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Prevalence and Antimicrobial Susceptibility Pattern of Uropathogenic Organisms Among Diabetic Patients Attending State Specialist Hospital, Maiduguri Nigeria.

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Abstract

Urinary tract infection (UTI) is the colonization of the urinary tract by pathogenic microorganisms. There is paucity of data on the development of multidrug resistant uropathogenic strains associated with Diabetes Mellitus (DM). In this cross-sectional study we investigated a total of three hundred and thirty (330) known diabetes mellitus (DM) patients, comprising of 06 (1.8%) Type I DM, 296 (89.7%) Type II DM and 28 (8.5%) Gestational Diabetes patients aged 21 to 80 years. The subjects consisted of 150 males (45.5%) and 180 (54.5%) females. Urine culture was carried out on CLED, MacConkey and blood agar and Kirby Bauer disc diffusion for antimicrobial susceptibility testing was carried out to determine the susceptibility of the isolated organisms to commonly used antimicrobials in the study area. The study revealed that one hundred and twenty-two (37%) yielded significant bacterial growth. The percentage distribution of the organisms isolated are as follows; Coagulase negative Staphylococci (10.6%), *Klebsiella spp.* (13.2%), *Coliforms spp.* (13.9%), Staphylococcus aureus (24.6%) and Escherichia coli has the highest occurrence of (37.7%). Gram negative bacteria isolated were highly susceptible to Ciprofloxacin (10 μ g), tarivid (10 μ g) and streptomycin (30 μ g); and moderately- to poorly sensitive to the other antibiotics used in the study. In conclusion female diabetics were at a higher risk for UTIs than males (p=0.000) and low educational level/social class was also a risk factor (p=0.04) when compared to subjects of higher educational level/social class.

Keywords: Antimicrobial Susceptibility, Uropathogenic Organisms, Diabetic Patients.

Introduction

Urinary tract infection (UTI) is the colonization of the urinary tract by pathogenic microorganisms. The infection can result to prolonged admissions in hospital, morbidity in general population and high financial cost implications to the patients and government (Ramakrishnan et al., 2005; Prakash et al., 2013). Majority of UTIs are caused by bacteria that are found in the bowel and live as normal flora and often result from faecal and perineal areas. These organisms are capable of invading the tissues of the urinary tract and adjacent tissues causing lower and upper urinary tract infections (Shilpi et al., 2013; Kumar et al., 2013). In general population and hospital set up, UTI is a common infection. Although there are new and more potent antibiotics in use, just as bacterial resistance persists (Patel et al., 2012). The spectrum of causative agents and their antimicrobial resistance pattern has been dynamic worldwide (Annapurna et al., 2014).

Urine culture is the most effective diagnostic tool employed in the diagnosis or monitoring the treatment of UTI (Onuoha and Fatokun, 2014). Lower UTI (cystitis) and upper UTI (pyelonephritis) are the two clinical entities mostly found in patients with symptomatic UTI. Lesions caused by UTI are severe and contribute to morbidity in the population resulting in loss of renal function, which leads to long-term illness (Lane et al., 2007). Due to their anatomical orientation: that is, the short distance between the anus and vagina which predispose women to higher risk of getting UTIs (Foxman, 2010). A second re-infection occurs in about 50% of all women with a first UTI within six months (Ehinmidu, 2003). Bacteria establish infection in the urinary tract only after overcoming possible elimination by normal flora during micturition and innate host defense mechanism in the bladder (Gupta et al., 2001). Common



symptoms of UTIs include burning sensation during urination, loss of bladder control, increased frequency of urination especially in small amounts, lower-back pain, cloudy and bloody or foulsmelling urine (Onifade and Anibijuwon, 2011). An estimated 150 million individuals are affected by UTI yearly on a global basis with a significant number of those affected being diabetics and are second on the list to catheterized patients (Stamm and Norrby, 2001). Due to the weakened immunity and metabolic disorders among diabetics, the effects of UTI are adverse in this category of individuals. Complications associated with UTI cases among diabetics increases the financial burden of health authorities. There is a wide range of organisms that cause UTI in humans and with a focus on people suffering from diabetes mellitus; these organisms are more resistant to most of the available antibiotics agents (Kayima et al., 1996). In order for health authorities to be able to curb UTI among diabetics, it is important that they have the information regarding the pathogens that are responsible for the UTI and their sensitivity to the available antibiotic agents. This information is largely missing in Nigeria especially in Borno state and this has created a big gap between the problem of UTI among diabetic patients and the appropriate solutions from the healthcare stakeholders.

Materials and Methods Study design

A cross-sectional survey designed to determine the disease period prevalence and profile of pathogenic bacteria associated with UTI among diabetic patients attending State Specialists Hospital (S.S.H.M.) in Maiduguri metropolis within a 3-month study interval (September-November, 2020). The study also surveyed the susceptibility pattern of the bacterial isolates to antibacterial agents commonly used in the study area.

Study area

State Specialists Hospital Maiduguri (S.S.H.M.) is a state healthcare facility located in the heart of the city of Maiduguri, on latitude 11°50'20.6"N and longitude 13°09'00.5"E, in Maiduguri, Borno State Nigeria. Maiduguri is the capital and the largest city of Borno State in North-eastern Nigeria. The city sits along the seasonal Ngadda River which disappears into the Firki swamps in the areas around Lake Chad (Britannica, 2019).

Study population

The study targeted both male and female diabetes mellitus patients of all ages attending State Specialists' Hospital Maiduguri (S.S.H.M.)

and has been diagnosed with diabetes mellitus (including all the types of DM). Baseline demographic data including age, gender, level of education and risk factors such as catheterization were also considered.

Sample size determination

The sample size of the study was determined from a standard formula for the calculation of minimum sample size for cross sectional studies/surveys as described in Charan and Biswas (2013).

Sample size (n) is given by the formula;

$$n = (\underline{Z_i} - \underline{d})^2 (\underline{P}) (\underline{1} - \underline{P}) \\ \underline{d}^2 \\ = 322 \ 1$$

Rounding up the figure to the nearest tens, the minimum sample size for this study is = 330 samples. Therefore, 330 mid-stream catch urine samples were collected and analyzed in the study.

Sample collection and storage *Sample collection*

The protocol for early-morning midstream urine sample collection and storage as described by Cheesbrough (2006) was described and duly followed in the study:

Sample storage

If the urine samples were not to be analyzed within one hour of collection, they were stored by refrigerating at 4-8°C by sealing in a plastic bag and placing them aseptically in the refrigerator avoiding contamination for a maximum of 24 hours prior to analysis. Urine samples that stayed for more than 24 hours after collection were discarded even if refrigerated as they were considered unfit for bacteriological analysis.

Statistical analysis of data

Data obtained from the study were analyzed using Statistical Package for Social Sciences (SPSS) version 16.0 for Microsoft windows and Microsoft Excel 2016 Data package for Windows 10. Important findings were presented on tables and in figures (pie-charts and barcharts) as percentages. Chi-square was used to test for statistical significance at 95% confidence level between the observed and expected data of each of the socio-demographic parameter for significant growth. A p-value of <0.05 was considered statistically significant.

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Result

Parameters		Value
Gender	Female	180 (54.5%)
	Male	150 (45.5%)
Marital Status	Married	325(98.5%)
	Single	05 (1.5%)
Type of DM	Gestational DM	28 (8.5%)
• •	Type 1 DM	06 (1.8%)
	Type 2 DM	296 (89.7%)
Duration of DM (ye	• 1	5.07±4.76
Pregnancy Status	Pregnant	25 (7.5%)
	Not Pregnant	155 (47%)
	Not Applicable*	150 (45.5%)
Nationality	Nigerian	328 (99.4%)
2	Others: Chadian	2 (0.6%)
Educational Level	Uneducated	122 (37%)
	Primary	19 (5.8%)
	Secondary	70 (21.2%)
	Tertiary	119 (36.1%)
Occupational	Civil Servants	101 (30.6%)
Status	Students	05(1.5%)
	Business/Farming	93 (28.2%)
	Pensioner	6 (1.8%)
	Housewife	125 (37.9%)
Family History of	Yes	243 (73.6%)
DM	No	63 (19.1%)
	Unsure	24 (7.3%)
Family History of	Yes	57 (17.3%)
UTI	No	184 (55.8%)
	Unsure	89 (27%)
Response to UTI	Yes	37 (11.2%)
Treatment	No	3 (0.9%)
	Unsure	21 (6.4%)
	Not Applicable	269 (81.5%)
Family History of	Yes	08 (2.4%)
Antibiotic Allergy	No	220 (66.7%)
	Unsure	102 (30.9%)
Family History of	Yes	00 (0%)
Antibiotic	No	229 (69.4%)
Resistance	Unsure	101 (30.6%)

Table 1. shows the socio-demographic distribution of the diabetic patients recruited in the study. 180 female and 150 male subjects were recruited where 325 (98.48%) were married while 5 (1.52%) were unmarried/single. On the type of DM, 296 (89.71%) were type II diabetic, 6 (1.81%) type I and 28 (8.48%) gestational diabetes mellitus. The average duration of DM by the subject is 5.07 ± 4.76 years. Of the 180 women recruited, 25 (1.4%) were pregnant while 155 (98.6%) were not pregnant. A total of 328 study subjects were Nigerians and 2 were foreigners (Chadians). Based on the educational levels of the subjects, 122 (36.95%) were uneducated, 19 (5.75%) had only primary education, 70 (21.2%) had secondary education and 119 (36.1%) subjects were educated to the tertiary level. Occupational distribution indicated that 101 (30.6%) of the subjects were civil servants, 5 (1.51%) students, 93 (28.18%) were either business persons or farmers, 125 (37.88%) housewives and 6 (1.83%) were pensioners. Distribution based on history of diabetes in the subject's family indicated that 243 (73.6%) of the subjects have a family history of DM, 63 (19.1%) have no family history of DM whereas 24 (7.3%) were unsure whether or not they have a family history of DM. The distribution for family history of UTI among the subject population indicated that 57 (17.3%) of the subjects had at least a close family member who had UTI in the past, 184 (55.8%) had no family history of UTI and 89 (27%) of the subjects were unsure. Among the patients that had family history of UTI, 33 (57.9%) responded well to treatment, 3 (5.3%) did not respond well to treatment and 21 (36.8%) were unsure of the response to treatment.

Parameters	Category	NBG	SG (>10 ³ /CFU)	Total	P-value	Remarks
	Female	96	84	180		
Gender	Male	112	38	150	0.000	S
	Total	208	122	330		
	Married	203	122	325		
Marital Status	Single	5	0	5	0.084	NS
	Total	208	122	330		
	No Education	79	43	122		
	Primary Edu.	5	14	19		
Educational Level	Sec. Edu.	42	28	70	0.04	S
	Tertiary Edu.	82	37	119		
	Total	208	122	330		
	Yes	57	35	92		
Antibiotic	No	132	78	210	0.849	NS
Administration in Last	Unsure	19	9	28		
Two Weeks	Total	208	122	330		
	21-30	9	10	19		
	31-40	27	16	43		
	41-50	65	45	110		
Age Range	51-60	76	26	102	0.077	NS
	61-70	22	18	40		
	71-80	9	7	16		
	Total	208	122	330		

Table 2 : Distribution of significant isolates obtained based on the socio-demographic data of the
subjects.

NOTE: NBG- no bacterial growth SG- significant growth, CFU- colony forming unit S- significant NS- not significant.



Table 2. shows the distribution of significant isolates obtained based on the socio-demographic data of the subjects. The test revealed a significant difference in infection between male and female subjects (p=0.000) where a significant increase in female than male subjects was observed. We observed a statistically significant difference in the prevalence of UTI based on the educational levels of the subjects (p=0.04). There was no statistical significance in the infections between marital status, antibiotic administration by the subjects or age range (p=0.084; p=0.077) respectively.

Microbial Culture	Outcome (n=330)	
Growth of Organism	122 (37%)	
No Growth of Organism	208 (63%)	
Co-infection (Candida spp.) *	06 (1.8%)	

 Table 3. Prevalence of Uropathogenic Organism in UTI in Diabetic Patients

Table 3. shows the disease period prevalence of Uropathogenic organisms in Diabetic patients in Maiduguri. 122 (37%) yielded significant bacterial growth and 208 (63%) yielded no bacterial growth on culture. Of the 37% that yielded significant bacterial growth, 6 (1.8%) appeared to be co-infected with *Candida spp*.

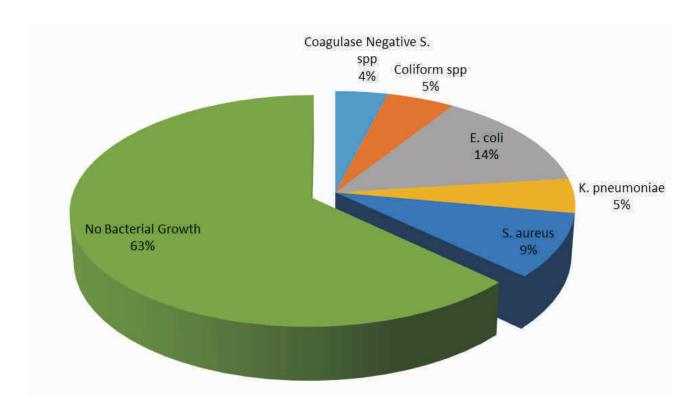
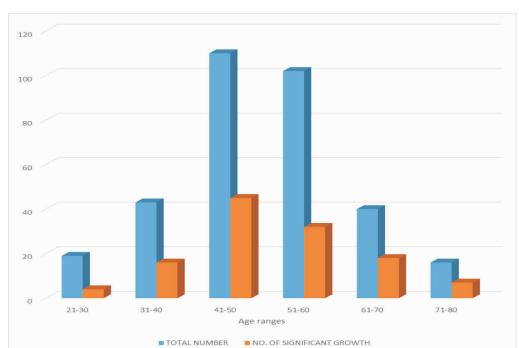


Figure 1: Distribution of Uropathogenic Organisms Isolated from Culture

Figure 1. shows 63% (208) of the subjects yielded no bacterial growth, whereas 37% (122) yielded significant bacterial growth. Of the type of organisms isolated, 14% were *Escherichia coli*, 9% *Staphylococcus aureus*, 5% *Klebsiella spp.*, 5% *Coliforms spp.*, and 4% Coagulase-negative *Staphylococci*. The percent distribution of the organisms that cause UTI are as follows; Coagulase negative *Staphylococci* (10.6%), *Klebsiella spp.* (13.2%), *Coliforms spp.* (13.9%), *Staphylococcus aureus* (24.6%) and *Escherichia coli* has the highest prevalence of (37.7%).



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Figure 2: Distribution of significant growth based on age range

Figure 2. shows the distribution of significant growth based on the age range of the study population. 4 out of 19 (21.1%) subjects in the 21-30 years age group yielded significant growth, 16 out of 43 (37.2%) for those aged 31-40; 45 out of 110 (41%) for those aged 41-50; 32 out of 102 (31.4%) for those aged 51-60; 18 out of 40 (45%) for those aged 61-70 and 7 out of 16 (43.75%) for the elderly 71-80 years old subjects.

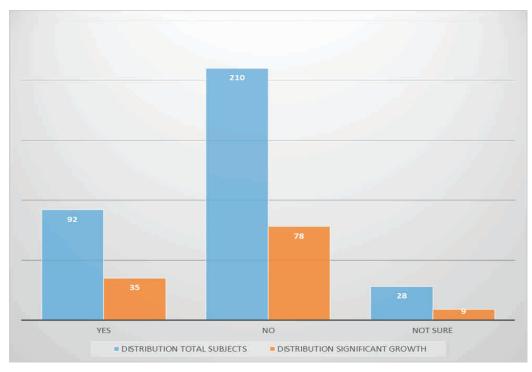


Figure 3: Distribution of significant growth based on whether or not the subjects are on antibiotic treatment

Figure 3 shows the distribution of significant growth based on whether or not the subjects have been on antibiotic treatment in the past two weeks. A total of 35 out of 92 (38%) subjects who have been on antibiotic treatment yielded significant bacterial growth; 78 out of 210 (37.1%) of those who are have not been on any kind of antibiotic treatment in the past two weeks yielded significant bacterial growth and 9 out 28 (32.1%) of those who are not sure of their antibiotic chemotherapy condition yielded significant bacterial growth.



Organism		Number
Coagulase Negative Staphylococcus		13 (3.9%)
Coliform spp.	Total	17 (5.1%)
	MDR Coliform spp.	01 (0.3%)
E. coli	Total	46 (13.9%)
	MDR E. coli	01 (0.3%)
Klebsiella spp.		16 (4.8%)
Staphylococcus aureus	Total	30 (9.1%)
	MDR Staphylococcus	2 (0.6%)
	aureus	
No Bacterial Growth		208 (63%)
Coinfection; with Candida spp.		06

Table 4. Distribution of Organisms Isolated from Culture

MDR: Multi-Drug Resistant

Organism	Antimicrobial	Sensitive	Resistant
Coliform spp. (n=17)	OFX	15 (88.2%)	02 (11.8%)
	NA	05 (29.5%)	12 (70.5%)
	PEF	12 (70.5%)	05 (29.5%)
	CN	04 (23.5%)	13 (76.5%)
	AU	05 (29.5%)	12 (70.5%)
	CPX	12 (70.5%)	05 (29.5%)
	SXT	09 (53%)	08 (47%)
	S	12 (70.5%)	05 (29.5%)
	PN	06 (35.3%)	11 (64.7)
	CEP	03 (17.6%)	14 (82.4)
<i>E. coli</i> (n=46)	OFX	40 (87%)	06 (13%)
	NA	09 (20%)	37 (80%)
	PEF	17 (37%)	29 (63%)
	CN	12 (26%)	34 (74%)
	AU	11 (24%)	35 (76%)
	CPX	39 (84.8%)	07 (15.2%)
	SXT	23 (50%)	23 (50%)
	S	40 (87%)	06 (13%)
	PN	10 (21.7%)	36 (78.3%)
	CEP	10 (21.7%)	36 (78.3%)

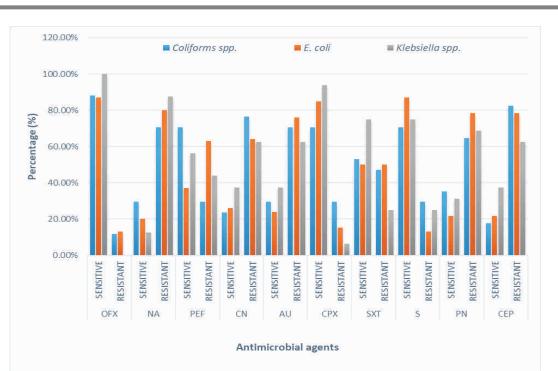
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<i>Klebsiella spp.</i> (n=16)	OFX	16 (100%)	0 (0%)
	NA	02 (12.5%)	14 (87.5%)
	PEF	09 (56.25%)	07 (43.75%)
	CN	06 (37.5%)	10 (62.5%)
	AU	06 (37.5%)	10 (62.5%)
	CPX	15 (93.75%)	01 (6.25%)
	SXT	12 (75%)	04 (25%)
	S	12 (75%)	04 (25%)
	PN	05 (31.25%)	11 (68.75%)
	CEP	06 (37.5%)	10 (62.5%)

Key: OFX: Tarivid 10dg, NA: Nalidixic Acid 30dg, PEF: Reflacine 10dg, CN: Gentamicin 10dg, AU: Augmentin 30dg, CPX: Ciprofloxacin 10dg, SXT: Sulfamethoxazole/Trimethoprim (Septrin) 30dg, S: Streptomycin 30dg, PN: Ampicillin 30dg, CEP Ceporex 10dg.

Organism	Anti-microbial	Sensitive	Resistant
Coagulase Negative	CN	08 (61.5%)	05 (38.5%)
Staphylococcus (n=13)	CPX	13 (100%)	00 (0%)
	S	11 (84.6%)	02 (15.4%)
	LEV	13 (100%)	00 (0%)
	СН	08 (61.5%)	05 (38.5%)
	E	09 (69.2%)	04 (30.8%)
	RD	09 (69.2%)	04 (30.8%)
	NB	00 (0%)	13 (100%)
	APX	00 (0%)	13 (100%)
	AMX	01 (7.7%)	12 (92,3%)
Staphylococcus aureus	CN	11 (36.7%)	19 (63.3%)
(n=30)	CPX	24 (80%)	06 (20%)
	S	25 (83.3%)	05 (16.7%)
	LEV	27 (90%)	03 (10%)
	СН	18 (60%)	12 (40%)
	E	19 (63.3%)	11 (36.7%)
	RD	23 (76.7%)	07 (23.3%)
	NB	04 (13.3%)	26 (86.7)
	APX	04 (13.3%)	26 (86.7%)
	AMX	09 (30%)	21 (70%)

Table 6. Anti-microbial Susceptibility Pattern for Gram Positive Organisms

Key: CN: Gentamycin 10dg, CPX: Ciprofloxacin 10dg, S: Streptomycin 30dg, LEV: Levofloxacin 20dg, CH: Chloramphenicol 30dg, E: Erythromycin 30dg, RD: Rifampicin 20dg, NB: Norfloxacin 10dg, APX: Ampiclox 20dg, AMX: Amoxicillin 20dg.



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Figure 3: Antimicrobial susceptibility pattern of isolated Gram-negative pathogens Figure 3. shows the bar charts for the antimicrobial susceptibility pattern of Gram negative uropathogens, isolated from the study.

Key: OFX: Tarivid 10dg, NA: Nalidixic Acid 30dg, PEF: Reflacine 10dg, CN: Gentamicin 10dg, AU: Augmentin 30dg, CPX: Ciprofloxacin 10dg, SXT: Sulfamethoxazole/Trimethoprim (Septrin) 30dg, S: Streptomycin 30dg, PN: Ampicillin 30dg, CEP Ceporex 10dg.

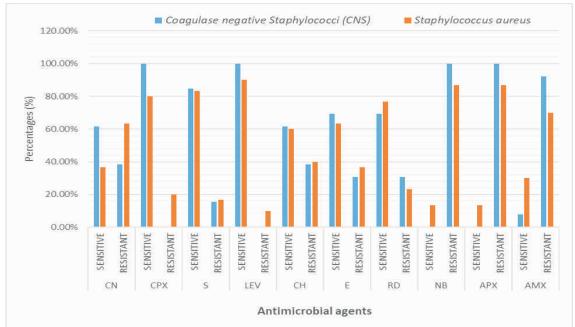




Figure 4. shows the bar chart for the antimicrobial susceptibility pattern of Gram positive uropathogens, isolated from the study.

Key: CN: Gentamycin 10dg, CPX: Ciprofloxacin 10dg, S: Streptomycin 30dg, LEV: Levofloxacin 20dg, CH: Chloramphenicol 30dg, E: Erythromycin 30dg, RD: Rifampicin 20dg, NB: Norfloxacin 10dg, APX: Ampiclox 20dg, AMX: Amoxicillin 20dg.



Discussion

Thirty-seven percent (37%) significant bacterial growth was observed in this study (Figure 4.1). This is in tandem to a study conducted in Kuwait (Sewify et al., 2016) that showed 35% positive to uropathogens and even a higher prevalence of 40% in a similar study conducted in Jos, Nigeria (Anejo-Okopi et al., 2017). Studies conducted in developed countries showed a much lesser prevalence of UTI among diabetics (4.69%) in the UK (Hirji et al., 2012) and 8.2% in the US (Yu et al., 2014). This was significantly higher in developing countries (24.0%) in Ethiopia (Yeshitela et al., 2012), (21%) in Nepal, (Simkhada, 2013), and (25.3%) in Saudi (Al-Rubeaan et al., 2013). A similar study conducted in Jos, Nigeria showed 40% prevalence of UTI among diabetic patients (Anejo-Okopi et al., 2017) which was higher than those obtainable in developed countries. Antimicrobial susceptibility testing was carried out on each of the isolates in the studies as shown on tables 5 and 6 for Gram- negative and Gram-positive bacteria respectively using Kirby Bauer disc diffusion technique as described (Cavalieri et al., 2005). Gram negative bacteria isolated (Coliform spp., E. coli and Klebsiella spp.) were highly sensitive (70%) to tarivid (OFX 10 μ g), ciprofloxacin (CPX 10µg) and streptomycin (S 30µg). The remaining isolated Gram-negative bacteria were moderately- or poorly sensitive to the other antibiotics used in the study. Gram positive bacteria isolated (Staphylococcus aureus and Coagulase Negative Staphylococci) were highly sensitive to ciprofloxacin (CPX $10\mu g$), streptomycin (S 30 μg) and levofloxacin $(20 \mu g)$, while they are moderately sensitive to chloramphenicol (30 µg), erythromycin (E 30 μg), rifampicin (RD 20 μg) and gentamicin (CN 10 µg). The Gram-positive bacteria remain highly resistant (10% sensitive) to ampiclox (APX 20 µg), amoxicillin (AMX 20 µg) and norfloxacin (NB 10 µg).

Escherichia coli was the most frequently isolated organism in this study (37.7%), followed by *Staphylococcus aureus* (24.6%), *Coliforms spp.* (13.9%), *Klebsiella spp.* (13.2%) and Coagulase Negative *Staphylococci* (10.6%) was the less frequently isolated uropathogen. This finding agrees with findings in a previous report in Kenya

(Simkhada, 2013) and Nepal (Sewify *et al.*, 2016) which indicated that *E. coli* as the most frequent uropathogen. This study however differs from that reported by Anejo-Okopi *et al.* (2017) in Jos, Nigeria who reported that Coagulase Negative *Staphylococci* was the frequently isolated uropathogen (37.5%), followed by *E. coli* (24%), *Klebsiella pneumoniae* (12.5%), *Staphylococcus aureus* (15%) and *Streptococcus spp.* (10%). They also reported *E. coli* and *Klebsiella pneumoniae* to be highly resistant to most antibiotics used for susceptibility testing and disagrees with the fact that they are both highly sensitive to tarivid, ciprofloxacin and streptomycin used in this study.

The distribution of significant growth based on gender, indicated a 25.3% prevalence among male subjects compared to 46.7% among the female subjects. The chi-square comparison between male and female positive subjects reveled that female were more at risk for UTI than male subjects (p=0.000). This agrees with the findings in previous report by Al-Rubean *et al.* (2013) in Saudi Arabia; Simkhada (2013) in Nepal (p=0.047) and Sewify *et al.* (2016) (p<0.0001).

The distribution of significant growth based on the age range of the study population (Figure 2) showed (21.1%) prevalence for subjects ranging between 21-30 years, (37.2%) for those aged 31-40, (41%) for those aged 41-50, (31.4%) for those aged 51-60, (45%) for those aged 61-70 and (43.75%) for subjects aged 71-80 years. The chi-square comparison of significant growth between age groups shows no significance in the age group relating to UTI.

Conclusion

Diabetes mellitus is characterized by immunosuppression in a number of individuals and urinary tract infection in this group of individuals causes significant morbidity and this increases the cost of management and treatment. It can be deducted from the findings of this study that although a control study was not conducted, the prevalence of UTI is high in diabetic patients compared to that reported in the non-diabetics. This is more pronounced in female diabetic patients who appear to be more at risk of UTI than male. In fact, studies have shown that diabetic patients are second to catheterized



patients on the risk of developing UTIs. This is further compounded by the fact that UTI is more common in underdeveloped poor nations of the world. Antimicrobial resistance is on the increase and the commonly used antimicrobial agents are becoming less and less effective. This makes the choices for antimicrobial therapy narrow and restricted to some broad spectrum stronger and more times, toxic antimicrobial agents. It is therefore very important to follow the gold standard in the diagnosis of UTIs and antimicrobial drug administration in implicated cases especially in the special risk group like diabetic patients.

Recommendations

Further research studies in different communities and environment should be organized, sponsored and coordinated by government or Non-Governmental Organization(s). Finding from this is a wakeup call for physicians to always request for a laboratory test for urine culture and sensitivity before concluding a urinary tract infection and prescribing an antimicrobial agent. All institutional laboratories should stick to the gold standard for the diagnosis and identification of UTIs (urine culture) and standard antimicrobial susceptibility testing should be performed before administering any antimicrobial drugs. Reference laboratories and quality control centers should develop an antibiogram with antimicrobial agents of less risk and high efficacy in special groups like the diabetics.

Declaration of Competing Interest

The authors declare that they have no competing interest.

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