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ASYMPTOMATIC BACTERIURIA IN AN APPARENTLY HEALTHY POPULATION AND ITS RELATION TO HYPERTENSION

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ABSTRACT

Background

Hypertension is a major health problem in sub-Sahara Africa. Several studies have suggested a role of asymptomatic bacteriuria (ASB) in the aetiology of hypertension, but there is a dearth of information on this association in Africa where the burden of hypertension is high. We investigated the prevalence of asymptomatic bacteriuria, its association with hypertension and determined the antibiotic resistance patterns of implicated bacterial isolates in an urban community of lle-Ife.

Methods

One hundred and seventy-four apparently healthy individuals were investigated for ASB. Relevant information was obtained from them with standard proforma. Their Blood pressure was measured with a standard mercury sphygmomanometer. All samples were processed on cysteine lactose electrolyte deficient medium and chocolate agar. Antimicrobial susceptibility testing was done using Kirby-Bauer disk diffusion technique. Results

Fifty (28.7%) individuals were positive for ASB. ASB was commonly detected among the female subjects (χ^2 =5.619; p-value = 0.01777), and among individuals in the age group of 50-59 years. Those that were hypertensive were two and a half times more likely to have ASB (Odd ratio=2.5; p-value=0.01369; CI=1.19-5.35). The highest percentage of hypertensive female participants with ASB was found in the age group of 30-39 years (33.3%) while among the male participants, the highest percentage was found in the age group of 60-69 years (9.5%). *Escherichia coli* (n=13; 26%) and *Staphylococcus aureus* (n=13; 26%) were the commonest organisms implicated in ASB. The majority of the isolates (>90%) were multidrug resistant. Isolates of *Escherichia coli* were commonly resistant to ampicillin (83.3%), ceftriaxone (72.7%) and cefepime (66.7%). Isolates of *Staphylococcus aureus* were all (100%) resistant to erythromycin, cloxacillin and streptomycin. All isolates were least resistant to cotrimoxazole (<8%).

Conclusion

Women as well as men in the age group of 50-59 years were more likely to develop ASB. ASB could be contributing to the rising incidence of hypertension in this environment. Co-occurrence of hypertension and ASB portends a grave problem for apparently healthy individuals in this environment.

Keywords: Asymptomatic bacteriuria, Hypertension, Escherichia coli, healthy individuals, urban community

LA BACTÉRIURIE ASYMPTOMATIQUE DANS UNE POPULATION APPAREMMENT EN BONNE SANTÉ ET DE SON RAPPORT À L'HYPERTENSION

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Résumé

Contexte: L'hypertension est un problème de santé majeur en Afrique subsaharienne. Plusieurs études ont suggéré un rôle de la bactériurie asymptomatique (ASB) dans l'étiologie de l'hypertension, mais il y a une pénurie d'information sur cette association en Afrique où la charge de l'hypertension est élevée.

Nous avons étudié la prévalence de la bactériurie asymptomatique, son association avec l'hypertension et déterminé les tendances de la résistance aux antibiotiques des isolats bactériens impliqués dans une collectivité urbaine d'Ile-Ife.

Les methods: 1 cent soixante-quatre personnes apparemment en bonne santé ont été examinés pour l'ASB. Les informations pertinentes ont été obtenues à partir de celles-ci avec une proforma standard. Leur pression artérielle a été mesurée à l'aide d'un sphygmomanomètre au mercure standard. Tous les échantillons ont été traités sur un milieu déficient en cystéine d'électrolyte de lactose et de chocolat. Les tests de sensibilité aux antimicrobiens a été effectuée à l'aide technique de diffusion disque Kirby-Bauer.

Résultats: Cinquante (28,7 %) personnes ont été positifs pour l'ASB. ASB est souvent détecté chez les sujets de sexe féminin ($\chi 2 = 5,619$; p = 0,01777), et parmi les individus dans le groupe d'âge 50-59 ans. Ceux qui n'ont de l'hypertension étaient deux fois et demie plus susceptibles d'avoir ASB (Odd ratio =2,5; valeur p =0,01369; IC = 1.19-5.35). Le plus haut pourcentage de participants féminins hypertendus avec ASB a été trouvé dans le groupe d'âge 30-39 ans (33,3 %) alors que chez les hommes, la proportion la plus forte a été observée dans le groupe d'âge 60-69 ans (9,5 %). L'Escherichia coli (n =13; 26 %) et Staphylococcus aureus (n =13; 26 %) ont été les plus fréquemment impliqués dans des organismes ASB. La majorité des isolats (>90 %) étaient multirésistantes. Les isolats d'Escherichia coli ont été fréquemment résistantes à l'ampicilline (83,3 %), à la ceftriaxone (72,7 %) et cefepime (66,7 %). Les isolats de Staphylococcus aureus ont été tous (100 %) résistantes à l'érythromycine, la cloxacilline et la streptomycine. Tous les isolats étaient résistants à au moins le cotrimoxazole (<8 %).

Conclusion: Les femmes ainsi qu'aux sujets dans le groupe d'âge 50-59 ans sont plus susceptibles de développer l'ASB. ASB pourraient contribuer à l'augmentation de l'incidence de l'hypertension dans cet environnement. La co-occurrence de l'hypertension et de l'ASB laisse présager un problème grave pour les personnes apparemment en bonne santé dans cet environnement.

Mots clés: La bactériurie asymptomatique, l'hypertension, l'Escherichia coli, les individus en bonne santé, communauté urbaine.

INTRODUCTION

Asymptomatic bacteriuria (ASB) is the presence of a positive urine culture with at least 105 cfu/ml collected from a patient with no symptoms or signs of urinary infection (1). ASB is common in people with abnormal genitourinary tract condition, and its prevalence varies among diverse populations, and depends on sex, age and conditions like diabetes mellitus or spinal cord injury and the presence of functional or structural genitourinary abnormalities (2). The prevalence of ASB increases with age in both men and women. In young women, the prevalence of ASB is 1-5%, and it increases to 6-16% in women over the age of 65 years (3). In healthy women above 80 years that reside in the community, the prevalence of ASB is about 20%. Asymptomatic bacteriuria is uncommon in healthy men before 60 years of age, but for ageing men in the community the prevalence rates of ASB is 3.6%-19% (3). Complications associated with asymptomatic bacteriuria include urolithiasis, genitourinary cancers, renal failure, hypertension and even death (4).

Hypertension is one of the major health problems in sub-Sahara Africa. It is the major cause of 50% of heart disease, stroke and heart failure. Due to significant improvements in the control of infectious diseases, and increased risk of cardiovascular disease (CVD) and kidney disease, attention has shifted to the control of non-invasive diseases and high blood pressure. However, unwillingness of patients with high blood pressure to seek for medical care, asymptomatic nature of the disease as well as poverty, increasing urbanization and bad eating habits have made the disease difficult to control, hence its rising incidence in Africa (5).

The role of asymptomatic bacteriuria (ASB) in the aetiology of hypertension has been reported by several authors in the past (4, 6-8). Those studies have shown that patients with renal scarring caused by pyelonephritis are more likely to develop hypertension and chronic kidney disease. For instance, Kass observed small differences in blood pressure between 444 bacteriuric and nonbacteriuric women who were watched for the development of high blood pressure in relation to E. coli bacteriuria at baseline. E. coli bacteriuria was associated with the development of hypertension during follow-up (1). In another study, Sinha and Postlethwaite reported that, a proportion of children who have suffered from a urinary tract infection (UTI) will go on to develop renal scarringwhich could lead to systemic arterial hypertension (8). A more recent study by Meiland et al. also suggested that bacteriuria may increase the risk of future hypertension in a population of asymptomatic women that were followed up (9). In spite of these reports, there is a dearth of information on the role of ASB in the aetiology of hypertension in Africa where the burden of hypertension is high, and its pathogenesis remains unclear. Considering these facts, we decided to screen apparently healthy urban community dwellers (men and women) between the age of 20 and 70 years for ASB, determine its association with hypertension and the susceptibility patterns of implicated pathogens.

METHODS Study population

The study was conducted in Ile-Ife, an urban community in South Western Nigeria. One hundred and seventy-four apparently healthy individuals within the age group of 20-70 years were recruited into the study from January to December, 2015. Informed consent was obtained from each participant prior to sample collection.

Collection and processing of samples

Midstream clean voided urine samples were collected from participants and sent to the laboratory for investigations. Asymptomatic bacteriuria was defined as the presence of 10⁵ bacteria in 1mL of urine. Plating of the samples was performed using a calibrated loop of 1 microliter on CLED and chocolate media (Oxoid, England), and incubated for 24h in aerobic conditions at 35°C. Bacterial identification was performed using conventional biochemical tests (10).

Blood pressure

Blood pressure was measured with a standard mercury sphygmomanometer (Accoson, England, United Kingdom) after the subject had been seated for five minutes. In this study, hypertension was defined as the previous use of antihypertensive medication (assessed at follow-up by the question: "Have you ever been treated with drugs for high blood pressure?") and/or a measured systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of 90 mm Hg or higher (11).

Antimicrobial susceptibility testing

Antibiotic susceptibility testing was done according to Clinical and Laboratory Standard Institute (CLSI) modified Kirby-Bauer method. A sterile cotton swab was dipped into each of the standardized solution of bacterial cultures and used for even inoculation of Mueller-Hinton plates (Himedia, Mumbai) and allowed to dry. Thereafter, antibiotic discs with the following drug contents: Amoxicillin (25µg), Ceftriaxone (30µg), Chloramphenicol (10 μg), Co-trimoxazole (25 μg), Erythromycin (10 μg), Gentamicin (10 µg), Ofloxacin (30µg), Perfloxacin (30µg), Tetracycline (30 µg), Amoxicillin/clavulanic acid (30 µg), and Cloxacillin (10 µg), Nitrofurantoin (300 µg), Cefuroxime (30 µg), Ceftaxidime (30µg), Nalidixic acid (30 µg), Penicillin (10 units), Streptomycin (10 µg), Cefepime (30µg) were placed on the plates, spacing them well to prevent the overlapping of inhibition zones. The plates were incubated at 37°C for 24 h, and the diameters were measured. The results were read and interpreted as recommended by the CLSI (10).

Statistical analysis

All data were analyzed with R Statistical package (12). Chi square (χ 2) test and t-test were used to test for statistical comparisons between the groups and a p< 0.05 was considered as statistically significant.

RESULTS

Fifty (28.7%) of 174 individuals that were investigated for ASB were positive, while 124 (71.3%) were negative. Of the 50 individuals that were positive for ASB, 34 (37%) were female and 16 (19.5%) were male. There was no statistical significant difference between the mean age of those with ASB (52.6800) and the mean age of those with ASB (50.1129) (t=-1.9653; p-value= 0.05167). Furthermore, as shown in table 1, the prevalence of ASB is significantly higher among the female subjects (χ^2 = 5.619; p-value = 0.01777).

The distribution of ASB among the various age groups revealed that the frequency of ASB increases with age and it is relatively higher among the female counterparts (Table 2).

TABLE 1: PREVALENCE OF ASB IN RELATION TO GENDER

Sex	Asymptom bacteriuria		P value				
	No Yes		_				
Female	58 (63.0)	34 (37.0)	χ ² = 5.619; p-value = 0.01777				
Male	66 (80.5)	16 (19.5)					
Total	124 (71.3)	50 (28.7)					
Mean age	50.1129	52.6800	t= -1.9653; p-value = 0.05167				

TABLE 2: PREVALENCE OF ASB IN RELATION TO AGE OF PATIENTS

Age (years)	Sex	No of subjects	No.with Asymptomatic bacteriuria (%)	ASB Total
20-29	Μ	2	0 (0)	0((0)
	F	1	0(0)	
30-39	Μ	5	0 (0)	3 (20)
	F	10	3 (30)	
40-49	М	22	3 (13.6)	9 (17.3)
	F	30	6 (20)	
50-59	Μ	38	10 (26.3)	33 (40.7)
	F	43	23 (53.5)	
60-69	Μ	13	3 (23.1)	5 (23.8)
	F	8	2 (25)	
≥70	Μ	2	0 (0)	0(0)
	F	0	0 (0)	

ASB and Blood Pressure

Of 174 individuals whose blood pressure was measured, 91 were hypertensive, while 83 were normotensive. Thirty-four (68%) individuals with high blood pressure had ASB while 16 (32%) individuals that were normotensive had ASB. Twenty-three (67.6%) of the 34 individuals with high blood pressure were females while 11(32.3%) were males. As shown in table 3, there was an association between asymptomatic bacteriuria and high blood pressure in this study (χ^{2} = 6.0783; p-value = 0.01369), and the hypertensive individuals were two and a half times likely to have ASB compared with those that are normotensive (Odd ratio=2.5; p-value=0.01369; CI=1.19-5.35).

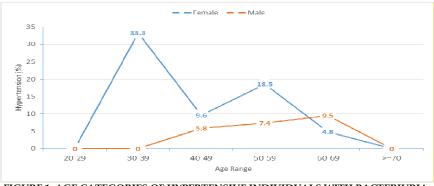
Figure 1 shows the age categories of healthy individuals with hypertension and bacteriuria. The

highest percentage of hypertensive female participants with ASB was found in the age group of 30-39 years (33.3%) followed by the age group of 50-59 years (18.5%). However, among the male participants, the percentage was highest in the age group of 60-69 years (9.5%) followed by the age group of 50-59 years (7.4%). No ASB was detected among the hypertensive female participants in the age groups of 20-29 years and 70 years and above. Among the hypertensive male participants, no ASB was detected in the age groups of 30-39 and 70 years and above.

Blood Pressure	- J I							Statistics					
		No (n=124))		Yes (n=50)	I	Total (n=174)	Chi-squared ; p-value	-squared ; p-value Odd Confidence ratio Interval				
	Male	Female	Total	Male	Female	Total							
High	35 (28.2)	22 (17.7)	57 (46)	11 (22)	23 (46)	34 (68)	91(52.3)	χ ² = 6.0783; p-value = 0.01369	2.50	1.19-5.35			
Normal	31 (25)	36 (29)	67 (54)	5 (10)	11 (22)	16 (32)	83(47.7)	1					

TABLE 3: PREVALENCE OF ASB IN RELATION TO PATIENTS' BLOOD PRESSURE

*Pearson's Chi-squared test with Yates' continuity correction





Frequency of Bacterial Isolates

Among all the bacterial species isolated from the urine samples of those with ASB, *Escherichia coli* (n=13; 26%) and *Staphylococcus aureus* (n=13; 26%) were the commonest, followed by *Klebsiella* spp (n=11; 22%) and *Pseudomonas aeruginosa* (n=10;

20%). *Pseudomonas aeruginosa* predominated (13) among the female subjects while *Staphylococcus aureus* (6) predominated in their male counterparts. *Morganella morgani* and *Proteus mirabilis* were isolated only from the female subjects.

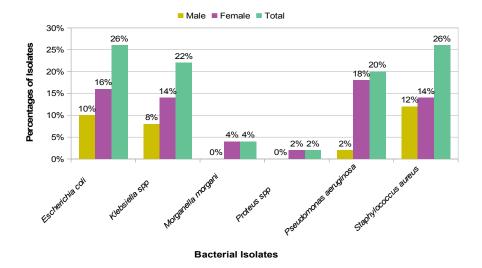


FIGURE 2: PERCENTAGES OF BACTERIAL ISOLATES IN RELATION TO SEX

Antimicrobial resistance patterns of the isolates

The majority of the Gram negative isolates were resistant to most of the antibiotics tested. Many isolates (>65%) of *Klebsiella, Pseudomonas* and *Morganella* were resistant to ampicillin, gentamicin, ceftriaxone and augmentin. Isolates of *Escherichia coli* exhibited high percentages of resistance to ampicillin (83.3%), erythromycin (83.3%) and

ceftriaxone (72.7%). *Staphylococcus aureus* isolates were commonly resistant to erythromycin (100%), tetracycline (92.3%), ampicillin (92.3%), cloxacillin (100%), penicillin (100%), and streptomycin (100%). All isolates were least resistant to cotrimoxazole (<30%).

Organisms	ERY	GEN	NIT	CEFT R	CEFT A	OFL O	AUG	TET	СОТ	AMP	CLO X	PE N	STR	CEFP
Escherichia coli (n=13)	5/6 (83.3)	8 (62.5)	4/9 (44.4)	8/11 (72.7)	9 (69.2)	6/12 (50)	8 (62.5)	0 (0)	1 (7.7)	5/6 (83.3)	NT	NT	NT	4/6 (66.7)
<i>Klebsiella</i> spp. (n=11)	1/1 (100)	9 (81.8)	7/10 (70)	9 (81.8)	9 (81.8)	7(63. 6)	7(63. 6)	0 (0)	0 (0)	10 (90.9)	NT	NT	NT	6 (54.5)
Morganella morgani (n=2)	0 (0)	2 (100)	0 (0)	2 (100)	1 (50)	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)	NT	NT	NT	0 (0)
Proteus spp (n=1)	1 (100)	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	NT	NT	NT	0 (0)
Pseudomonas aeruginosa (n=10)	1/1 (100)	8 (80)	4 (40)	6/8 (75)	4/7 (57.1)	5 (50)	7 (70)	3 (30)	3 (30)	7 (70)	NT	NT	NT	4/7(5 7.1)
Staphylococcus aureus (n=13)	13 (100)	9 (69.2)	NT	NT	0 (0)	NT	NT	12 (92.3)	1 (7.7)	12 (92.3)	13 (100)	13 (10 0)	13 (100)	0 (0)

TABLE 3: ANTIMICROBIAL RESISTANCE PATTERNS OF THE ISOLATES

NT= Not tested; ERY=Erythromycin; GEN= Gentamicin; NIT=Nitrofurantoin; CEFTR=Cetfriaxone; OFLO=Ofloxacin; AUG=Augmentin; TET=Tetracycline; COT=Cotrimoxazole; AMP=Ampicillin; CLOX=Cloxacillin; PEN=Penicillin; STR=Streptomycin; CEFP=Cefepime

Multi drug resistance

Multi-drug resistance in this study was defined as resistance of an isolate to three or more classes of antibiotics (Magiorakos *et al.*, 2012). Majority of the isolates (>90%) were multidrug resistant. 92.3% and 90.9% of *Escherichia coli* and *Pseudomonas*

TABLE 5: MULTIDRUG RESISTANCEPATTERNS OF THE ISOLATES

12 ≥ 3 Escherichia coli (13)0 (0)1(7.7)12 (92.3)Klebsiella spp (11)0 (0)0 (0)11 (100)Morganella morgani (2)0 (0)0 (0)2 (100)Proteus spp (1)0 (0)0 (0)1 (100)Pseudomonas aeruginosa (11)0 (0)1 (9.1)10 (90.9)Staphylococcus aureus (13)0 (0)0 (0)13 (100)	Organisms		No of isolates resistant to classes of antibiotics (%)					
Klebsiella spp (11) 0 (0) 0 (0) 11 (100) Morganella morgani (2) 0 (0) 0 (0) 2 (100) Proteus spp (1) 0 (0) 0 (0) 1 (100) Pseudomonas aeruginosa (11) 0 (0) 1 (9.1) 10 (90.9)		1	2	≥3				
Morganella morgani (2) 0 (0) 0 (0) 2 (100) Proteus spp (1) 0 (0) 0 (0) 1 (100) Pseudomonas aeruginosa (11) 0 (0) 1 (9.1) 10 (90.9)	Escherichia coli (13)	0 (0)	1(7.7)	12 (92.3)				
Proteus spp (1) 0 (0) 0 (0) 1 (100) Pseudomonas aeruginosa (11) 0 (0) 1 (9.1) 10 (90.9)	Klebsiella spp (11)	0 (0)	0 (0)	11 (100)				
Pseudomonas aeruginosa (11) 0 (0) 1 (9.1) 10 (90.9)	Morganella morgani (2)	0 (0)	0 (0)	2 (100)				
	Proteus spp (1)	0 (0)	0 (0)	1 (100)				
<i>Staphylococcus aureus</i> (13) 0 (0) 0 (0) 13 (100)	Pseudomonas aeruginosa (11)	0 (0)	1 (9.1)	10 (90.9)				
	Staphylococcus aureus (13)	0 (0)	0 (0)	13 (100)				

DISCUSSION

Asymptomatic bacteriuria (ASB) in healthy people is a minor problem that requires no treatment or clinical follow up, but it is considered relevant when there are underlying conditions; such as pregnancy, renal transplantation, severe neutropenia, urologic disorders (13).

The prevalence of ASB in the studied population was 28.7%, and ASB was commonly detected among the female subjects ($\chi^2 = 5.8098$; p-value = 0.01594). Our finding is comparable to the reports of previous investigators in Nigeria (14, 15). This might be due to the fact that women possess shorter urethra, which gives bacteria from the urethral meatus and the perineum a shorter distance to the bladder (16).

The prevalence of ASB was highest in the age group of 50-59 years. Among the male subjects, the prevalence of ASB increased with age and peaked at the age group of 50-59 years. Likewise, among the females, the prevalence of ASB peaked at age group 50-59 years. This finding could be attributed to changes in postmenopausal status or presence of comorbidities. This is likely true of the later as 25.9% of participants with ASB and hypertension were found in the age group 50-59 years old.

The role of ASB in the aetiology of hypertension has been reported by several investigators in the past but the pathogenesis is not understood (4, 6–8). For example, a cohort study of 444 women who were followed for the development of hypertension in relation to *E. coli* bacteriuria at baseline suggests that bacteriuria increase the chance to develop hypertension, and that those who were hypertensive were more likely to develop ASB than *aeruginosa* isolates were resistant to three or more classes of antibiotics respectively. All isolates (100%) of *Klebsiella* spp, *Morganella morgani, Proteus* spp., and *Staphylococcus aureus* were resistant to three or more classes of antibiotics

those who were normotensive . Considering the fact that the incidence of hypertension is increasing in Africa due to poverty, urbanization, bad eating habit, etc, and the possibility of ASB is adding to this increase. Thus, of the 174 individuals that were studied, thirty-four (68%) of 91 hypertensive individuals had ASB, while 16 (32%) of 83 normotensive individuals had ASB which suggested an association between asymptomatic bacteriuria and hypertension (χ^2 = 6.0783; p-value = 0.01369), and those who were hypertensive were two times more likely to have ASB (Odd ratio=2.5; p-value=0.01369; CI=1.19-5.35) when compared with those that were normotensive. Our finding agrees with the observations of previous investigators that reported an association between bacteriuria and hypertension (4, 7, 8). Although, we did not determine whether bacteriuria preceded hypertension or vice versa, neither did we prove that a causal relationship exists. A plausible explanation for our findings would be that hypertension arises secondary to renal scarring caused by the uropathogens, even though the participants were asymptomatic at the time the study was conducted. This finding suggests that ASB may have a role to play in the aetiology of hypertension in this environment. Co-occurrence of hypertension and ASB may portend a grave problem for individuals in this environment. Hence, the nature of this association needs to be investigated in future studies because of the grave effect of hypertension in our society.

The commonest pathogens implicated in ASB were *Escherichia coli* (26%), *Staphylococcus aureus* (26%), *Klebsiella* spp (22%) and *Pseudomonas aeruginosa* (20%). The aetiology of ASB varies from one geographical location to another and with patients' conditions. Globally, *E. coli* is the commonest uropathogens implicated in ASB (17–20). A previous study in the study environment also reported it as the commonest pathogen implicated in ASB (21). Therefore, its preponderance in this study agrees with the reports of previous investigators.

Isolation of *S. aureus* as uropathogen is not exclusive to our study. A previous study in Ile-Ife by Odetoyin *et al.* (22) and across the globe similarly reported it as a commonly isolated organism from patients with ASB (18, 23, 24). *Staphylococcus aureus* has in recent times been implicated in complicated UTI (25). The other isolates in this study included *Klebsiella* spp and *Pseudomonas aeruginosa* which have also been implicated in UTI (26).

Contrary to earlier studies (27-30), this study has demonstrated that in vitro, co-trimoxazole is the single most efficacious antibiotic against all the strains of uropathogens isolated, with sensitivity rate as high as 100% against Proteus, Morganella, Klebsiella, 93% against E. coli and Staphylococcus aureus but lower (70%) for Pseudomonas aeruginosa. In Africa, there are reports of increasing resistance to this drug due to its availability over the counter and its indiscriminate use for unrelated conditions (14, 22). Likewise, the second most effective antibiotic in this study is tetracycline, with 100% sensitivity against E. coli, Klebsiella, Morganella, Proteus, 70% against Pseudomonas aeruginosa, a pattern which is dissimilar to other studies in Africa (14, 27, 31). The efficacies of co-trimoxazole and tetracycline in this study may be due to the fact that people have shifted to newer drugs like the cephalosporins and quinolones for treatment which favours resistance to them due frequent use and the older drugs like tetracycline and co-trimoxazole which have been neglected are now becoming effective due to lack of frequent use. Hence, frequent use of an antibiotic is a risk factor for its resistance.

Surprisingly, Nitrofurantoin an old drug and ofloxacin a relatively new drug demonstrated a rather low *in vitro* sensitivity of less than 50% for *E. coli, Klebsiella* spp, *Pseudomonas aeruginosa.* Fluoroquinolone resistance (FQR) in UTI pathogens has been increasing globally. The Study for Monitoring Antimicrobial Resistance Trends (SMART) collected 1,116 FQR gram-negative urinary pathogens from hospitalized patients in 33 countries during 2009-2010. FQR rates varied widely from country to country with a range of 6% to 75%. Regional FQR rates were 23.5% in North America, 29.4% in Europe, 33.2% in Asia, 38.7% in

REFERENCES

- 1. Kass EH. Prevention of apparently noninfectious disease by detection and treatment of infections of the urinary tract. J Chronic Dis. 1962;15(7):665-73.
- 2. Sharma BD, Bansal R, Gupta B. Asymptomatic bacteriuria in diabetics. Journal, Indian Acad Clin Med. 2012;13(1):55–9.
- 3. Nicolle LE. Asymptomatic Bacteriuria and Bacterial Interference. Microbiol Spectr. 2015;3(5). Available from: http://www.asmscience.org/content/journal/mic robiolspec/10.1128/microbiolspec.UTI-0001-2012
- 4. Geerlings S. Asymptomatic Bacteriuria (ASB), Renal Function and Hypertension, Chronic Kidney Disease. In: Isbn:-51-0171-0, InTech A from:hyperten, editors. Monika Göőz (Ed) [Internet]. ISBN:-51-0171-0, InTech, Available from:hypertension; 2012. p. 953-78. Available from:

http://www.intechopen.com/books/chronickidney-disease/asymptomatic-bacteriuria-asbrenal-function-and Latin America, and 25.5% in the South Pacific (32). Studies across Nigeria also reported various degree of FQR up to 50% which is almost comparable to the present study (33–35). Over the counter use of these drugs in Nigeria has probably led to such low degree of sensitivity of uropathogens to this drug. Resting such antibiotic from use by making it unavailable on the market and/or restricting its use may allow it to recover its potency.

Sensitivities to gentamicin and ampicillin which are also commonly prescribed for treatment of UTI are also relatively low, with overall sensitivities of only 61.4% and 40% respectively. Studies done in Nigeria showed similar trends as well (5, 31, 36–39).

Conclusion: The prevalence of significant bacteriuria among healthy people was at 27.8%. The most commonly implicated pathogens were *Escherichia coli* and *Staphylococcus aureus*. Cotrimoxazole was the most efficacious antibiotic to all the uropathogens isolated. The high rate of resistance to ofloxacin, augmentin, ampicillin and gentamicin may prevent the use of these antibiotics for empiric treatment of UTI in Nigeria. The association of ASB and hypertension was established in this study and the co-occurrence of them could portend a grave problem for apparently healthy individuals in this environment.

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- Mann DL, Zipes DP, Libby P, Bonow RO, Braunwald E. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. Elsevier Heal Sci. 2015;
- Kunin CM, McCormack RC. An epidemiologic study of bacteriuria and blood pressure among nuns and working women. N Engl J Med. 1968;278(12):635–42.
- Freedman LR. The Relation of Bacteriuria to Hypertension The Milbank Memorial Fund Quarterly . Vol. 47. In: No 3, Part 2: Preventive Approaches to Chronic Diseases Proceedings of a Conference on Chronic Diseases Held in , Massachusetts June, 1969 (Jul, 1969), pp 33-42. 1969. p. 4-6.
- 8. Sinha MD, Postlethwaite RJ. Urinary tract infections and the long-term risk of hypertension. Curr Paediatr. 2003;13(7):508-12.
- 9. Meiland R, Geerlings SE, Stolk RP, Hoepelman AI, Peeters PH, Coenjaerts FE, et al. Escherichia coli bacteriuria in female adults is associated with the development of hypertension. Int J Infect Dis. 2010 Apr;14(4):e304–e307.

- 10. (CLSI) C and LSI. Performance Standards for Antimicrobial Susceptibility Testing. In: CLSI supplement. 2016. p. M100S.
- 11. Rodriguez CJ, Swett K, Agarwal SK, Folsom AR, Fox ER, Loehr LR, et al. Systolic Blood Pressure Levels Among Adults With Hypertension and Incident Cardiovascular Events: The Atherosclerosis Risk in Communities Study. JAMA Intern Med [Internet]. 2014 Aug;174(8):1252-61. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC 4573449/
- 12. R Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna, Austria; 2017. Available from: https://www.rproject.org/
- Nicolle L. Asymptomatic bacteriuriaWhen to screen and when to treat. Infect Dis Clin North Am [Internet]. 2003;17(2):367–94. Available from: http://linkinghub.elsevier.com/retrieve/pii/S089 1552003000084
- Timothy O, Olusesan F, Adesola B, Temitayo A, David F, Ige O. Antibiotic resistance pattern of bacterial isolates from cases of urinary tract infections among hospitalized and out-patients at a tertiary health facility in South Western Nigeria. Ann Trop Med Public Heal [Internet]. 2014;7(2):130-5. Available from: http://www.atmph.org/article.asp?issn=1755-6783%5Cnyear=2014%5Cnvolume=7%5Cnissue =2%5Cnspage=130%5Cnepage=135%5Cnaulast =Timothy
- Olowe OA, Makanjuola OB, Olabiyi KO, Akinwusi PO, Alebiosu CO, Isawumi MA, et al. Asymptomatic bacteriuria among elderly and middle-aged rural community-dwellers in South-Western Nigeria. Infect Drug Resist. 2013;6:55–8.
- Nalini R, Ramya JE, Meenakshi B, Palniappan N, Poongodi S. Recent Sensitivity Pattern of *Escherichia coli* in Urinary Tract Infection. Res Rev J Microbiol Biotechnol. 2014;3:31–5.
- 17. Onoh RC, Umeora OUJ, Egwuatu VE, Ezeonu PO, Onoh TJP. Antibiotic sensitivity pattern of uropathogens from pregnant women with urinary tract infection in Abakaliki, Nigeria. Infect Drug Resist [Internet]. 2013;6:225-33. Available from: http://doi.org/10.2147/IDR.S46002
- Sabharwal ER. Antibiotic susceptibility patterns of uropathogens in obstetric patients. North Am J Med Sci [Internet]. 2012;4(7):316-9. Available from: http://www.embase.com/search/results?subactio n=viewrecord&from=export&id=L365291873%5 Cnhttp://www.najms.org/temp/NorthAmJMedS ci47316-5025477_012345.pdf%5Cnhttp://dx.doi.org/10.410 3/1947-2714.98591
- Fareid MA. Frequency and Susceptibility Profile of Bacteria Causing Urinary Tract Infections among Women. New York Science Journal; 2012. (2: 284–298; vol. 5).

- Poolman JT. Escherichia coli. In: International Encyclopedia of Public Health [Internet]. Recent Advances on Physiology Pathogenesis and Biotechnological Applications; 2017. p. 585-93. Available from: http://linkinghub.elsevier.com/retrieve/pii/B978 012803678500504X
- 21. Ochada N, Nasiru I, Thairu Y, Okanlowan M, Abdulakeem Y. Antimicrobial Susceptibility Pattern of Urinary Pathogens Isolated from Two Tertiary Hospitals in Southwestern Nigeria. African J Clin Exp Microbiol [Internet]. 2014;16(1):12. Available from: http://www.ajol.info/index.php/ajcem/article/vi ew/110717
- 22. Odetoyin WB, Aboderin AO, Ikem RT, Kolawole BA, Oyelese AO. Asymptomatic bacteriuria in patients with diabetes Mellitus in Ile-Ife, South-West, Nigeria. East Afr Med J. 2008;85(1):18-23.
- 23. Omoregie R. Observed changes in the prevalence of uropathogens in Benin City, Nigeria. Nz J Med Lab Sci. 2008;29-31(Table 1):29-31.
- 24. Bolaji RO, Onaolapo JA, Ibrahim YKE, Igwe JC. Incidence Of Uropathogens From Asymptomatic Bacteriuric Pregnant Women In Zaria, Nigeria. Nig Journ Pharm Sci. 2013 Mar;12(1):1-8.
- Ajayi AB, Nwabuisi C, Aboyeji AP, Ajayi NS, Fowotade A, Fakeye OO. Asymptomatic Bacteriuria in Antenatal Patients in Ilorin, Nigeria. Oman Med J [Internet]. 2012 Jan 14;27(1):31–5. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC 3282126/
- 26. Flores-Mireles A, Walker J, Caparon M, Hultgren S. Urinary tract infection: Epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol [Internet]. 2015;13(5):269-84. Available from: http://doi.org/10.1038/nrmicro3432
- UWAEZUOKE, J C; OGBULIE JN. Antibiotic Sensitivity Pattern of Urinary Tract Pathogens in Port – Harcourt, Nigeria. Journal of Applied Science and Environmental Management. 2006. 103-107 p. (3: 103-107; vol. 10).
- Sohail M, Khurshid M, Murtaza Saleem HG, Javed H, Khan AA. Characteristics and antibiotic resistance of urinary tract pathogens isolated from Punjab, Pakistan. Jundishapur J Microbiol [Internet]. 2015;8(7):e19272. Available from: http://doi.org/10.5812/jjm.19272v2
- George C, Norman G, Ramana Gv, Mukherjee D, Rao T. Treatment of uncomplicated symptomatic urinary tract infections: Resistance patterns and misuse of antibiotics. J Fam Med Prim Care [Internet]. 2015;4(3):416. Available from: http://www.jfmpc.com/text.asp?2015/4/3/416/161 342
- 30. Nzalie RNT, Gonsu HK, Koulla-Shiro S. Bacterial Etiology and Antibiotic Resistance

Profile of Community-Acquired Urinary Tract Infections in a Cameroonian City. Int J Microbiol. 2016;2016:6.

- 31. Gta J, Ue E, En A, Jg D. Urinary tract infections at a Nigerian university hospital: Causes, patterns and antimicrobial susceptibility profile. J Microbiol Antimicrob [Internet]. 2011;3(6):153-9. Available from: http://www.academicjournals.org/JMA
- 32. Bouchillon S. Fluoroquinolone Resistance Among Gram-Negative Urinary Tract Pathogens: Global Smart Program Results, 2009-2010. Open Microbiol J [Internet]. 2012;6(1):74-8. Available from: http://benthamopen.com/ABSTRACT/TOMICR OJ-6-74
- 33. Ogbolu D, Alli A, Anorue M, Daini O, Oluwadun A. Distribution of plasmid-mediated quinolone resistance in Gram-negative bacteria from a tertiary hospital in Nigeria. Indian J Pathol Microbiol. 2016; 59(3): 322. Available from: <u>http://www.ijpmonline.org/text.asp?2016/59/3/32</u>
- Odetoyin BW, Hofmann J, Aboderin AO, Okeke IN. Diarrhoeagenic Escherichia coli in mother-child Pairs in Ile-Ife, South Western Nigeria. BMC Infect Dis. 2016;16(1).

2/188108

- 35. Odetoyin BW, Labar AS, Lamikanra A, Aboderin AO, Okeke IN. Classes 1 and 2 integrons in faecal Escherichia coli strains isolated from mother-child pairs in Nigeria.
- Odetoyin WB, Aboderin AO, Ikem RT, Kolawole BA, Oyelese AO. Asymptomatic bacteriuria in patients with diabetes Mellitus in Ile-Ife, South-West, Nigeria. East Afr Med J. 2008;85(1).
- Oladeinde B, Omoregie R, Olley M, Anunibe J. Urinary tract infection in a rural community of Nigeria. N Am J Med Sci [Internet]. 2011;3(2):75-7. Available from: http://doi.org/10.4297/najms.2011.375
- Iregbu K, Nwajiobi-Princewill P. Urinary tract infections in a Tertiary Hospital in Abuja, Nigeria. African J Clin Exp Microbiol [Internet]. 2013;14(3):169-73. Available from: http://www.ajol.info/index.php/ajcem/article/vi ew/91754
- 39. Akingbade O, Balogun S, Ojo D, Akinduti P, Okerentugba PO, Nwanze JC, et al. Resistant plasmid profile analysis of multidrug resistant *Escherichia coli* isolated from urinary tract infections in Abeokuta, Nigeria. Afr Health Sci. 2014;14:4. Available from: http://doi.org/10.4314/ahs.v14i4.8