

Prevalence of Asymptomatic Bacteriuria among Pregnant Women seen at a Tertiary Hospital in Northern Nigeria

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Abstract The importance of screening for asymptomatic bacteriuria in pregnancy can never be overemphasized. This study was done to determine the prevalence of asymptomatic urinary tract infection, the bacteriological profile and antimicrobial susceptibility pattern of the isolates, amongst pregnant women attending their first antenatal clinic. Two hundred and twenty-seven pregnant women presenting for the first antenatal clinic visit at the Barau Dikko Teaching Hospital, Kaduna were recruited for the study using systematic random sampling method, relevant demographic and clinical characteristics were obtained from proformas given to the pregnant women to fill. Clean catch mid-stream urine samples were collected and processed using standard bacteriological methods. The modified Kirby-Bauer method (Disk diffusion) was used for antimicrobial susceptibility testing according to Clinical Laboratory Standards Institute (CLSI, 2012) guidelines. Prevalence of AB was 19.8% and isolates recovered included *Staphylococcus aureus* (51.1%), *Escherichia coli* (28.9%), *Proteus mirabilis* (11.1%) and *Staphylococcus saprophyticus* (8.9%). Bacterial isolates from this study were most sensitive to Gentamycin, followed by Amoxicillin/Clavulanic acid, and least susceptible to Cotrimoxazole. The prevalence of asymptomatic bacteriuria among pregnant women presenting for the first antenatal clinic visit at the Barau Dikko Teaching Hospital, Kaduna is high. Follow up studies are required to determine if routine screening by urine culture should be advocated for all pregnant women at booking.

Keywords: Antimicrobial susceptibility, Asymptomatic bacteriuria, Pregnancy, Prevalence, Kaduna.

INTRODUCTION

Asymptomatic bacteriuria (AB) is not a clinical term, but it is a medical microbiological diagnosis determined by culturing urine specimen that had been collected in a manner to minimize contamination and transported to the laboratory in a timely fashion to limit bacterial growth (Lindsay *et al* 2005). It is regarded as the presence of $\geq 10^5$ colonies of bacteria/ml urine from a specimen obtained by the clean catch, midstream collection method (Cheesbrough 2009).

Asymptomatic bacteriuria may precede symptomatic urinary tract infection characterized by dysuria, frequency, pain, fever, which accounts for over 6 million outpatients visit each year.

The incidence of bacteriuria in pregnant women is approximately the same as that in non-pregnant women, however, recurrent bacteriuria is more common during pregnancy (Peterside *et al.* 2007).

Asymptomatic bacteriuria (AB) occurs in 2.5-10% of pregnant women (Teodor *et al.*, 2016.) It typically occurs during early pregnancy, with only approximately a quarter of cases identified in the second and third trimesters (Zakazaka, *et al.*, 2017).

Various maternal physiologic and anatomic factors predispose to AB, with an ensuing complication of upper urinary tract infection. Such factors include urinary retention caused by the weight of the enlarging uterus and urinary stasis due to progesterone-induced ureteral smooth muscle relaxation. Blood-volume expansion is accompanied by increases in the glomerular filtration rate and urinary output. Loss of ureteral tone combined with increased urinary tract volume results in urinary stasis, which with the presence of vesicoureteral reflux predispose some women to upper urinary tract infections (UTIs) and acute pyelonephritis (Kazemier *et al.*, 2015).

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This increases the risk for pre-term delivery, low birth weight, foetal and perinatal mortality. This risk is reduced by 70 to 80 percent if bacteriuria is eradicated (Schieve *et al.*, 1994), through screening and aggressive treatment of pregnant women with AB.

This study aims to determine the prevalence of AB in pregnancy, associated risk factors, its etiological agents and their antimicrobial susceptibility pattern.

MATERIALS AND METHODS

Study design, period and area

The hospital-based, cross-sectional study was carried out from June - August, 2018 at the Barau Dikko Teaching Hospital in Kaduna. Kaduna State is about 300km North of Abuja, the capital city of Nigeria. It is predominantly a Hausa speaking town in Nigeria, however it is quite heterogeneous in population, in terms of religion, ethnic group, and culture. The Barau Dikko Teaching Hospital is a tertiary health care centre. This hospital is a major referral centre for Kaduna and its environs however it caters not only for Kaduna citizens but for people from other parts of the North and the South of the country.

Sample size;

Using a prevalence of AB of 15% as reported by Ezeome (Ezeome *et al.*, 2006), and the formula $n = Z^2P(1-P)/d^2$, an attrition rate of 10%, the calculated minimum sample size for this study is 227.

The study population

All pregnant women who came for antenatal check-up without any sign and symptom of UTI but willing to participate in the study were enrolled. A total of 227 study participants were selected during the study period using systematic random sampling method.

Inclusion criteria; Women that consent to participate in the study and are 18 years or above, whose pregnancy can be accurately dated by Last Menstrual Period (LMP) or early ultrasound scan and with singleton pregnancy.

Exclusion criteria; Women less than 18 years, that do not consent to take part in the study, those who were not certain of their LMP and did not have an early ultrasound scan to date the pregnancy, with signs and symptoms of urinary tract infection (UTI). Also, women with a history of urolithiasis, urological surgery, urogenital fistula and active bleeding and those who are currently on antimicrobials or had taken

antimicrobials within two weeks were excluded from the study.

Collection of sociodemographic and clinical data

After taking written informed consent of the patients, socio-demographic and clinical data of the study participants were collected by nurses through face-to-face interviews using coded, structured and pre-tested questionnaires.

Collection of urine samples

Urine specimens were collected from the pregnant women, who were also instructed by trained nurses about collection of mid-stream urine, to reduce the chance of contamination. About 10 to 15 mL of mid-stream urine was collected from every pregnant woman in a sterile screw-capped, wide-mouth container. It was then delivered to the Hospital Research laboratory and processed within 1–2 hours for microbiologic analysis.

Sample culture, isolation and identification of associated bacteria

Samples were cultured on dried plates of blood agar and cysteine lactose electrolyte deficient agar (CLED), using a calibrated wire loop to inoculate 0.002ml of urine on all plates. Incubation was carried out aerobically at 37°C for 18-24 hours. In the present study, cut-off values of conventional semi-quantitative evaluation (S-QBC) for significant bacteriuria were determined as 10^5 colony forming units (cfu)/ml.² Suspected bacterial species were characterised by colonial morphology, gram stain followed by microscopic examination, motility test and biochemical tests. Isolates were identified to species level using standard methods according to Clinical and Laboratory Standard Institute Guidelines (CLSI, 2008) The antibiotic susceptibility of each isolate was tested manually on Mueller-Hinton agar, according to standardized guidelines for disc diffusion by the Kirby Bauer method (CLSI, 2012). Antibiotic discs were procured from oxoid®

Statistical Data Analysis

All relevant data were entered and analyzed with IBM Statistical Package for the Social Sciences (IBM SPSS Statistics; Armonk, NY, USA) software version 20. Data were summarized using cross tab and frequency tables. Bivariate and multivariate logistic regression models were applied to check for statistically significant association between the dependent and independent variables.

The *p*-value below 0.05 was considered as statistically significant.

Ethical clearance for this study was obtained from the Ethics committee of the Barau Dikko Teaching Hospital, Kaduna.

RESULTS

The mean age of the patients included in the study was 25.8 years (standard deviation 4.5 years). Range was from 15-44 years. The majority of study participants (84.1%) attended secondary school and above (Table 1). All were married, with parity ranging between zero and nine.

Forty – five of the 227 urine specimens screened yielded significant growth using the semi quantitative bacterial colony count of 10^5 organisms/ml of urine as an indication of significant bacteriuria. This gave a prevalence of 19.8%. Bacteria isolated include *Staphylococcus aureus*, which was the most common (51.1%), *E. coli* (28.9%), *Proteus mirabilis* (11.1%) and *Staphylococcus saprophyticus* (8.9%). (Table 2) Although, there was no particular trend in infection rate amongst the different age groups (Table 3), the highest rate of infection was seen in the 20-24 age group. Age, level of education, occupation marital order and sexual activity of participants did not have particular significance on the prevalence of asymptomatic bacteriuria. However, parity and previous episodes of Urinary tract Infection (UTI) prior to pre-natal care initiation showed significant difference. (Table 4)

Some organisms (*S.aureus* (95.7%), *E.coli* (100%), *S.saprophyticus*(100%),) showed good susceptibility to Gentamycin, others like *P.mirabilis* showed variable susceptibilities to Nitrofurantoin(40%), Ceftazidime(80%), and Ampicillin(100%). There was a high degree of resistance to Sulfaamethoxazole-Trimethoprim by all the organisms isolated (*S.aureus* 91.3%, *E.coli* 84.6%, *S. saprophyticus* 100%, *P.mirabilis* 100%) (Table 5).

DISCUSSION

This study showed that the overall prevalence of asymptomatic bacteriuria among pregnant women attending the antenatal clinic of BDTH, Kaduna was 19.8%, which is higher than the reported prevalence in most of previous studies, where the prevalence of asymptomatic bacteriuria in pregnancy varied from 2.5-10%. (Teodor *et al.*, 2016, Bandyopadhyay S *et al.*, 2005, Olusanya *et al.*) However, the prevalence

in this study is lower than what has been reported in Ile-Ife (Aboderin *et al.*) (26%) and Abuja (Urombo *et al.*) (49.5%). These differences may be attributed to variations in population characteristics with regards to age, parity, socioeconomic status, tribe and religion.

No significance was found for age, level of education, occupation, marital order and sexual activity. However, pregnant women with higher parity were more likely to have AB. Study of the prevalence of bacteriuria shows that it generally increases with age and sexual activity. In addition, occurrence of bacteriuria during pregnancy increases with trimester, which agrees with the work of Ajayi *et al* In the present study, all the subjects in their second and third trimesters were visiting the antenatal clinic for the first time, hence it could not be established if they carried infection from the first trimester. The study also confirmed that multiparity is associated with increased bacteriuria in pregnancy. This is in line with the study done by Ajayi *et al.*, (2012) Previous episodes of UTI prior to pre-natal care initiation showed significant difference ($p=0.009$) and patients were more likely to have asymptomatic bacteriuria than their counterparts who had no previous episodes of overt UTI (Table 4)

The most common organism isolated was *S. aureus* (51.1%), followed by *E. coli* (28.9%), *Proteus mirabilis* (11.1%) and *S. saprophyticus* (8.9%). Studies done by Akerele *et al*, 2006 (Benin), Ajayi *et al*, 2012 (Ilorin) and Oyegade *et al*, 2004 (Ado-Ekiti) also found *S. aureus* as the predominant isolate, in their respective areas.

This study revealed that Gentamycin and Amoxicillin-clavulante were very effective against urinary isolates. Some isolates demonstrated varying susceptibilities to Nitrofurantoin, Ceftazidime and Ampicillin. There was a high degree of resistance to cotrimoxazole by all isolates. (Table 5)

Out of the 45 isolates on which susceptibility testing were carried out, more than 50% were multidrug resistant. Cefoxitin disc diffusion was used in the detection of possible *mecA*-mediated oxacillin resistance (CLSI, 2012), 69.6% of the *S. aureus* were possible Methicillin resistant *S. aureus*.(CLSI, 2012). This can be confirmed during subsequent research by testing specifically for the *mecA* gene or for the protein expressed by it, the penicillin binding protein 2a (PBP2a). These are the most accurate methods for the prediction of resistance to oxacillin (CLSI, 2012).

The high resistance profile of isolates seen in this study may be attributed to over the counter sale of antibiotics and a high rate of self-medication in the general population leading to antibiotic abuse, misuse or underuse. These all serve as potent drivers for antimicrobial resistance.

CONCLUSION

The prevalence of AB amongst pregnant women attending antenatal booking clinic in BDTH, Kaduna is high. *S. aureus* and *E. coli* were the dominant pathogens isolated. Many of the isolates were resistant to antibiotics frequently used in the treatment of urinary tract infections. Amoxicillin-clavulanate and Gentamycin had the highest sensitivity pattern to these uropathogens.

Table 1: Socio-demographic characteristics of pregnant women attending a tertiary hospital in Northern Nigeria.

Age range	Frequency	Percentage (%)
15-19	9	4.0
20-24	63	27.8
25-29	61	26.9
30-34	57	25.1
35-39	31	13.7
40-44	6	2.6
TOTAL	227	100.0
LEVEL OF EDUCATION		
TERTIARY	94	41.4
SECONDARY	97	42.7
PRIMARY	28	12.3
OTHERS	8	3.5
TOTAL	227	100.0
OCCUPATION		
CIVIL SERVANT	33	14.5
PUBLIC SERVANT	1	0.4
SELF EMPLOYED	88	38.8
HOUSE WIFE	66	29.1
APPLICANT	4	1.8
CORPER	3	1.3
STUDENT	25	11.0
OTHERS	7	3.1
TOTAL	227	100.0
MARITAL STATUS		
SINGLE	0	0.0
MARRIED	227	100.0
TOTAL	227	100.0

Table 2: Organisms recovered in urine samples of pregnant women with AB

Organism	Frequency	Percentage (%)
<i>Escherichia coli</i>	13	28.9
<i>Staphylococcus aureus</i>	23	51.1
<i>S. Saprophyticus</i>	4	8.9
<i>Proteus mirabilis</i>	5	11.1
Total	45	100.0

Table 3: Prevalence Of Ab In Relation With Socio-Demographic Characteristics Of Pregnant Women In A Tertiary Hospital In Northern Nigria

Socio-demographic data	ORGANISMS		Odds Ratio	P-value
	Isolated (%)	Not isolated (%)		
Educational level				
<Secondary	8 (17.8)	27	1.186	0.625
≥Secondary	37 (15.6)	155		
TOTAL	45 (100)	182		
Occupation				
Employed	20 (44.4)	109	1.134	0.061
Unemployed	25 (56.8)	73		
TOTAL	45 (100)	182		
Parity				
Nulliparous	12 (26.7)	50 (27.8)		0.042
Primiparous	11 (24.4)	45 (25.0)		
Multiparous	22 (48.9)	85 (47.2)		
Family type				
Polygamy	5 (11.1)	16 (8.8)		0.638
Monogamy	40 (88.9)	166 (91.2)		

TABLE 4: INFLUENCE OF RISK FACTORS ON AB

Risk factor	Organisms		Statistics
	Isolated	Not isolated	
Sexual Activity			p = 0.433
ACTIVE	42	175	OR=0.560 (0.139-2.257)
NOT ACTIVE	3	7	
TOTAL	45	182	
PREG/UTI			p = 0.009
YES	28	74	OR=2.404 (1.228-4.704)
NIL	17	108	
TOTAL	45	182	
PREG/PM			p = 0.957
YES	18	72	OR=1.019 (0.523-1.983)
NIL	27	110	
TOTAL	45	182	

Key

PREG: pregnancy

UTI: urinary tract infection

PM: PRE-PREGNANCY MORBID CONDITIONS

TABLE 5 Sensitivity pattern of organisms cultured from cases of significant bacteriuria

ORGANISM	ANTIBIOTICS (SINGLE DISCS)							
S	F	SXT	CAZ	AMP	CRO	CN	AUG	FOX
<i>S.aureus</i>	S- 47.8% R- 47.8% I- 4.4%	S- 8.7% R- 91.3%	S- 26.1% R- 73.9%	S- 20% R- 80%	S- 26.1% R-73.9%	S- 95.7% R- 4.3%	S- 33.3% R- 66.7%	S- 30.4% R- 69.6%
<i>E.coli</i>	S- 69.2% R- 30.8%	S- 15.4% R- 84.6%	S- 54.5% R- 45.5%	S- 25% R- 75%	S- 63.6% R- 27.3% I- 9.1%	S- 100%	S- 76.9% R- 23.1%	-----
<i>S.saprophyticus</i>	S- 75% R- 25%	R- 100%	R- 100%	S- 50% R- 50%	R- 100%	S- 100%	S- 100%	-----
<i>P.mirabilis</i>	S- 40% R- 60%	R- 100%	S- 80% R- 20%	S- 100%	S- 80% R- 20%	S- 60% R- 40%	S- 100%	-----

KEY

F – Nitrofurantoin, SXT – Sulfamethoxazole-Trimethoprim, CAZ – Ceftazidime, AMP – Ampicillin, CRO – Ceftriaxone, CN – Gentamycin, AUG – Amoxicillin clavulanate, FOX - Cefoxitin

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