to the hospital has been reported [4]. Most of these organisms are multidrug resistant strains [4][35]. Due to the increased resistance to antibiotics by strains of *K. pneumonia*, it is becoming increasingly difficult to treat these infections. Rath and Padhy [36] in an earlier study carried out in India isolated extended spectrum beta lactamase (ESSL) and cephalosporinase enzymes

producing *K. oxytoca and K. pneumoniae* in non-hygienic communities and clinical settings. The prevalence rates of ESBL resistance were 81.715 and 74.07% for *K. oxytoca* and *K. pneumoniae* respectively. Apart from Peflacine, the isolates in our study showed resistance to all other antibiotics used and ranged from 18.70 and 56.25% for ciprofloxacin and tarivid, respectively. Furthermore, Rath and Padhy [36] showed that the isolates *K. pneumoniae* strains were highly resistant to several antibiotics such as ampicillin, norfloxacin, ciprofloxacin, and imipenem. Hou *et al* [37] characterized 38 MDR *K. pneumoniae* isolates from China that possesses atleast 7 antibiotics resistance determinants that drives its resistance to aminoglycosides, macrolides, quinolones and beta-lactams. This explains the resistance displayed by our isolates to these classes of antibiotics. Tian *et al* [38] linked *K. pneumoniae* carbapenem resistance to increased mortality of *K. pneumoniae* in blood stream infection patients. Despite the fact that *Klebsiella* species are not a predominant cause of UTI, they are capable of causing kidney disease even among patients getting infected for the first time [39]. Moreover, infections with multidrug resistant *Klebsiella* strains are more likely to lead to death than are infections with most *E. coli* strains.

5. CONCLUSIONS

The result obtained in this study shows that *Klebsiella pneumoniae* infection is a common hospital acquired urinary tract infection in Etim Ekpo general hospital of Akwa Ibom state, Nigeria. Females are more likely to be infected than their male counterparts. Also, the higher rate of occurrence amongst the in-patients is an indication that the hospitalized patients with low immunity are more vulnerable to KP. Furthermore, our study also revealed that multidrug resistant strains of *Klebsiella pneumonia* are prevalent in a community clinical setting and this could further narrow the spectrum of available potent antibiotics in its management and possibly lead to longer stay in the hospital. Efforts should be made to trace the source of these MDR KP pathogens and also channeled to hospitals and other healthcare systems to prevent the nosocomial spread of the organism.

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